



Atypical Femoral Fracture in Patients on Long Term Bisphosphonate Therapy: A Proposed Pathway for Recognition and Management

Anahit Mahlangu^{1*}, Dongwoo Mokoena², Grace Wolde³

¹Department of Medical Sciences, Levantine Academy of Medical Sciences, Saudi Arabia

²Department of Medical Sciences, Hejaz Institute for Advanced Medical Sciences, Nigeria

³Department of Medical Sciences, Siberian Graduate Institute of Medical Sciences, Nigeria

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Abstract

Atypical femoral fractures are uncommon stress-type fractures of the subtrochanteric region and femoral shaft that occur with little or no trauma and are associated with long term antiresorptive treatment. They are easy to miss. Prodromal thigh or groin pain is frequently attributed to the spine or the hip, the early radiographic sign is a subtle thickening of the lateral cortex, and the opposite femur, which is often affected, may not be imaged at all. This article proposes a stepwise pathway for orthopaedic departments, assembled from the case definition and recommendations of the American Society for Bone and Mineral Research task force and from the published surgical literature. The pathway covers six steps: recognising the prodrome, obtaining full-length radiographs of both femora, applying the published case definition, stratifying the lesion as complete, incomplete with pain or incomplete without pain, choosing between intramedullary fixation and supervised conservative care, and coordinating the medical review of bone-active treatment. The pathway is a proposal. It has not been applied or validated in a patient series here, it does not offer new treatment or dosing advice, and its individual steps rest on evidence of varying strength, which the article sets out. The measures that a department could use to audit the pathway are described.

Keywords: *Atypical femoral fracture, Bisphosphonates, Osteoporosis, Subtrochanteric fracture, Intramedullary nailing, Clinical pathway*

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1. Introduction

Bisphosphonates are the most widely prescribed treatment for osteoporosis, and their capacity to reduce vertebral and hip fractures is supported by large randomised trials. From 2005 onward, clinicians began to report an unusual pattern of femoral fracture in patients who had taken these drugs for several years. [Odvina et al. \(2005\)](#) described low-energy fractures with delayed healing and biopsy evidence of severely suppressed bone turnover. Reports from Singapore drew attention to subtrochanteric insufficiency fractures with a characteristic radiographic appearance in women on alendronate ([Goh et al., 2007](#)), and

* Corresponding author: Anahit Mahlangu, Department of Medical Sciences, Levantine Academy of Medical Sciences, Saudi Arabia. E-mail: anahit.mahlangu@levantine.edu

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series from New York described a simple transverse fracture with thickened cortices in the femoral shaft (Lenart *et al.*, 2008; Neviaser *et al.*, 2008).

A task force of the American Society for Bone and Mineral Research (ASBMR) gave the entity a case definition in 2010 and revised it in the light of further evidence (Shane *et al.*, 2010; Shane *et al.*, 2014). The fractures are rare in absolute terms, and for most patients with osteoporosis the benefit of treatment outweighs the risk by a wide margin (Black *et al.*, 2020). For the orthopaedic surgeon, though, the problem is not prescribing policy. It is that the patient with an evolving atypical fracture often presents weeks or months before the bone breaks, and the opportunity to prevent a complete fracture is lost if the presentation is not recognised.

This article proposes a pathway for recognising and managing atypical femoral fracture in an orthopaedic department. It is built from published guidance and surgical series. It is a proposed procedure and has not been applied to patients or validated here; no case is reported. Its purpose is to turn scattered recommendations into a sequence that a department can adopt, adapt and audit.

2. Background

Three bodies of evidence shape the pathway: what an atypical fracture is, how strongly it is tied to treatment, and how it behaves once it has formed.

