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Predictors of survival after intramedullary nail fixation of completed or impending pathologic femur fractures from metastatic disease

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ABSTRACT

Background: Surgical decision-making can be challenging when treating patients with osseous metastases. Numerous factors, including expected duration of survival, must be considered to ensure optimal operative stabilization of the affected bone. However, life expectancy of patients with metastatic carcinoma is often difficult to estimate. The goal of our study was to assess the associations of various clinical and demographic factors with survival time after intramedullary nail fixation of impending or completed pathologic femur fractures.

Methods: One hundred thirty-eight consecutive patients treated with intramedullary nail fixation for impending or completed pathologic femur fractures between 2005 and 2017 were included in this study. Factors related to patient survival were assessed with Cox multivariate survival analysis. For all analyses, $p < 0.05$ was considered significant.

Results: The median overall postoperative survival time was 8.4 months. Lower hemoglobin concentration ($p = 0.001$), lower albumin concentration ($p = 0.002$), and having a group 2 primary cancer ($p = 0.001$) were associated with shorter survival on multivariate analysis. When considering the subgroup of 88 prophylactically stabilized patients, lower hemoglobin concentration ($p = 0.005$), lower albumin concentration ($p = 0.015$), and having a group 2 primary cancer ($p = 0.037$) were predictive of shorter survival.

Conclusion: Several factors are associated with shorter survival after intramedullary nail fixation of pathologic femur fractures. These factors should be considered by orthopedic surgeons when educating patients and determining appropriate treatment.

1. Introduction

End-of-life care for oncology patients involves a delicate balance of risks, benefits, and durable comfort. The concept of end-of-life care is particularly pertinent for patients with metastatic long bone lesions who have experienced fracture or are at risk of fracture. These patients tend to be frail and to have high risk of perioperative morbidity and mortality [1]. As such, the benefit of functional improvements must be weighed against anticipated life expectancy when assessing operative interventions, choosing implants, and educating patients. With the advancement of intramedullary nail fixation systems, the risk of perioperative morbidity has decreased, making fixation an option for many patients with femoral lesions.

It is often difficult to predict the duration of survival for these patients, particularly for potential surgical candidates. Studies have found several factors associated with survival time in patients with metastatic osseous disease who undergo surgical fixation, including cancer type; functional status; presence and number of bone and visceral metastases; hemoglobin concentration; and physician-estimated survival time [2–10]. Unfortunately, many of these studies have analyzed heterogeneous populations treated with multiple fixation types for weightbearing and nonweightbearing extremities [2,3,8].

The femur commonly requires operative stabilization for impending or completed pathologic fracture. Few studies have assessed patients with metastatic bone disease treated exclusively with intramedullary fixation of the femur [11–17], and only 3 studies have assessed risk factors for mortality in this population [13,15,16]. This is important because the femur is a weightbearing long bone, and intramedullary nailing is a relatively common palliative procedure in this population. The goal of our study was to assess the associations of various clinical

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and demographic factors with duration of survival after intramedullary nail fixation of impending or completed pathologic femur fractures.

2. Methods

This study was approved by our institutional review board. Patients treated with intramedullary nail fixation for an impending or completed metastatic femur fracture between January 2005 and April 2017 at our institution were considered for inclusion. Patients treated with antegrade or retrograde intramedullary nails were included, irrespective of location of femoral fracture. For patients who were ultimately treated with bilateral femoral intramedullary nails, we selected only the first operative side to obtain a unique patient population. We excluded patients who did not have confirmed pathologic diagnosis of metastasis before intramedullary nail fixation; those with tumor that eroded into bone from a pre-existing soft tissue mass in the thigh; those who had concomitant surgery of another extremity; those with primary osseous lesions; and those treated with other reconstructive or stabilization methods (e.g., total joint arthroplasty, hemiarthroplasty). In total, 138 patients were included in the study.

2.1. Data collection

Medical records were reviewed for demographic and other patient characteristics. Imaging and clinical reports were used to confirm the presence of other metastases. Eastern Cooperative Oncology Group (ECOG) scores were recorded directly from clinical notes or estimated by 1 reviewer on the basis of notes. Most mortality data were acquired from the United States Social Security Death Index. Other collected data included presence of other metastases; laboratory values; type of primary cancer; chemotherapy history; and whether the fracture was treated prophylactically.

Indications for intramedullary nailing were determined according to the operative note and other clinical notes. These notes were used to establish whether the surgery was performed for pathologic fracture fixation or for prophylactic fixation of impending fractures. If further clarification was required, preoperative imaging and the final radiology report were reviewed to determine whether a fracture was evident before surgery.

