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Biomechanical model of a high risk impending pathologic fracture of the femur: Lesion creation based on clinically implemented scoring systems

Gerald E. Alexander III [a], Sergio Gutierrez [b], Aniruddh Nayak [b], Brian T. Palumbo [a], David Cheong [a,c], G. Douglas Letson [a,c], Brandon G. Santoni [b,*]

[a] Department of Orthopaedic Surgery and Sports Medicine, University of South Florida College of Medicine, Tampa, FL USA
[b] Phillip Spiegel Orthopaedic Research Laboratory, Foundation for Orthopaedic Research & Education, Tampa, FL USA
[c] H. Lee Moffitt Cancer Center, Tampa, FL USA

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ABSTRACT

Background: Multiple classifications combine objective and subjective measures to predict fracture risk through a metastatic lesion. In our literature review, no studies have attempted to validate this predicted fracture risk from a biomechanical perspective. The study goal was to evaluate proximal femur strength after creating osteolytic defects. We report a standardized technique to re-create a metastatic lesion.
Methods: Eight femoral matched pairs were procured and a standardized technique was used to create an osteolytic femoral neck defect in one femur with the contralateral specimen serving as the control. Femurs were loaded to failure in a material testing machine at 2 mm/s. Failure load (N) and location of failure were documented. 3D finite element (FE) femur models with and without the lesions were developed to predict von Mises stresses in the femoral neck and compare between the two models.
Findings: Femurs containing the osteolytic defect failed at significantly lower loads than the intact specimens in a reproducible manner (intact: 10.69 kN (3.09 SD); lesion: 5.56 kN (2.03 SD), $p<0.001$). The average reduction in failure load was 48%, and the fracture pattern was consistent in all specimens. FE model comparison similarly predicted significantly higher von Mises stress at the lesion.
Interpretation: Our methods and pathologic fracture model represent the clinical parameters of metastatic bone disease and suggest a significant reduction in structural integrity of the lesion-containing femur. Prophylactic surgical fixation may be warranted clinically to reduce the risk of pathologic fracture. Our model technique is reproducible and may be used in future studies.

1. Introduction

Impending pathologic fracture is a challenging problem in patients with metastatic bone disease. These lesions carry risk of fracture depending on the origin of the primary cancer, including the lung, breast, prostate, thyroid, kidneys, and occasionally other primary carcinomas. In general, metastatic lesions are classified as osteolytic, osteoblastic or mixed, and occur more commonly in the proximal portion of the extremities (Coleman, 2001). Osteolytic and mixed metastatic tumors alter the native cancellous and cortical architecture rendering the osseous tissues prone to pathologic fracture, especially in the weight-bearing lower extremities. Fracture can occur with minimal activity, such as rolling over in bed or rising from a chair (Coleman, 2001), and catastrophic results have been reported. These injuries are associated with increased mortality rates, as published reports have found survival to be decreased approximately 50% once a fracture occurs (Hirsh, 2009). This has led to an increase in prophylactic fixation and radiotherapy for treatment of at risk lesions (Algan and Horowitz, 1996; Dutka et al., 2006; Mrozek et al., 2005; van der Linden et al., 2003).

Numerous criteria and scoring systems have been proposed to guide the decision-making process of the orthopedic surgeon in choosing when to prophylactically treat high-risk lesions. Proposed classifications, including the Mirels' score (Mirels, 1989), combine objective and subjective measures, including lesion type, size, location, and pain, to best predict the risk of fracture through a metastatic lesion. Other classification systems, such as that proposed by Harrington, include percentage of axial cortical involvement, percentage of circumferential cortical involvement, and absolute lesion size (Harrington, 1986). The Mirels' score is most commonly used due to its simplicity and its reproducibility (Damron et al., 2003; Evans et al., 2008; Jawad and Scully, 2010; Mac Niocaill et al., 2011).

Biomechanical studies have attempted to help physicians define the structural risk of impending fractures. Prior in vitro studies have

* Corresponding author at: Foundation for Orthopaedic Research & Education, Tampa, FL 33637 USA.
E-mail address: bsantoni@foreonline.org (B.G. Santoni).

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analyzed various defects in animal specimens using both physical and finite element methods, demonstrating decreased strength in defect models (Hipp et al., 1989, 1990, 1991; McBroom et al., 1988). Human cadaveric studies showed similar decreases in strength, but the lesions created were large cortical defects, clinically representative of a pathologic fracture as opposed to an impending fracture (Cheal et al., 1993; Kaneko et al., 2007; Keyak et al., 2005). More recently, studies have utilized computed tomography imaging in conjunction with finite element analysis to predict the risk of fracture, especially as it pertains to reductions in bone strength associated with osteoporosis or cancer (Kaneko et al., 2008; Keyak et al., 2005).

In our review of the literature, we found that no standardized method has been reported to create a realistic and repeatable model of impending fracture. This remains a constant obstacle in biomechanical studies which attempt to assign risk through gross mechanical testing. The development and characterization of a clinically-based model of impending fracture may serve to reinforce existing clinical recommendations for prophylactic, surgical intervention for the treatment of impending fractures. Therefore, the purpose of the current research was to develop a standardized, reproducible technique of creating an impending fracture in a cadaver model based on clinically relevant criteria that could be easily implemented in future biomechanical studies to evaluate, for example, invasive and non-invasive modalities with which to augment the impending fractures.

