

Distribution of atypical fractures and cortical stress lesions in the femur: implications on pathophysiology

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ABSTRACT

Introduction: Some authors have hypothesised that atypical femur fractures occur due to tensile mechanism of failure. We studied the distribution of such lesions along the femur shaft to determine if they concentrate in regions that are subject to tensile loading.

Methods: From May 2004 to March 2010, radiological reviews of 48 patients aged 69 +/- 10.4 (range 47–92) years with atypical femoral fractures and lesions were performed. The absolute distance of each lesion from the greater trochanter and the ratio of the distance of each lesion from the greater trochanter expressed as a percentage of the entire femur length were measured.

Results: All periosteal reactions and cortical stress lesions occurred in the lateral cortex. There were 35 right femoral lesions (28 complete fractures and seven cortical stress reactions), with a median distance of 108.3 +/- 54.0 (range 67.0–270.4) mm from the greater trochanter and a median ratio of 23.9 +/- 11.7 (range 15.7–58.6) percent of the entire femoral length. There were 38 left femoral lesions (27 complete fractures and 11 cortical stress reactions), with a median distance of 109.9 +/- 43.1 (range 73.6–246.2) mm from the greater trochanter and a median ratio of 24.4 +/- 9.1 (range 16.3–51.1) percent of the entire femoral length.

Conclusion: Based on previously established femoral shaft loading characteristics, atypical lesions were clustered at the region of maximal tensile loading. No lesion occurred in regions that were subject to compressive loading. This unique distribution supports a tensile mechanism of failure in such lesions.

Keywords: advanced glycation end products,

atypical fracture, lateral periosteal reaction, tension failure

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INTRODUCTION

Atypical fractures of the femur have generated heightened interest with the release of the American Society for Bone and Mineral Research (ASBMR) task force report. This is due to their probable association with prolonged bisphosphonate therapy, among other risk factors. Features of prodromal thigh pain, bilateral involvement, transverse pattern with absence of comminution and occurrence with minimal or no trauma⁽¹⁾ all point toward a stress fracture evolving under systemic influence.

The association of these fractures with lateral cortical thickening and periosteal reaction of the lateral cortex⁽²⁾ is opposed to the typically medial locality of proximal femoral fatigue fractures that have previously been described in young athletes.^(3,4) The latter have been attributed to excessive compressional strain,⁽⁵⁾ and are located in the proximal third of the medial femur cortex, a region known to be subjected to the highest compressional strain.⁽⁵⁾ Isaacs et al recently described this fracture as tensional failure of the femoral cortex.⁽⁶⁾ If this were so, the distribution of these lesions in the femur should mirror the tensile stress distribution along the femoral cortex.

We hypothesised that atypical fractures, being tensional failures of the femoral cortex, exhibit a distribution corresponding to the tensile stress distribution along the femur. We aimed to study the distribution of atypical fractures and stress lesions along the femur shaft to determine if they concentrate in regions that are subject to tensile loading.

METHODS

From our institution's database of 3,104 low-energy femoral fractures occurring from May 2004 to March 2010, 48 atypical femoral fractures, comprising low-energy or spontaneous fractures with a transverse or short oblique configuration, as well as radiological suggestion of lateral cortical thickening, were identified. Exclusion

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Fig. 1 Radiograph shows the ratio between the distance of fracture/lesion from the greater trochanter (y) over the entire femur length (x).

criteria were patients with established metastatic bony involvement, metabolic bone diseases, any form of metaphyseal involvement and those with high energy trauma. This study was approved by the institutional review board.

A total of 44 female patients aged 69 ± 10.4 (range 47–92) years had fractures in association with prolonged bisphosphonate therapy. These bisphosphonates included alendronate (Merck, Sharpe and Dohme, Whitehouse Station, NJ, USA) ($n = 39$), zoledronate (Novartis, Basel, Switzerland) ($n = 1$), risedronate (Sanofi-Aventis, Paris, France) ($n = 2$) and alendronate, followed by risedronate ($n = 2$). The duration of bisphosphonate therapy averaged 4.0 ± 2.2 (range 2.0–10.0) years.