2.1. The case definition

Under the revised ASBMR definition the fracture must lie along the femoral diaphysis, from just distal to the lesser trochanter to just proximal to the supracondylar flare, and at least four of five major features must be present. These are: association with minimal or no trauma; a fracture line that originates at the lateral cortex and is substantially transverse, though it may become oblique as it crosses medially; a complete fracture extending through both cortices, possibly with a medial spike, or an incomplete fracture involving only the lateral cortex; no or minimal comminution; and localised periosteal or endosteal thickening of the lateral cortex at the fracture site, often described as beaking or flaring (Shane *et al.*, 2014). Minor features, none of them required, include generalised cortical thickening of the shafts, prodromal pain, bilateral involvement and delayed healing. Femoral neck, intertrochanteric and periprosthetic fractures and pathological fractures through tumour are excluded.

2.2. Association with antiresorptive treatment

The link with bisphosphonates is supported by consistent observational evidence, although causation in the individual patient cannot be proved. A Swedish national study with radiographic adjudication found a strong relative association between bisphosphonate use and atypical fracture with a small absolute risk (Schilcher *et al.*, 2011). A secondary analysis of the major randomised trials found too few subtrochanteric and diaphyseal fractures to confirm or exclude an effect (Black *et al.*, 2010). Data from a large health maintenance organisation in California showed that incidence rises with duration of use (Dell *et al.*, 2012), and later work indicated that risk falls quickly after the drug is stopped (Schilcher *et al.*, 2014). The proposed mechanism is that prolonged suppression of remodelling allows microdamage to accumulate at the lateral cortex, where tensile stress is highest, but this remains a hypothesis (Shane *et al.*, 2014). Atypical fractures also occur in people who have never taken an antiresorptive drug.

2.3. Natural history and the opposite femur

The lesion behaves as a stress fracture. It begins as a focal thickening of the lateral cortex, may develop a transverse radiolucent line, and can progress to a complete fracture after trivial load. Pain in the thigh or groin precedes complete fracture in a large proportion of reported patients (Kwek *et al.*, 2008). Cortical stress lesions with a visible lucent line and accompanying pain appear more likely to progress than painless thickening alone (Koh *et al.*, 2010). The opposite femur is affected in a substantial minority of patients, sometimes without symptoms, which is the reason every published recommendation calls for it to be imaged (Shane *et al.*, 2010).

3. The Proposed Pathway

The pathway has six steps. Table 1 lists each with its purpose and the published basis for it, and Figure 1 shows the branching that follows from the classification of the lesion. The steps are set out in order below. Where the supporting evidence is weak, the text says so.

Table 1: Steps of the proposed pathway, their purpose and their published basis		
Step	Purpose	Published basis
1. Recognise the prodrome	Identify thigh or groin pain in a patient on antiresorptive treatment	Kwek et al., 2008
2. Image both femora	Full-length views to find cortical thickening and contralateral lesions	Shane et al., 2010
3. Apply the case definition	Separate atypical from ordinary osteoporotic and pathological fractures	Shane et al., 2014
4. Stratify the lesion	Complete; incomplete with pain; incomplete without pain	Koh et al., 2010
5. Choose surgical or conservative care	Stabilise complete fractures; prevent progression of incomplete ones	Banffy et al., 2011 ; Egol et al., 2014
6. Coordinate medical review	Reassess antiresorptive treatment, calcium and vitamin D with the prescriber	Adler et al., 2016

3.1. Step 1: Recognise the prodrome

Any patient who has taken a bisphosphonate or another potent antiresorptive agent for several years and reports a dull or aching pain in the thigh or groin should be regarded as having a possible stress lesion of the femur until imaging shows otherwise. The pain is typically worse on weight bearing and may have been present for weeks. In practice it is commonly ascribed to lumbar spine disease, hip arthritis or trochanteric bursitis. The pathway therefore begins with a prompt in the history: duration and type of osteoporosis treatment should be asked about in every older patient with unexplained thigh pain.

