Is It Appropriate to Treat Sarcoma Metastases With Intramedullary Nailing?

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Received: 8 March 2016 / Accepted: 30 August 2016 / Published online: 1 November 2016
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Abstract

Background Patients with primary bone and soft tissue sarcoma are at risk for skeletal metastases. Although uncommon, these metastases can result in impending or pathologic fractures. Intramedullary nailing traditionally has been an accepted form of palliative treatment for patients with metastatic carcinoma, but we could find no studies that report specifically on intramedullary nailing of metastatic sarcoma lesions.

Questions/purposes We asked: (1) What is the survival of patients with an impending or pathologic fracture from a sarcoma metastasis? (2) What proportion of patients treated with intramedullary nailing subsequently underwent a revision procedure or nail removal during their lifetimes?

Methods Between 1996 and 2014, we performed 40 intramedullary nailing procedures in 34 patients with multifocal metastases from sarcomas who showed signs or symptoms of impending fracture or who presented with a

pathologic fracture. All of these patients are accounted for, either through the time of death or to the present, and all are included at a mean of 13 months (range, 0.3–86 months) in this retrospective study. During the study period, we generally applied the same surgical indications for patients with nailing of metastatic sarcoma lesions as we did for patients with metastatic carcinoma; in general, we used intramedullary nailing (with or without cement) rather than resection for diaphyseal lesions with less cortical destruction and no substantial soft tissue mass or metadiaphyseal lesions that could be adequately supplemented with cementation. The goal was to use this approach when it would allow immediate weightbearing, or in patients whose medical conditions were such that a more-extensive procedure seemed unsafe. During the same period, an additional 58 patients underwent resection procedures for metastatic sarcomas to long bones because they either did not meet the above indications, had a solitary resectable metastasis, or because of surgeon preference; these patients were excluded from this study. The median age of the patients was 52 years (range, 27–81 years). Eleven patients with 11 impending or pathologic fractures were documented to have received either preoperative or postoperative radiation therapy and 29 patients received some form of chemotherapy.

Results Thirty (88%) patients died during the period of observation, at a median of 5 months (range, 0.3–80 months) after surgery. Twenty-nine patients (85%) underwent no additional surgery and retained their original intramedullary nail. One patient (3%) underwent nail removal for infection, and four patients (12%) underwent further surgical revision secondary to local progression.

Conclusions Patients with an impending or pathologic fracture from multifocal metastatic sarcoma to a long bone have a dismal prognosis, but they may gain short-term

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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benefit from surgical fixation with the goal of reducing pain and maintaining mobility. Although we have no group for comparison, such as treating with radiotherapy alone or resection and an endoprosthesis, our findings suggest that use of intramedullary nails is helpful for providing fixation that in most instances lasts for the lifetime of patients with multifocal bone metastases from sarcomas.

Level of Evidence Level IV, therapeutic study.

Introduction

Metastatic sarcoma to the skeleton is uncommon. However, like metastatic carcinoma, sarcoma metastases can lead to morbidity from impending or pathologic fractures of the long bones [10, 11]. Although treatment of metastatic carcinoma with intramedullary nailing has become a standard treatment option for long bone metastases [2, 4, 7, 9], there is no such standard for metastatic sarcoma nor could we find any studies that have specifically addressed the treatment of sarcoma metastasis with intramedullary nailing.

Given that sarcomas are aggressive, that they commonly recur after margin-positive resections, and that they can seed the tissues when incised or traversed, the standard surgical treatment for primary bone sarcomas is wide resection [3, 5, 8]. Wide resection does provide effective local control, but it also involves a major reconstruction procedure, with its attendant risks, a sometimes-prolonged hospital stay, and lengthy recovery period. Although this is acceptable for resection of a primary sarcoma in a patient with a realistic chance at cure and prolonged life, it could be considered overtreatment in a patient with metastatic sarcoma whose lesion calls for palliative management of an impending or pathologic fracture. Although a lesser procedure such as intramedullary nailing is an attractive option, it would not address the concerns regarding the possibility of local progression that could result in inadequate fixation of an impending or pathologic fracture.

The purpose of this study was to assess patients treated at our cancer center to evaluate the adequacy of fixation after intramedullary nailing in patients with multifocal sarcoma metastases who underwent palliative treatment of one or more long bone metastases. We asked: (1) What is the survival of patients with an impending or pathologic fracture from a sarcoma metastasis? (2) What proportion of patients treated with intramedullary nailing subsequently underwent a revision procedure or nail removal during their lifetimes?