Two patients had normal bone mineral density (BMD), 19 were osteopaenic, ten were osteoporotic and the rest had no documented BMD results at the time of fracture. A radiological review of all the available radiographs of each patient was performed with respect to the absolute distance of each atypical fracture/stress lesion from the greater trochanter, and the ratio of the distance of each atypical fracture/stress lesion from the greater trochanter expressed as a percentage of the entire femur length.

All measurements were performed on strict anteroposterior radiographs of the intact femur, where

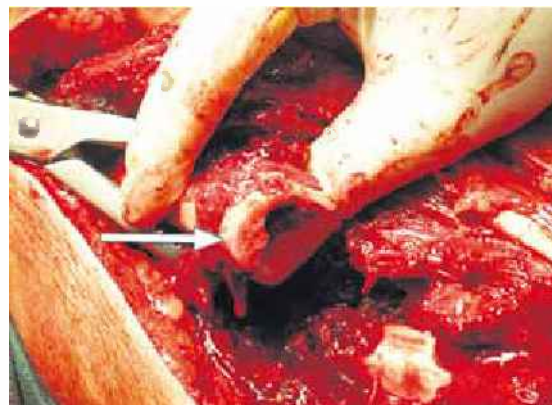


Fig. 2 Intraoperative photograph of the localised periosteal reaction of the femur cortex, through which the fracture occurred.

possible. The intact femur was measured for femoral length, and the lengths were assumed to be equal for both femurs. In patients who did not have an intact femur for reference, a strict anteroposterior postoperative radiograph of the fractured femur was measured. The tip of the greater trochanter was identified. A line was then drawn through this point, perpendicular to the axis of the femoral shaft. Another line, parallel to the first was drawn through the lowermost point of the femoral condyles. The distance between these two lines was the femoral length (Fig. 1). The greater trochanter was used as a reference, as it is the starting point for most intra- and extramedullary fixations for these lesions.

In similar fashion, the tip of the greater trochanter was identified in a strict anteroposterior radiograph of the respective femur. A line was then drawn through this point, perpendicular to the axis of the femoral shaft. Another perpendicular line was then dropped from this line to the lateral cortical aspect of a complete fracture, and this distance was measured (Fig. 1). The distance of the cortical stress lesion was measured in a similar way to that used for measuring atypical fractures described above. The reference point of the stress lesion was taken to be the region with the widest cortical thickness on the anteroposterior radiograph.

To determine the approximate magnification in femoral radiographs performed at our institution, ten femoral radiographs were obtained using the standard technique, with a radiopaque ruler placed horizontally at the level of the greater trochanter. For each case, the magnified ruler distance was measured twice. The average measurement was divided by the true ruler distance to obtain the magnification factor. The magnification was then averaged to obtain the estimated magnification for femoral radiographs. The estimated magnification obtained (9.98%) was used to correct the absolute distances measured.