3.2. Step 2: Image both femora

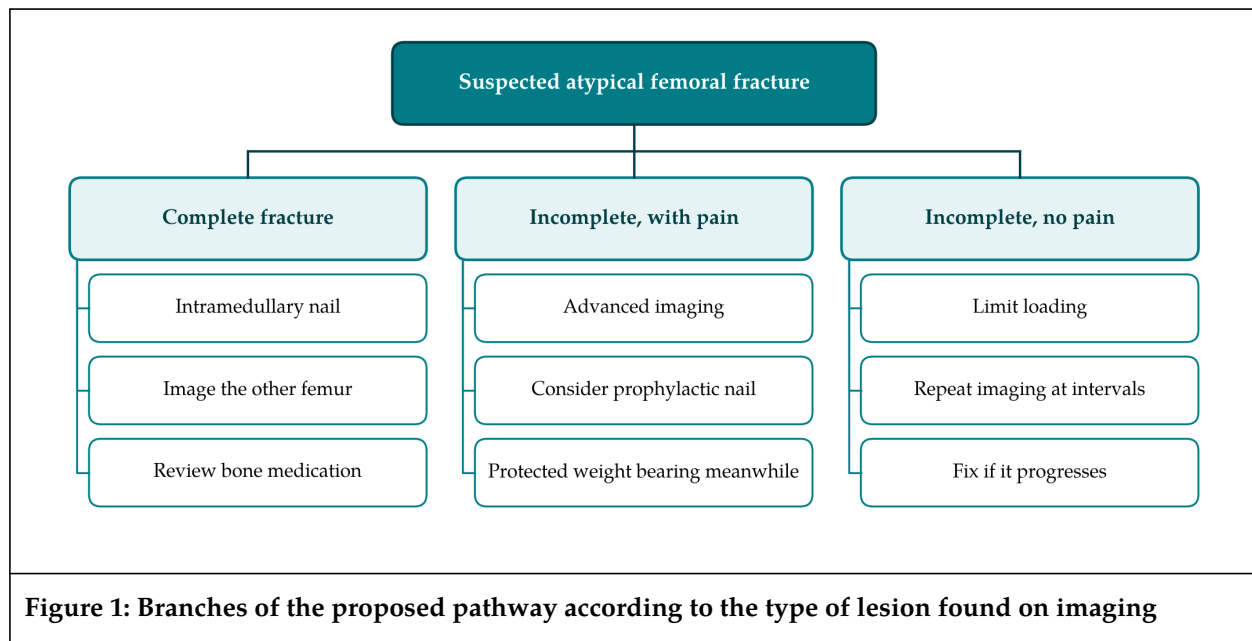
Anteroposterior and lateral radiographs should include the whole length of both femora, from hip to knee. A radiograph of the pelvis or hip alone will miss a diaphyseal lesion. The reader looks for a focal bump on the lateral cortex, with or without a transverse lucent line. If radiographs are normal or equivocal and suspicion remains, magnetic resonance imaging or a radionuclide bone scan can show a stress reaction before cortical change is visible, and the long femur images produced by some dual-energy X-ray absorptiometry scanners have been used for the same purpose ([Shane et al., 2014](#)).

3.3. Step 3: Apply the case definition

The radiographs are assessed against the major features listed above. The step matters because ordinary osteoporotic fractures of the subtrochanteric region and shaft are more common than atypical ones and are spiral or comminuted in pattern, and because metastatic disease must not be mistaken for either. Recording which features are present, in the notes and in the operative record, also makes later audit and reporting to pharmacovigilance schemes possible.

3.4. Step 4: Stratify the lesion

Lesions are placed in one of three groups. A complete fracture needs fixation. An incomplete fracture with pain, and particularly one with a visible lucent line, carries a meaningful risk of completion ([Koh et al., 2010](#)). An incomplete fracture without pain, seen as cortical thickening alone, is the least likely to progress. Both femora are stratified separately, since a patient may have a complete fracture on one side and an incomplete lesion on the other.



