

Predicting Need for Fixation of Atypical Femoral Fracture

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Context: Predictors of the requirement for fixation have not been reported in incomplete atypical femoral fractures. The clinical features of incomplete atypical femoral fractures should be reviewed to predict the requirement for surgical intervention in this condition.

Objective: Our purposes were (1) to evaluate the clinical results of incomplete atypical femoral fracture and (2) to determine the factors associated with the requirement for fixation in incomplete atypical femoral fractures.

Design, Setting, and Patients: We retrospectively reviewed the medical records of 51 patients with a total of 65 incomplete atypical femoral fractures from 3 tertiary referral centers. Minimum follow-up was 12 months (mean, 19.8 months; range, 12–82 months).

Intervention: The study consisted of fixation-requiring and non-fixation-requiring groups.

Main Outcome Measure: The main outcome measure was the requirement for fixation.

Results: Thirty-one (47.7 %) hips required internal fixation. Cox regression analysis showed that the subtrochanteric location was significantly associated with the requirement for fixation (hazard ratio, 2.713; 95% confidence interval, 1.189–6.189)

Conclusions: About one-half of incomplete atypical femur fractures required surgical intervention, and subtrochanteric involvement could be used as a predictor of the requirement for fixation in these conditions. (*J Clin Endocrinol Metab* 98: 2742–2745, 2013)

Bisphosphonates have been proven to be effective for reducing the risk of osteoporotic fractures and have been prescribed worldwide to prevent and treat osteoporosis (1–3). However, long-term use of bisphosphonates have recently been found to be associated with atypical femoral fractures, which has increased concerns regarding osteoporosis treatment (4–9).

Recently, the American Society for Bone and Mineral Research (ASBMR) atypical femoral fractures task force described several radiographic features to define an atypical

femoral fracture. All of the major features should be present to diagnose an atypical fracture. These major features include location in the subtrochanteric or diaphyseal region, a transverse or short oblique fracture configuration, minimal or no associated trauma, a medial spike when the fracture is complete, involvement of lateral cortex when the fracture is incomplete, and absence of comminution (10).

Although incomplete fractures are also included in the ASBMR criteria, an incomplete atypical femoral fracture can be easily undiagnosed or misdiagnosed until the frac-

Table 1. Characteristics of Fixation-Requiring Group and Non-Fixation-Requiring Group

	Fixation-Requiring Group (n = 26)	Non-Fixation-Requiring Group (n = 25)	P Value
Sex (female/male)	25:1	25:0	1.000
Age, y	70.4 ± 8.3	70.4 ± 8.1	.989
BMI, kg/m ²	22.0 ± 4.3	23.9 ± 3.0	.074
Duration of bisphosphonates, y	4.1 ± 3.7	4.8 ± 4.0	.518
History of bisphosphonate use, n			.743
Yes	19	20	
No	7	5	
Location of involvement, n			.095
Subtrochanteric	12	6	
Diaphyseal	19	28	
T-score of total femur	-1.7 ± 1.5	-2.1 ± 1.1	.296
Bone mineral density, g/cm	0.696 ± 0.217	0.673 ± 0.157	.694
Osteocalcin, ng/ml	13.2 ± 12.6	14.9 ± 8.7	.679
Use of teriparatide, n			.153
Yes	7	12	
No	19	13	

ture becomes complete. In addition, the natural course of an incomplete atypical femur fracture is unknown, and treatment guidelines for incomplete atypical femoral fractures have not been established (11, 12).

Our study purposes were (1) to evaluate the clinical results of incomplete atypical femoral fractures and (2) to determine factors associated with the requirement for fixation in incomplete atypical femoral fractures.

Subjects and Methods

We retrospectively reviewed the medical records for 65 incomplete atypical femoral fractures in 51 patients who were treated at 4 hospitals from June 2004 to March 2011. The inclusion criteria were incomplete atypical femoral fractures defined by the ASBMR on radiographs (10) and follow-up for a minimum of 12 months.

Of the 14 patients with bilateral involvement, 2 had had subtrochanteric fractures on one side and femoral shaft fractures on the other side. Of the fractures in the remaining 37 patients, 12 were diagnosed as incomplete atypical fractures, when the contralateral femur sustained a complete atypical femur fracture.