2. Methods

Sixteen ($n = 16$) donor-matched femur specimens were dissected from eight fresh-frozen human cadavers (average age: 62.2 (10.3 SD); range: 48–76 yrs.), leaving the bone devoid of any soft tissue. To exclude pre-existing disease or trauma, initial anterior–posterior and lateral radiographs were taken of each hip following femur extraction. Bone mineral density (BMD) values were assessed by dual energy X-ray absorptiometry (DEXA) (Lunar Prodigy, GE Healthcare, Madison, WI, USA), with average BMD values of 0.861 g/cm^2 (0.150 SD) (range: 0.598–1.28 g/cm^2) and an average T-score of −0.72 (range: −3.2 to 1.6). The specimens were wrapped in saline soaked gauze and stored at −70 °C in sealed plastic bags.

One right or left femur from each matched pair was enrolled in the "high-risk" impending pathologic fracture study arm. "High-risk" was defined according to the clinically relevant Mirels' score (Table 1) (Mirels, 1989). As this was a cadaveric study, pain as a contributing factor in defining pathologic fracture risk was removed as a scoring metric. Thus, the lesion was created to satisfy a score of nine by being osteolytic (3 points), encompassing greater than 2/3 of the bony diameter (3 points), and located in the proximal femur (3 points). In addition to Mirels' score, Harrington's proposed classification criteria of lesion size greater than 25 mm and axial cortical involvement of greater than 50% were incorporated into the lesion design.

Table 1
Mirels' score of impending pathologic fractures. A score of 1 through 3 is assigned to each of the four categories [lesion type, size, anatomic location, and pain] resulting in a minimum score and a maximum score of 12. Metastatic lesion with a score higher than 8 are generally considered to be at higher risk of eventual fracture and the practitioner should consider prophylactic fixation.

Mirels' score	Type	Size	Location	Pain
1	Osteoblastic	<1/3	Upper extremity	Mild
2	Mixed	1/3–2/3	Lower extremity	Moderate
3	Osteolytic	>2/3	Peritrochanteric	Mechanical

2.1. Creation of the high risk lesion

A cortical defect was drilled through the femoral head articular surface at the fovea using a 3/16 in drill bit (Fig. 1A). This defect size and location were chosen because it allowed easy access to the canal of the femoral neck and resulted in minimal biomechanical bias of the model according to an a priori finite element stress analysis. A curved curette was inserted through the femoral head defect. The curette was used to shell out a canal defect of the inferior portion of the femoral neck (Fig. 1B). Sequential AP radiographs were taken throughout the process to ensure proper lesion size and location. The defect was enlarged until it encompassed 2/3 of the entire width of the femoral neck, in accordance with the Mirels' scoring system, which was measured throughout lesion creation on AP fluoroscopy images.

After creating the osteolytic defect in the femoral neck, a 25 mm diameter circle was drawn on the outer cortex of the calcar to outline the proposed cortical insult. The defect was centered over the inferomedial femoral neck, above the level of the lesser trochanter. An AP radiograph was taken, and cortical thickness in the area of the planned defect was measured and recorded. A high-speed burr was then taken to the outer cortex of the pre-defined area and the cortical bone was carefully debrided. Serial radiographs were taken throughout the debridement process, until a defect encompassing 50% of the cortical thickness was measured as compared to the initial film (Fig. 1C). The thinned cortical region was checked with fluoroscopy to ensure uniformity throughout the circular area. The size of the cortical insult as well as the reduction in cortical thickness were chosen based on Harrington's criteria, which classifies lesions as high risk if they radiographically appear to involve 50% or more of the diaphyseal cortex with a lesion size 25 mm in length or greater (Harrington, 1986). The same author created all lesions to promote reproducibility of the technique.

2.2. Specimen testing

All specimens were thawed at room temperature overnight (25 °C) before biomechanical testing. The femur was shortened by 50% and approximately 5 in of the distal femur was potted in 1.5 in diameter polyvinylchloride (PVC) pipe in a custom-designed aluminum fixture with high strength resin (Bondo body filler, 3M Collision Repair Solutions, St. Paul, MN, USA). Two wood screws were placed through the construct to confer rotational stability to the potted femur. The custom-designed aluminum box was secured in a servo electric TestResources biaxial loading frame (TestResources Model 800LE, Shakopee, MN, USA). We employed a biomechanical testing model similar to prior studies (Olsen et al., 2011; Zdero et al., 2008). In order to simulate the anatomic alignment and joint reactive force vector of the femur, the specimen was oriented such that it was in 20° of lateral tilt in the coronal plane (Stoffel et al., 2008). The specimen was aligned to neutral in the sagittal and axial planes. The test frame actuator was equipped with a 22 kN load cell and custom-made load application device consisting of a titanium acetabular cup with a lipped ultra-high molecular weight polyethylene (UHMWPE) liner (Stryker, Kalamazoo, MI, USA) (Fig. 2) of diameter slightly larger than the femoral head. Each specimen was loaded with a continuous axial compressive load at a rate of 2 mm/s (Olsen et al., 2011; Schileo et al., 2008; Stoffel et al., 2008) until catastrophic failure of the femur occurred. This displacement rate is more consistent with those of daily living, as opposed to those experienced during a sideways fall, which have been estimated at 100 mm/s (de Bakker et al., 2009). Construct stiffness (N/mm) was derived from the linear portion of the force versus displacement curve below 1500 N. Continuous live fluoroscopy video data (GE FlexiView 8800,GE Healthcare, Waukesha, WI, USA) was collected throughout each biomechanical test and evaluated post hoc to determine differences in failure location and