3.5. Step 5: Choose surgical or conservative care

For complete fractures the task force recommends intramedullary nailing, which protects the whole femur and allows healing by endochondral repair, a process less dependent on the remodelling that antiresorptive drugs suppress than the direct healing sought with rigid plate fixation (Shane *et al.*, 2010). Surgeons should expect technical difficulty from the bowed, brittle femur and a narrow canal, and should counsel patients that union is usually achieved but is slower than after an ordinary femoral shaft fracture (Egol *et al.*, 2014).

For incomplete fractures with pain, the task force advises that prophylactic nailing be considered; where the pain is minimal, a trial of conservative treatment with limited weight bearing is reasonable, with fixation if symptoms and imaging have not improved after two to three months (Shane *et al.*, 2010). A comparative series supports this caution, since most incomplete fractures managed without surgery in that report progressed to complete fracture, and hospital stay was shorter after prophylactic fixation than after fixation of a completed fracture (Banffy *et al.*, 2011). For incomplete fractures without pain, the pathway follows the task force in advising reduced loading and repeat imaging until the lesion has resolved. The choice in each case belongs to the surgeon and the patient, and the evidence behind it consists of case series, not trials.

3.6. Step 6: Coordinate medical review

An orthopaedic pathway should not end at the wound. The task force recommends that potent antiresorptive treatment be stopped once an atypical fracture is diagnosed, that calcium and vitamin D status be assessed and corrected, and that the further management of osteoporosis be reviewed (Shane *et al.*, 2014). These decisions lie with the physician responsible for the patient's bone health, and the pathway's requirement is only that the referral is made and documented before discharge. The use of teriparatide to promote healing has been described in case reports and small series; the task force regarded the evidence as limited and inconclusive, and this article makes no recommendation on it. General guidance on reviewing the need for continued bisphosphonate treatment after several years, including the concept of a drug holiday for patients at lower risk, is given by a separate ASBMR task force (Adler *et al.*, 2016) and draws on the extension of the alendronate trials (Black *et al.*, 2006).

4. Fitting the Pathway to a Department

The pathway asks for little that a department does not already have. Its first two steps depend on the people who see the patient first: emergency clinicians, general practitioners and fracture clinic staff. A

short prompt on the request form for hip and femur radiographs, asking about antiresorptive treatment, and a standing arrangement with radiology that full-length views of both femora follow any report of focal lateral cortical thickening, would address the two commonest points of failure. Steps three to five can be captured on a single proforma that records the features of the case definition, the stratification of each femur and the agreed plan. Step six is most reliably delivered where a fracture liaison service or an orthogeriatric team already reviews patients with fragility fractures.

5. Limitations and What Remains to Be Shown

The pathway is proposed and untested. It combines recommendations that are themselves based largely on observational studies, case series and expert consensus, and following it cannot be assumed to improve outcomes until that has been measured. A department adopting it could audit several things: the proportion of patients with an atypical fracture who had imaging of the opposite femur; the interval between first presentation with prodromal pain and diagnosis; the proportion of incomplete lesions that progressed to complete fracture under conservative care; time to union after fixation; and whether medical review took place. Comparison with the period before adoption would give a first indication of its value.

Several matters remain uncertain in the literature and are not resolved by a pathway. The threshold at which a painless incomplete lesion warrants fixation is not defined. The benefit of anabolic treatment for healing is unproven. The best management of osteoporosis after an atypical fracture, in a patient who remains at high risk of ordinary fragility fractures, is a matter of specialist judgement. Rarity makes randomised trials difficult, so registries with radiographic adjudication are likely to remain the main source of better evidence ([Schilcher et al., 2011](#)).

6. Conclusion

Atypical femoral fracture is rare, but it announces itself in advance more often than most fractures do, and both the warning and the lesion in the opposite femur are frequently overlooked. The six-step pathway proposed here arranges existing guidance into a sequence that begins with a question about treatment history and ends with a documented medical review. It is offered as a framework for local adaptation and audit. Whether it shortens the time to diagnosis or reduces the number of incomplete lesions that go on to break is a question for departments that choose to adopt and evaluate it.

Conflict of interest

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