Patients and Methods

A retrospective study of the musculoskeletal oncology database at the University of Texas MD Anderson Cancer

Center identified 34 patients with metastatic sarcoma from 1996 to 2014 who had impending (26) or pathologic (14) fractures from bone metastases. All of these patients had multiple metastases to bone and organs. All patients were accounted for until death or current followup. The median followup for all patients was 13 months (range, 0.3–86 months). The primary diagnoses were: osteosarcoma (four), hemangiopericytoma (five), leiomyosarcoma (five), alveolar soft parts sarcoma (four), angiosarcoma (three), spindle cell sarcoma (three), undifferentiated pleomorphic sarcoma (two), liposarcoma (two), fibrosarcoma (one), myxofibrosarcoma (one), epithelioid hemangioendothelioma (one), synovial sarcoma (one), Ewing's sarcoma (one), and neurofibrosarcoma (one). Forty intramedullary nailings were performed for these 34 patients. There were 24 femoral nails, 15 humeral nails, and one tibial nail (Table 1). Three patients underwent nailing of an additional extremity and one patient underwent nailing of three additional extremities owing to multiple long bone metastases. Eighteen nailings (45%) were performed open with curettage and cement supplementation, and 22 nailings (55%) were performed closed. The median patient age was 52 years (range, 27–81 years). Eleven patients with 11 impending or pathologic fractures received either preoperative or postoperative radiation therapy. The radiation therapy delivered at our institution was at doses that typically are used for metastatic carcinoma (20–30 Gy).

Our current indications for intramedullary nailing of sarcoma metastases are essentially identical to indications for intramedullary nailing for metastatic carcinoma. These include impending or pathologic fractures of a long bone without significant cortical destruction or substantial soft tissue mass. The rationale is that the nail, with or without cement supplementation, must be able to provide adequate support for immediate weightbearing. If immediate weightbearing would not be possible, then resection and endoprosthetic reconstruction would be the preferred procedure. Another important consideration is the patient's overall medical condition and projected life expectancy. All of these patients had multiple metastases to bone and organs and we generally prefer resection, when possible, of a solitary sarcoma metastasis. An exception may be made as it relates to the radiographic features of the metastasis and immediate weightbearing if the patient is debilitated from their malignancy, has limited preoperative mobility, and is not medically fit for a resection procedure. These indications have been applied consistently for at least the past decade through our multidisciplinary preoperative conference. However, surgeon preference is deferred to when a general consensus is not achieved.

After reviewing our data with a statistician, we determined that our numbers were too small to perform a