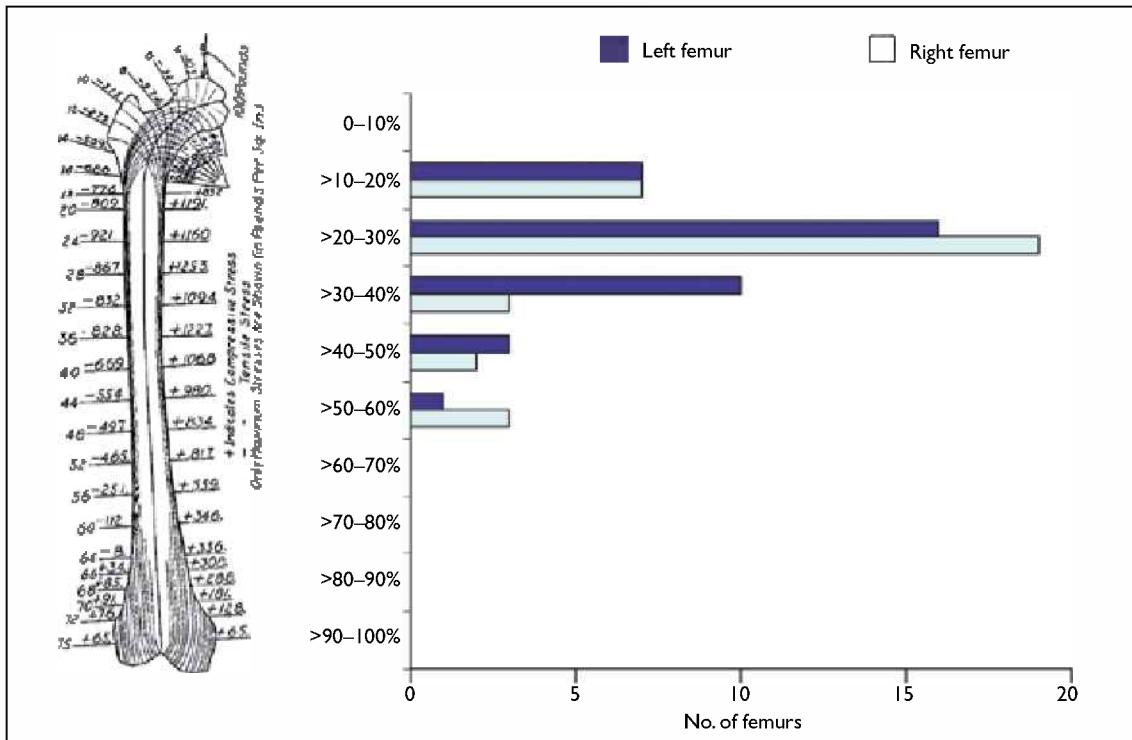


Fig. 3 Graph shows the concentration of lesions (similar for both femurs) at 20%–30% of the femoral length from the greater trochanter, which corresponds to the region of highest tensile stress, as illustrated on the femoral sketch by Koch.⁽¹⁵⁾

RESULTS

All periosteal reactions and cortical stress lesions occurred in the lateral cortex. Of the 35 right femoral lesions, 28 were complete fractures and seven were cortical stress reactions. The median distance of the lesions from the greater trochanter was 108.3 ± 54.0 (range 67.0–270.4) mm. The median ratio was $23.9\% \pm 11.7\%$ (range 15.7%–58.6%) of the entire femoral length. Of the 38 left femoral lesions, 27 were complete fractures and 11 were cortical stress reactions. The median distance of the lesions from the greater trochanter was 109.9 ± 43.1 (range 73.6–246.2) mm. The median ratio was $24.4\% \pm 9.1\%$ (range 16.3%–51.1%) of the entire femoral length.

DISCUSSION

Atypical femur fractures have been recently described in association with prolonged bisphosphonate therapy, among other risk factors, but their pathogenesis is still subject to much speculation.⁽⁷⁻¹⁰⁾ There is good reason to believe that these fractures are stress fractures of the femur occurring with minimal or no trauma, and are preceded sometimes by prodromal discomfort in the affected thigh.⁽²⁾ However, a closer observation of proximal femoral stress fractures in athletes would point to a stark difference in their pathogenesis. These fractures are known to involve the medial cortex of the proximal

third of the femur,^(3,4) a region established to be subject to the highest compressional loading.⁽⁵⁾ This is consistent with overuse injuries and failure of the cortical bone in compression.

Atypical femur fractures appear to have their origin in the lateral femoral cortex. The presence of a lateral cortical thickening in these fractures was earlier described by Kwek et al,⁽²⁾ and this localised periosteal reaction of the lateral cortex (Fig. 2) has been classified by the ASBMR task force report as a minor feature of atypical femur fractures.⁽¹⁾ In addition, a distinct thickening of the lateral cortex in the contralateral femur was also observed in some patients presenting with these fractures. These lesions, in the presence of a “dreaded black line” and pain, have a very high likelihood of progression to complete fractures.⁽¹¹⁾ That these lesions actually start from and progress from the lateral cortex is well illustrated on the radiograph of an incomplete stress fracture.⁽¹²⁾ The unique distribution of such fractures along the femur shaft and their association with prior bisphosphonate therapy first led to their being reported as subtrochanteric fractures involving strictly the meta-diaphyseal region by Goh et al.⁽¹³⁾ There seems to be some minor discrepancies in the distribution, as another study⁽¹⁴⁾ has classified them as femur shaft fractures.