After diagnosis of incomplete atypical fractures, patients were initially treated nonoperatively with limited weight-bearing using an assistive device. During study periods, the indications for internal fixation were complete fracture or intractable pain on weight bearing, even after nonoperative treatment including protected weight-bearing and pain control. The patients who underwent internal fixation were categorized to the fixation-requiring group. Routine follow-up was conducted every 2 to 3 months until the lesion of the incomplete fracture was healed and annually thereafter until discharge upon clinical determination of a healed status.

We assessed patient characteristics including age, sex, body mass index (BMI), duration of bisphosphonates, location of involvement (subtrochanteric and diaphyseal), T-score of total femur, bone mineral density, osteocalcin, and use of teriparatide to determine factors associated with requirement for fixation.

The Fisher exact test was performed for categorical variables and the Mann-Whitney *U* test for continuous variables. Cox regression analysis using the enter method was performed to determine factors associated with requirement for fixation. Statistical analyses were conducted with the SPSS for Windows statistical package, version 16.0 (SPSS, Chicago, Illinois).

The design and protocol of this study were approved by the institutional review board in each hospital, who waived the informed consent.

Results

Thirty-one (47.7%) hips required internal fixation at the mean of 9.4 months (range, 1–26 months). Among them, 17 hips required internal fixations for intractable pain, and 14 hips required internal fixation for complete fractures. All patients could ambulate independently and perform daily living activities at the mean follow-up of 19.6 months (range, 12–82 months). There were no significantly different variables between fixation-requiring and non-fixation-requiring groups (Table 1). Of the 51 patients, 19 patients (22 hips) used teriparatide for a mean of 4.6 months (range, 1–10 months). The independent variables tested for the multivariate analyses included age, BMI, location of involvement, history of bisphosphonate use, and teriparatide use as confounding factors. In Cox regression analysis, the subtrochanteric location was significantly associated with the requirement for fixation (hazard ratio, 2.713; 95% confidence interval, 1.189–6.189) (Table 2 and Figure 1A).

Discussion

Atypical femoral fractures have been an increasing concern in the treatment of osteoporosis, especially with bisphospho-

Table 2. Cox Regression Analysis for Requirement for Fixation

	Hazard Ratio	95% Confidence Interval	P Value
Age	1.036	0.988–1.086	.141
BMI	0.955	0.860–1.061	.389
History of bisphosphonate use			.954
Yes	0.971	0.357–2.643	
No	1		
Location of involvement			.018
Subtrochanteric	2.714	1.189–6.189	
Diaphyseal	1		
Teriparatide use			.210
Yes	0.575	0.242–1.367	
No	1		

nates (13–17). Our objectives were to evaluate the clinical results with incomplete atypical femoral fractures and to determine factors associated with the requirement for fixation in these conditions. Although 48% of incomplete fractures required internal fixation, multivariate analysis showed that subtrochanteric involvement was significantly associated with the requirement for fixation.

We cannot draw a definite conclusion about the association between atypical femoral fractures and bisphosphonate use in this study. However, 76.5% patients (39 of 51) had a history of bisphosphonate use before diagnosis of atypical femoral fractures in this study.

Several studies have demonstrated that prophylactic fixation could be necessary in an incomplete atypical femoral fracture, because it is easy for the fracture to progress to a complete fracture, and complete fractures have higher rates of perioperative complications (10, 12, 18, 19). In particular, prodromal pain should be considered an indication for surgical intervention, because it indicates an impending complete fracture. We totally agree with this concern and therefore used internal fixation as the treatment when patients had intractable pain during the study periods.