Table 1. Characteristics of study population

Patient number	Age (years)	Tumor	Location	Fracture/union	Curette/cement	Radiation	Chemotherapy	Other metastasis	Survival (months)	Revision/removal	Mobility	Major complications
1	53	Leiomyosarcoma	Femur, diffuse	No	No	No	Yes	Yes	2.5	No	Walker	
2	74	Angiosarcoma	Femur, diffuse	No	No	No	Yes	Yes	0.3	No	Bedridden	
3	35	Osteosarcoma	Humerus, proximal	No	Yes	No	Yes	Yes	1	No	Not applicable	
4	44	Liposarcoma	Tibia proximal	Yes/no	Yes	Yes, 30 Gy	Yes	Yes	7	No	Walker	
5	34	Synovial sarcoma	Femur, subtrochanter	Yes/no	Yes	No	No	Yes	0.5	No	Crutches	Acute arrest
6	49	Hemangiopericytoma	Humerus, distal	No	Yes	Yes, 30 Gy	Yes	Yes	15.5	No	Not applicable	
7	55	Hemangiopericytoma	Humerus, proximal	No	Yes	Yes, 20 Gy	Yes	Yes	6.5	No	Not applicable	
8	62	Pleomorphic	Femur, proximal	No	Yes	No	No	Yes	9	No	Walker	
9	30	Neurofibrosarcoma	Humerus, diaphysis	Yes/no	No	No	Yes	Yes	0.6	No	Not applicable	
10	39	Osteosarcoma	Humerus, diaphysis	Yes/yes	No	No	Yes	Yes	55	Yes, nail removal	Not applicable	Infection
11	73	Hemangiopericytoma	Femur, proximal	No	No	No	Yes	Yes	4	No	Wheelchair	
12	43	Liposarcoma	Humerus, proximal	No	Yes	No	Yes	Yes	1.5	No	Not applicable	
13	64	Leiomyosarcoma	Femur, subtrochanter	No	Yes	No	Yes	Yes	5.5	No	Walker	
14	69	Leiomyosarcoma	Femur, diaphysis	No	No	Yes, 30 Gy	No	Yes	3.5	No	Walker	
			Femur, proximal	No	Yes	No	No	Yes	1	No	Walker	Intraoperative cortical perforation
15	78	Fibrosarcoma	Femur,	Yes/no	Yes	No	No	Yes	21.5	Yes	Walker	Local progression
			humerus, diaphysis	Yes/no	Yes	No	No	Yes	9	No	Not applicable	
			Femur, distal	No	Yes	No	No	Yes	9	No	Wheelchair	
			Humerus, diffuse	Yes/no	No	No	No	Yes	3	No	Not applicable	
16	47	Alveolar soft parts sarcoma	Femur, distal	No	Yes	No	Yes	Yes	29	No	Cane	
17	65	Angiosarcoma	Humerus, diaphysis	Yes/no	Yes	No	Yes	Yes	6.5	No	Not applicable	
18	81	Pleomorphic	Femur, proximal	No	No	No	No	Yes	8	No	Walker	
19	36	Alveolar soft parts sarcoma	Humerus, diaphysis	Yes/yes	No	No	Yes	Yes	7	No	Not applicable	Fracture tip of nail
20	69	Osteosarcoma	Humerus, proximal	Yes/no	No	Yes, 30 Gy	Yes	Yes	3.5	No	Not applicable	
21	28	Ewing's	Femur, diaphysis	Yes/yes	No	Yes, 20 Gy	Yes	Yes	86-alive	No	No assistive device	
22	71	Leiomyosarcoma	Femur, proximal	No	No	Yes, 35 Gy	Yes	Yes	42	Yes, endoprosthesis	No assistive device	Local progression
23	61	Unclassified spindle cell	Femur, diffuse	No	Yes	Yes, 30 Gy	No	Yes	5	No	Walker	
24	64	Unclassified spindle cell	Femur, diffuse	No	No	No	Yes	Yes	3	No	Walker	
25	29	Alveolar soft parts sarcoma	Humerus, diffuse	No	No	No	Yes	Yes	48-alive	No	Not applicable	
			Femur, distal	No	No	No	Yes	Yes	37-alive	No	Walker	
26	49	Hemangiopericytoma	Humerus, proximal	Yes/no	No	No	Yes	Yes	0.6	No	Not applicable	
			Femur, subtrochanter	Yes/no	No	No	Yes	Yes	0.6	No	Wheelchair	
27	45	Myxofibrosarcoma	Femur, subtrochanter	No	Yes	No	Yes	Yes	13	No	Cane	
28	64	Hemangiopericytoma	Femur, subtrochanter	No	Yes	Yes, 30 Gy	Yes	Yes	5	No	Walker, long distances only	
29	45	Angiosarcoma	Femur	No	No	No	Yes	Yes	1	No	Walker	

Table 1. continued

Patient number	Age (years)	Tumor	Location	Fracture/union	Curette/cement	Radiation	Chemotherapy	Other metastasis	Survival (months)	Revision/removal	Mobility	Major complications
30	61	Epithelioid hemangioendothelioma	Humerus, diaphysis	No	No	No	Yes	Yes	13-alive	No	Not applicable	
31	46	Unclassified spindle cell	Femur, diffuse	No	No	No	Yes	Yes	13-alive	No	Walker	
32	51	Osteosarcoma	Femur, neck	No	No	Yes, 20 Gy	Yes	Yes	5	Yes, endoprosthesis	Walker	Local progression
33	80	Leiomyosarcoma	Humerus, diaphysis	Yes/no	No	No	No	Yes	1	No	Not applicable	
34	27	Alveolar soft parts sarcoma	Femur, subtrochanter	No	Yes	Yes, 37.5 Gy	Yes	Yes	80	Yes allograft prosthetic composite	No assistive device	Local progression

meaningful statistical analysis looking for factors predictive of survival or success of nailing in the presence of an impending or pathologic fracture, therefore no statistical analysis was performed.