In this study, atypical fractures and femoral stress

lesions are clustered around a median ratio of 23.9% (right femur) and 24.4% (left femur) of the entire femur from the greater trochanter. The maximal ratio from the greater trochanter was 58.6%. These ratios, in combination with their lateral distribution, corresponded to the region of highest tensile stress distribution in the femoral shaft described in Koch's classic article,⁽¹⁵⁾ as shown in Fig. 3. Going beyond the junction of the mid-shaft and lower third of the femur, where there is a change of loading conditions from tension to compression, these lesions actually do not occur. Atypical fractures and stress lesions exhibit a distribution corresponding to the tensile stress distribution along the femur, further affirming the possibility that they represent tensile failures of the cortical bone. This supports Isaacs et al's theory,⁽⁶⁾ and should be differentiated from femoral stress fractures in athletes, which are compressional failures due to excessive compressional loading.

While various biochemical abnormalities are being studied, it would be worthwhile to look into possible contributors to tensional bone failure. Among various pathogenetic mechanisms listed by the recent task force report, alterations to the normal pattern of collagen cross-linking seem a plausible mechanism for tensional failure. This can be a result of changes to the maturity of cross-links formed by enzymatic processes or the accumulation of advanced glycation end-products. The latter have been experimentally shown to occur in association with high doses of bisphosphonates in animal models.⁽⁷⁾

In conclusion, atypical femur fractures and cortical stress lesions were clustered at the region of maximal tensile loading. No lesion occurred in regions subject to compressive loading. This unique distribution supports a tensile mechanism of failure in such lesions.

REFERENCES

1. 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; 25:2267-94.
2. 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; 39:224-31.
3. Butler JE, Brown SL, McConnell BG. Subtrochanteric stress fractures in runners. *Am J Sports Med* 1982; 10:228-32.
4. Leinberry CF, McShane RB, Stewart WG Jr, Hume EL. A displaced subtrochanteric stress fracture in a young amenorrhoeic athlete. *Am J Sports Med* 1992; 20:485-7.
5. Oh I, Harris WH. Proximal strain distribution in the loaded femur. An in vitro comparison of the distributions in the intact femur and after insertion of different hip-replacement femoral components. *J Bone Joint Surg Am* 1978; 60:75-85.
6. Isaacs JD, Shidiak L, Harris IA, Szomor ZL. Femoral insufficiency fractures associated with prolonged bisphosphonate therapy. *Clin Orthop Relat Res* 2010; 468:3384-92.
7. Tang SY, Allen MR, Phipps R, Burr DB, Vashishth D. Changes in non-enzymatic glycation and its association with altered mechanical properties following 1-year treatment with risedronate or alendronate. *Osteoporos Int* 2009; 20:887-94.
8. Iwata K, Allen MR, Phipps R, Burr DB. Microcrack initiation occurs more easily in vertebrae from beagles treated with alendronate than with risedronate. *Bone* 2006; 38(Suppl):42.
9. Donnelly E, Gladnick BP, Meredith DS, Lane JM, Boskey AL. Bisphosphonate treatment reduces cortical tissue heterogeneity in postmenopausal women with fractures. *Transactions Orthopaedic Research Society 56th Annual Meeting*. New Orleans, 2010.
10. Allen MR, Iwata K, Phipps R, Burr DB. Alterations in canine vertebral bone turnover, microdamage accumulation, and biomechanical properties following 1-year treatment with clinical treatment doses of risedronate or alendronate. *Bone* 2006; 39:872-9.
11. Koh JS, Goh SK, Png MA, Kwek EBK, Howe TS. Femoral cortical stress lesions in long-term bisphosphonate therapy: a herald of impending fracture? *J Orthop Trauma* 2010; 24:75-81.
12. Kwek EB, Koh JS, Howe TS. More on atypical fractures of the femoral diaphysis. *N Engl J Med* 2008; 359:316-7.
13. Goh SK, Yang KY, Koh JS, et al. Subtrochanteric insufficiency fractures in patients on alendronate therapy: a caution. *J Bone Joint Surg Br* 2007; 89:349-53.
14. Neviaser AS, Lane JM, Lenart BA, Edobor-Osula F, Lorich DG. Low-energy femoral shaft fractures associated with alendronate use. *J Orthop Trauma* 2008; 22:346-50.
15. Koch JC. The laws of bone architecture. *Am J Anat* 1917; 21:177-298.