The Influence of Femoral Geometry and Demographic Factors on Atypical Femoral Fractures

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Introduction: Osteoporosis is a bone disorder characterized by the deterioration of bone microarchitecture. This results in bone fragility fractures among older individuals and is a significant societal burden. In the United States alone, osteoporosis affects approximately 10 million individuals aged 50 and above, with an additional 35 million at risk of developing osteoporosis. This contributes to a staggering 1.5 million fragility fractures every year[1]. The foundational treatment of osteoporosis is bisphosphonates, which work by promoting apoptosis of osteoclasts that are actively engaged in mineral degrading on the bone surface[2]. While bisphosphonates have proved to be efficacious, studies have shed light on potential adverse effects stemming from prolonged bisphosphonate consumption. The spectrum of side effects notably includes osteonecrosis of the jaw and, importantly for this study, atypical femoral fractures (AFF)[3]. Intriguingly, similar adverse manifestations have been reported in osteoporotic patients who have been administered other anti-resorptive medications, such as denosumab[4]. Atypical femoral fractures, although less common, represent a potentially severe adverse effect of bisphosphonate and denosumab treatments. The estimated incidence of these fractures is 1.74 fractures per 10,000 patient-years, yet their underlying pathophysiology remains poorly understood[5]. Considering the profound implications for osteoporotic patient outcomes on anti-resorptive treatment, there is a crucial need to enhance our understanding of the pathophysiology and biomechanics that cause atypical femoral fractures. Our study aims to investigate these aspects by conducting specific demographic and radiological measurements that have been established as influential factors in the pathogenesis of AFFs, ultimately striving toward better prevention, diagnosis, and treatment strategies.

Figure 1: Left Hip, Atypical Femur Fracture. Key: 1, distance from lesser trochanter to atypical femur fracture; 2a, medial cortical thickness; 2b, lateral cortical thickness; 3, femoral offset; 4, femoral neck angle.

Methods: We conducted a retrospective analysis of 57 patients who experienced AFFs after being treated with bisphosphonates for a prolonged time (range: 1-19 years). An age-matched control group of 66 patients was also identified. The AFF group consisted of 54 females and three males with an average age of 67.4 ± 9.5 years, while the control group consisted of 63 females and three males with an average age of 69.5 ± 8.6 years. A retrospective chart review was performed to collect the demographic data shown in Table 1. We used Sectra MSK (Version 24.2.6.5829) to measure the following parameters on hip X-rays: 1) the distance from the lesser trochanter to the atypical femur fracture, 2) medial and lateral cortical thickness, 3) femoral offset, and 4) femoral neck angle (Figure 1). The average distance from the distal lesser trochanter to the atypical femur fracture was 77.0 mm. Therefore, this distance was used to measure the control group parameters. A pooled t-test was performed to calculate p-values for lateral cortical thickness, femoral offset, and femoral neck angle, and a Mann-Whitney U test was performed to calculate the medial cortical thickness p-value.

	AFF (n=57)	Control (n=66)	P-value
Age (years)	67.4 ± 9.5	69.5 ± 8.6	0.2148*
Sex			
Male	3 (5.3)	3 (4.5)	1.0000
Female	54 (94.7)	63 (95.5)	
BMI (kg/m²)	26.7 ± 4.7	28.2 ± 7.7	0.4333*
Laterality			
Right	21 (36.8)	29 (43.9)	
Left	21 (36.8)	30 (45.5)	
Bilateral	15 (26.4)	7 (10.6)	
Previous Fracture (low energy)	23 (40.4)	13 (19.7)	**0.0168**
Parent Fractured Hip	4 (7.0)	10 (15.2)	0.2544
Rheumatoid Arthritis	11 (19.6)	6 (9.1)	0.1211
Steroid Use (> 3 months)	22 (38.6)	8 (12.1)	**0.0008**
Excessive Alcohol Intake	2 (3.5)	4 (6.1)	0.6849
Rheumatoid Arthritis	11 (19.6)	6 (9.1)	0.1211
History of Secondary Osteoporosis	9 (15.8)	2 (3.0)	**0.0225**
Parent Fractured Hip	4 (7.0)	10 (15.2)	0.2544

Table 1: Patient Demographic Data

Results: The AFF group had 21 right, 21 left, and 15 bilateral AFFs, and the control group had 29 right, 30 left, and seven bilateral comparison hips. Patients in the AFF group were more likely to have had prior fragility fractures (p=.0168), chronic steroid use (p=.0008), and secondary osteoporosis (p=.0225) compared to the control group. For the AFF group, the average distance from the distal lesser trochanter to the AFF was 77.0 mm. At this level, the average medial and lateral cortical thicknesses were 7.747 ± 1.70 mm and 11.068 ± 2.32 mm in the AFF group (p = 0.854), and 7.695 ± 1.60 mm and 7.975 ± 1.73 mm (p = <.0001) in the control group. The femoral offset was greater in the AFF group, with an average of 43.856 ± 7.23 mm, versus the control group, whose average was 41.870 ± 6.94 mm (p = 0.0464). Lastly, there was no significant difference in the femoral neck angle between the two groups, as the AFF group averaged 129.781° ± 3.95° and the control group averaged 131.453° ± 3.32° (p = 0.9968) (Table 2).

	Atypical Femur Fracture (n=73)	Control (n=73)	P-value
Distance from lesser trochanter to AFF (mm)	77.099 ± 46.22	-	-
Medial Cortical Thickness (mm)	7.747 ± 1.70	7.695 ± 1.60	0.854
Lateral Cortical Thickness (mm)	11.068 ± 2.32	7.975 ± 1.73	< .0001*
Femoral Offset (mm)	43.856 ± 7.23	41.870 ± 6.94	0.0464*
Femoral Neck Angle (degrees)	129.781° ± 3.95	131.453° ± 3.32°	0.9968

Table 2: Radiologic Measurements

Discussion: The etiologies of AFFs remain incompletely elucidated, although existing literature implicates an intricate interplay among patient-specific variables, hip geometric characteristics, and dysregulated bone remodeling processes. Our findings show that a prior history of fractures, concomitant secondary osteoporosis, and corticosteroid use (> three months) are significantly higher in patients with AFFs. In terms of femoral geometry, we found an increase in the femoral offset and lateral cortical thickness in the AFF cohort. Contrary to existing studies, our analyses did not discern significant deviations in the femoral neck-shaft angle among our study subjects[6]. Recent advances in imaging analyses, including CT and MRI finite element analyses, will facilitate further examination of the influence of these biomechanical factors on the microarchitecture of AFFs. By integrating these findings with demographic and risk factor data, clinicians may be better equipped to predict which patients are at a high risk of developing AFFs before initiating bisphosphonate therapy. This information could help inform decisions about alternative osteoporosis treatments or the implementation of more frequent bisphosphonate-free holidays for high-risk patients.

Clinical Significance: The demographic and biomechanical factors predisposing patients to atypical femoral fractures (AFFs) provide invaluable insights for the targeted management of osteoporotic patients on anti-resorptive therapies, notably bisphosphonates and denosumab. Our findings offer a foundation for risk stratification algorithms that could inform clinical decision-making, potentially guiding the selection of alternative therapeutic options or the implementation of drug holidays for patients identified as high-risk for AFF development.

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