Results

Thirty (88%) patients died during the period of observation. The median postoperative survival after surgery was 5 months (range, 0.3–80 months). As noted, with the numbers we had, we could not distinguish any clinical factors that might have indicated poorer or more-prolonged survival. Eleven patients (32%) presented with 14 pathologic fractures: nine humerus, four femur, and one tibia. Only three of these fractures achieved union before the patients died.

Twenty-nine patients (85%) underwent no additional surgery and retained their original intramedullary nail. Fifteen patients (60%) who underwent lower extremity nailing could ambulate postoperatively with a walker, three (12%) required no assistive devices, three (12%) ambulated via wheelchair, two (8%) ambulated with a cane, one (4%) ambulated with crutches, and one (3%) was bedridden. Five patients (15%) underwent additional surgery. Of the patients who underwent nail revisions, the median survival was 42 months (range, 4–80 months), and the median time to additional surgery from the initial nail placement was 12 months (range, 4–56 months). One (3%) nail was removed for infection. This patient had a healed fracture and was treated successfully with nail removal, débridement, and antibiotics. One (3%) amputation was performed for advanced local progression that was not amenable to local resection and reconstruction. Three (9%) additional patients underwent revision surgery secondary to local progression. Two of these patients received endoprostheses and the third patient received an allograft prosthetic composite. All four patients who had substantial local progression had lesions develop in femoral nailings (femoral neck, femoral shaft, subtrochanteric, and proximal). The three patients who underwent revision surgery had lesions in the proximal region of the femur whereas the patient who had an amputation had a lesion in the femoral shaft. Three of the four patients with substantial local progression had received radiation therapy, two had the lesion curetted at the time of nail insertion, and three had received chemotherapy. One patient had a new lesion develop remote from the original metastasis. This occurred in one of the patients who had revision surgery, and after their revision procedure, a new lesion developed at the tip of the endoprosthetic stem. Two other complications occurred related to the nailing. In one patient the distal cortex of the femur was penetrated during nailing and

required a supplemental plate. A second patient experienced a fracture at the tip of their humeral nail 16 days before death. This was managed conservatively. In addition, one death occurred shortly after surgery in a 34-year-old patient with metastatic synovial sarcoma. He had acute shortness of breath develop and cardiovascular collapse resulting in death on postoperative Day 16.

Discussion

Although intramedullary nailing is common palliative treatment for metastatic carcinoma, we could find no reports on the outcomes of the palliative treatment of sarcoma metastases to bone. Intramedullary nailing of sarcoma metastases is an attractive option because it can be done quickly and with limited incisions, and it provides immediate stability allowing early mobilization. However, one concern with this intralesional approach is that the entire bone could be seeded with sarcoma, perhaps resulting in local progression that may lead to a second resection procedure. Although this concern also exists regarding carcinoma, adjuvant therapies like radiation therapy and bisphosphonates make this complication seem less likely, whereas most primary bone sarcomas do not respond to radiation therapy. Whether seeding resulting from intramedullary nailing of metastatic sarcomas results in clinical problems during the lifetimes of these patients because of local recurrences is not known. We sought to determine how many patients underwent removal or revision of their intramedullary nails and the length of survival of patients after intramedullary nailing for metastatic sarcoma.

There are limitations to this study. Its retrospective design likely introduces some selection bias, as does participation of multiple surgeons and lack of a standard treatment algorithm. The selection of patients for intramedullary nailing could have been influenced by such things as tumor size, patient performance status, surgeon preference, and sarcoma type. All 34 patients (100%) in this series had multifocal metastases, and this may indicate that patients with more advanced disease were selected for nailing. However, selection bias for this circumstance should be deemed appropriate since avoiding a more major procedure such as radical resection would be desirous in patients with advanced disease. The small number of patients studied precluded statistical analysis of factors associated with improved or poorer survival; future, multicenter studies will need to address this topic. We did not assess pain level or quality of life postoperatively, so we can comment only on the frequency of revision, survival of the nail, and survival of the patient. Given the dearth of information on this topic, we believe some valuable information is still gained from our study, but the absence

of other outcomes does reduce the usefulness of this study. Future studies should assess those aspects more carefully to ensure we really are providing adequate palliation for these patients.