Teriparatide has been suggested as a nonsurgical intervention for atypical femoral fractures, (12) and has been reported to enhance bone healing in patients with delayed healing or nonunion (20–23). However, there was a lack of evidence for the efficacy of teriparatide in several epidemiologic and observational cohort studies on atypical femoral fractures. Recently, a prospective study reported that teriparatide use is associated with increased bone remodeling in patients with atypical femoral fractures (24). However, this study presented bone remodeling of distal radius and tibia not the involved femur. Use of teriparatide was not associated with reducing the requirement for fix-

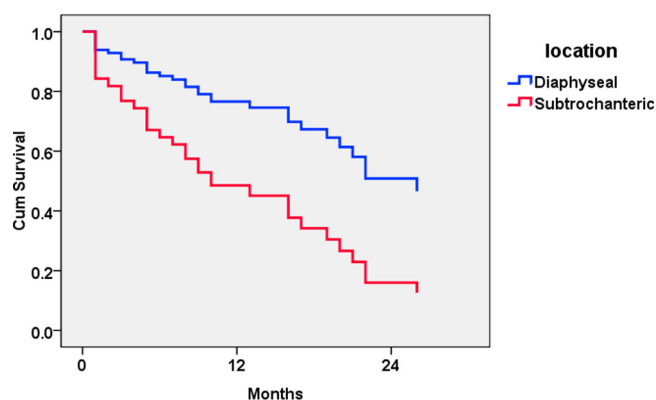
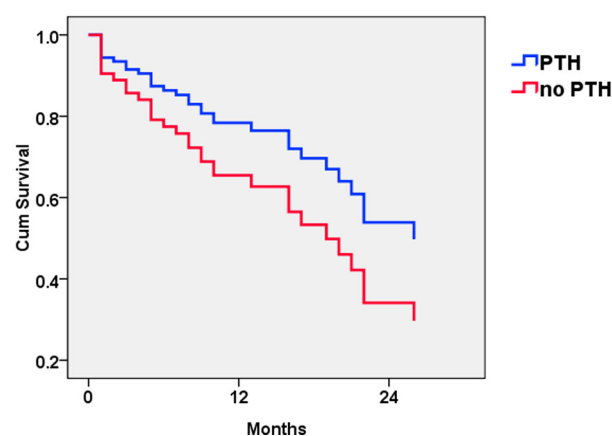
A**Survival Curve with Requirement of Fixation as an End Point****B****Survival Curve with Requirement of Fixation as an End Point**

Figure 1. A, Survival curve with requirement for fixation as an end point according to the involved location ($P = .018$). B, Survival curve with requirement for fixation as an end point according to the use of teriparatide ($P = .210$).

ation in our study (Figure 1B). Although use of teriparatide could be an alternative option during conservative treatment, evidence of its usefulness is still lacking, and well-designed studies are necessary to verify the efficacy of teriparatide for these conditions.

Our study had several limitations. First, it was hard to avoid the pitfalls of selection bias and information bias because of the retrospective design of the study. Surgeons who are aware of the high risk of a complete fracture in the subtrochanteric region might prefer elective fixation. However, our indication for fixation was not the location of involvement but intractable pain, which indicates an impending complete fracture before it occurs. Second, we simplified the main outcome to the requirement for fixation, although there might be a substantial difference in morbidity between patients who have elective fixation and those who need fixation after a complete fracture. However, there was no significant difference in the clinical re-

sults between the 2 groups in this study. Despite these limitations, this is the first study presenting a predictor of the requirement for fixation in incomplete atypical femoral fractures. About one-half of incomplete atypical femur fractures required surgical intervention, and clinicians should be cautious when treating nonsurgical patients with subtrochanteric involvement.