The type of primary cancer was confirmed by femur biopsy in 70 patients. In 54 patients, a pre-existing biopsy from a different metastatic site was considered the tissue diagnosis. In 10 patients, biopsies were deficient and nondiagnostic, although clinical correlation with imaging and clinical presentation enabled clinicians to determine the primary cancer diagnosis. In the remaining 4 patients, biopsy results were nondiagnostic for the specific primary cancer and were categorized as metastatic carcinoma of unknown origin.

Hemoglobin concentrations recorded within 5 days before surgery were considered. Albumin and calcium concentrations within 1 month before surgery were also recorded.

Thirty-day complication rates were assessed. Major medical complications included deep venous thrombosis, pulmonary embolism, pneumonia, myocardial infarction, arrhythmia, cerebrovascular accident, and renal failure. Wound complications included surgical site infection and hematoma formation.

2.2. Statistics

Survival analysis was performed for the full population with univariate and multivariate Mantel-Cox regressions. Univariate analysis was performed by dichotomizing each variable, with the exception of cancer type. Patients were grouped on the basis of relative cancer aggressiveness according to a study by Katagiri et al. [5]. Group 1 (rapid growth) consisted of those with lung carcinoma, gastric carcinoma, melanoma, or hepatocellular carcinoma. Group 2 (moderate growth) consisted of those with previous sarcoma or other carcinomas. Group 3 (slow growth) consisted of those with breast carcinoma, prostate carcinoma, renal cell carcinoma, thyroid carcinoma, multiple myeloma, or lymphoma.

The mean (± standard deviation) age of the full cohort was 60 ± 13 years. Therefore, we used age 60 years as a binary threshold. The mean hemoglobin concentration (based on 137 patients) was 11 ± 1.9 g/dL; therefore, we used 11 g/dL as the binary threshold. The mean albumin concentration (based on 117 patients) was 3.6 ± 0.6 g/dL and was used to calculate mean corrected calcium concentration (9.4 ± 0.8 g/dL). Thresholds were set at 3.5 g/dL for albumin and 9.5 g/dL for corrected calcium. Univariate analysis was also used to assess how various factors, including type of visceral metastasis and number of visceral metastases, influenced survival in the 65 patients with visceral metastases. An additional multivariate Cox regression model was created to determine the associations of assessed factors with survival within the subgroup of 88 patients treated prophylactically for impending pathologic fractures. Complication rates were compared between the completed and impending fracture cohorts via chi-squared analysis. For all assessments, significance was set at $p < 0.05$. Factors with $p < 0.20$ on univariate analysis were included in the final multivariate model.

3. Results

3.1. Demographic characteristics

Eight-eight patients (64%) were treated prophylactically. Eighty-one women (59%) were included in this study. Breast carcinoma and multiple myeloma were the most common cancer types, each occurring in 29 patients (21%). Lung carcinoma (15%) and renal cell carcinoma (8.7%) were the next most common primary tumor types. Prostate carcinoma (5.1%) and thyroid carcinoma (3.6%) were less common, and 35 patients (25%) had primary tumors classified as “other.” Twenty-four patients were assigned to group 1; 30 patients to group 2; and 84 patients to group 3. Visceral metastases were present in 65 patients (47%), and additional bone metastases in bones other than the femur were present in 110 patients (80%) at the time of surgery (Table 1).

Of the 50 patients with completed fractures, 22 (44%) continued with systemic therapy after intramedullary rod fixation. Of the 88 patients with prophylactically stabilized impending fractures, 47 (54%) continued with systemic therapy after surgery. Of the patients with impending fractures, 8 (9%) patients had local treatment of visceral metastases, whereas 5 (10%) patients with completed fractures had analogous treatment of visceral metastases.

3.2. Thirty-day complication rates

Eighteen patients (13%) of the overall population had complications within 30 days. Of these, 16 patients (12%) had major medical complications, and 3 patients (2.2%) had wound complications. When considering stabilization of impending versus completed fractures, there were no significant differences between cohorts ($p > 0.25$; Table 2).

3.3. Survival analysis

The median postoperative survival time for the overall population was 8.4 months (Fig. 1). Univariate analysis showed significantly shorter survival in those with visceral metastases (median, 5.6 versus 16 months, $p < 0.001$, Fig. 2), lower hemoglobin concentration (4.1 versus 18 months, $p < 0.001$, Fig. 3), lower albumin concentration (2.4 versus 16 months, $p < 0.001$, Fig. 4), more aggressive primary cancers (3.4 months for group 1, 3.0 months for group 2, and 18 months for group 3, $p < 0.001$, Fig. 5), and older age (7.0 versus 12 months, $p = 0.048$, Fig. 6) (Table 3). With the exception of age, visceral