The median survival of our patients was 5 months. This suggests that, in most cases, an intramedullary nail is sufficient to provide fixation for the duration of the patients' lives because it is so short. Given that the median survival for the patients who required revision surgery was eight times greater than the median survival of the group as a whole, expected survival may be an important variable that should be considered when determining if a patient with sarcoma metastases is an appropriate candidate for intramedullary nailing. In comparison, Miller et al. [6] also found that the median survival for patients with carcinoma, lymphoma, myeloma, and one case of leiomyosarcoma undergoing revision surgery was greater than that of patients who did not require revision surgery (3.2 years vs 0.6 years). These findings are similar to our findings for patients with metastatic sarcoma. Unfortunately, given our small sample size and the lack of a dedicated treatment algorithm, we cannot make any definitive recommendations regarding the assessment of patient survival. However, these findings should highlight the need for a reliable survival assessment tool for this population rather than relying on a surgeon's "best guess" that has been developed solely from their personal experience.

In this series, intramedullary nailing resulted in stable, durable fixation in 29 of 34 (85%) patients for the remainder of their lives. Given that this was a palliative procedure, durable is defined as a single procedure that provides adequate bony support until the time of death. Although the other goals of the procedure are to provide pain control and/or allow for activities of daily living, as mentioned previously, we do not have preoperative and postoperative pain scores, therefore we are not able to determine success from the standpoint of pain and function. However, intramedullary nailing is an accepted and widely used treatment to improve pain and function in patients with impending and pathologic fractures that develop from carcinoma metastases [2, 4, 7, 9]. As it has been shown that adequate palliation is achieved with intramedullary nailing of carcinoma metastases, a similar conclusion could be drawn for patients with metastatic sarcoma because it is an identical procedure that simply is being used for a different malignancy. This may not be a fair conclusion as local progression of sarcoma metastases occur at such a rate that the nail may not provide adequate bony support for the remaining survival time of the patient. Because there are no other studies to our knowledge that have evaluated intramedullary nailing of sarcoma metastases, we compared our results with those of studies of metastatic carcinoma. Alvi and Damron [1] reported that 8% (five of 60) of patients

treated with an intramedullary nail for impending or pathologic fractures caused by carcinoma, myeloma, or lymphoma underwent revision surgery, and four of these revisions (7%) were related to local progression. In a similar report, Miller et al. [6] reported that 9% (10 of 112) of their patients underwent revision surgery. Three (3%) of these revisions were attributable to local progression. In comparison, it is clear that the risk of revision in our series is higher, especially when the revision is performed for local progression. This is not surprising given that the standard treatment for sarcomas is wide resection. The four patients in our series who underwent additional surgery owing to disease progression had progression at only the site of the original metastasis rather than new sites of disease throughout the reamed portion of the bone. This allowed salvage by resection and proximal femur replacement rather than resection of the entire bone in three of these patients. After revision surgery, one of these patients had further tumor progression in the affected bone at the tip of the endoprosthesis stem, but additional surgery was not needed. We assume that this was attributable to seeding from the prior nailing procedure rather than a new metastasis. Given the short survival and limited postoperative imaging for many of these patients, we cannot comment further regarding the incidence of tumor seeding. However, it does not appear to be a clinically relevant issue as there were no cases of new lesions from tumor seeding resulting in a change in the management of the patients. Therefore, despite intralesional management of a sarcoma metastasis and the hypothetical concerns of sarcoma seeding from reaming, 97% of our patients avoided amputation.

Our results indicate that in patients with an impending or pathologic fracture in the setting of multifocal sarcoma metastases, intramedullary nailing of sarcoma bone metastases can provide fixation that should last for the duration of the patient's lifetime in most instances. This is primarily because the survival of these patients is dismal. Nevertheless, 85% of patients retained their original implant and 98% had successful limb salvage surgery despite intralesional treatment. Although we do not have data regarding the quality of life of these patients after their treatment, these results support the contention that intramedullary nailing is an acceptable treatment option. Although we have no comparison group, it likely avoids the morbidity and potential complications of alternative

procedures such as resection and endoprosthesis reconstruction for palliative management of impending and pathologic fractures of sarcoma metastases and likely provides better bony stability than would be expected from radiation therapy alone. It also is clear that there is no good solution for these patients and that better systemic treatments and local control methods are needed to improve our ability to provide them with palliation.

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