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References

1. Bilezikian JP. Efficacy of bisphosphonates in reducing fracture risk in postmenopausal osteoporosis. *Am J Med.* 2009;122:S14–S21.
2. Black DM, Schwartz AV, Ensrud KE, et al. Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. *JAMA.* 2006;296:2927–2938.
3. Pols HA, Felsenberg D, Hanley DA, et al. Multinational, placebo-controlled, randomized trial of the effects of alendronate on bone density and fracture risk in postmenopausal women with low bone mass: results of the FOSIT study. Fosamax International Trial Study Group. *Osteoporos Int.* 1999;9:461–468.
4. Lenart BA, Lorch DG, Lane JM. Atypical fractures of the femoral diaphysis in postmenopausal women taking alendronate. *N Engl J Med.* 2008;358:1304–1306.
5. Neviaser AS, Lane JM, Lenart BA, et al. Low-energy femoral shaft fractures associated with alendronate use. *J Orthop Trauma.* 2008;22:346–350.
6. Kwek EB, Goh SK, Koh JS, Png MA, Howe TS. An emerging pattern of subtrochanteric stress fractures: a long-term complication of alendronate therapy? *Injury.* 2008;39:224–231.
7. Goh SK, Samuel M, Su DH, Chan ES, Yeo SJ. Meta-analysis comparing total hip arthroplasty with hemiarthroplasty in the treatment of displaced neck of femur fracture. *J Arthroplasty.* 2009;24:400–406.
8. Lee YK, Ha YC, Park C, Yoo JJ, Shin CS, Koo KH. Bisphosphonate use and increased incidence of subtrochanteric fracture in South Korea: results from the National Claim Registry. *Osteoporos Int.* 2013;24:707–711.
9. Capeci CM, Tejwani NC. Bilateral low-energy simultaneous or sequential femoral fractures in patients on long-term alendronate therapy. *J Bone Joint Surg Am.* 2009;91:2556–2561.
10. Shane E, Burr D, Ebeling PR, et al. Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res.* 2010;25:2267–2294.
11. La Rocca Vieira R, Rosenberg ZS, et al. Frequency of incomplete atypical femoral fractures in asymptomatic patients on long-term bisphosphonate therapy. *AJR Am J Roentgenol.* 2012;198:1144–1151.
12. Ha YC, Cho MR, Park KH, Kim SY, Koo KH. Is surgery necessary for femoral insufficiency fractures after long-term bisphosphonate therapy? *Clin Orthop Relat Res.* 2010;468:3393–3398.
13. Silverman SL, Ott SM, Dell RM. Bisphosphonates and atypical femoral fractures. *N Engl J Med.* 2010;363:1083; author reply 1084–1085.
14. Stevenson JC. Bisphosphonates and atypical femoral shaft fractures. *N Engl J Med.* 2011;365:377; author reply 377.
15. Lenart BA, Neviaser AS, Lyman S, et al. Association of low-energy femoral fractures with prolonged bisphosphonate use: a case control study. *Osteoporos Int.* 2009;20:1353–1362.
16. Park-Wyllie LY, Mamdani MM, Juurlink DN, et al. Bisphosphonate use and the risk of subtrochanteric or femoral shaft fractures in older women. *JAMA.* 2011;305:783–789.
17. Maravic M, Ostertag A, Cohen-Solal M. Subtrochanteric/femoral shaft versus hip fractures: incidences and identification of risk factors. *J Bone Miner Res.* 2012;27:130–137.
18. Banffy MB, Vrahas MS, Ready JE, Abraham JA. Nonoperative versus prophylactic treatment of bisphosphonate-associated femoral stress fractures. *Clin Orthop Relat Res.* 2011;469:2028–2034.
19. Prasarn ML, Ahn J, Helfet DL, Lane JM, Lorch DG. Bisphosphonate-associated femur fractures have high complication rates with operative fixation. *Clin Orthop Relat Res.* 2012;470:2295–2301.
20. Black DM, Kelly MP, Genant HK, et al. Bisphosphonates and fractures of the subtrochanteric or diaphyseal femur. *N Engl J Med.* 2010;362:1761–1771.
21. Abrahamsen B, Eiken P, Eastell R. Cumulative alendronate dose and the long-term absolute risk of subtrochanteric and diaphyseal femur fractures: a register-based national cohort analysis. *J Clin Endocrinol Metab.* 2010;95:5258–5265.
22. Lo JC, Huang SY, Lee GA, et al. Clinical correlates of atypical femoral fracture. *Bone.* 2012;51:181–184.
23. Abrahamsen B, Eiken P, Eastell R. Subtrochanteric and diaphyseal femur fractures in patients treated with alendronate: a register-based national cohort study. *J Bone Miner Res.* 2009;24:1095–1102.
24. Chiang CY, Zebaze RM, Ghasem-Zadeh A, Iuliano-Burns S, Hardidge A, Seeman E. Teriparatide improves bone quality and healing of atypical femoral fractures associated with bisphosphonate therapy. *Bone.* 2013;52:360–365.