Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Atypical subtrochanteric and diaphyseal femoral fractures: second report of a Task Force of the American Society for Bone and Mineral Research.

Bibliographic Source(s)

Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM, Cosman F, Curtis JR, Dell R, Dempster DW, Ebeling PR, Einhorn TA, Genant HK, Geusens P, Klaushofer K, Lane JM, McKiernan F, McKinney R, Ng A, Nieves J, O'Keefe R, Papapoulos S, Howe TS, van der Meulen MC, Weinstein RS, Whyte MP. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a Task Force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2014 Jan;29(1):1-23. [107 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Shane E, Burr D, Ebeling PR, Abrahamsen B, Adler RA, Brown TD, Cheung AM, Cosman F, Curtis JR, Dell R, Dempster D, Einhorn TA, Genant HK, Geusens P, Klaushofer K, Koval K, Lane JM, McKiernan F, McKinney R, Ng A, Nieves J, O'Keefe R, Papapoulos S, Sen HT, van der Meulen MC, Weinstein RS, Whyte M, American Society for Bone and Mineral Research. 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 Nov;25(11):2267-94. [177 references]

Recommendations

Major Recommendations

Note from the American Society for Bone and Mineral Research (ASBMR) and the National Guideline Clearinghouse (NGC): This document should be considered an update and companion to the first report, because much of the information in the first report has not been included here but is still valid and useful. Please refer to the 2010 original task force report for additional information (see the "Availability of Companion Documents" field).

ASBMR Task Force 2013 Revised Case Definition of Atypical Femur Fractures (AFFs)

To satisfy the case definition of AFF, the fracture must be located along the femoral diaphysis from just distal to the lesser trochanter to just proximal to the supracondylar flare.

In addition, at least 4 of 5 Major Features must be present. None of the Minor Features are required but have sometimes been associated with these fractures.

Major features[a]

- The fracture is associated with minimal or no trauma, as in a fall from a standing height or less
- The fracture line originates at the lateral cortex and is substantially transverse in its orientation, although it may become oblique as it progresses medially across the femur
- Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex
- The fracture is noncomminuted or minimally comminuted
- Localized periosteal or endosteal thickening of the lateral cortex is present at the fracture site ("beaking" or "flaring")

Minor features

- Generalized increase in cortical thickness of the femoral diaphyses
- Unilateral or bilateral prodromal symptoms such as dull or aching pain in the groin or thigh
- Bilateral incomplete or complete femoral diaphysis fractures
- Delayed fracture healing

Changes from the 2010 original task force report are bold.

[a]Excludes fractures of the femoral neck, intertrochanteric fractures with spiral subtrochanteric extension, periprosthetic fractures, and pathological fractures associated with primary or metastatic bone tumors and miscellaneous bone diseases (e.g., Paget's disease, fibrous dysplasia).

Update on Medical Management

The natural history of AFFs suggests that they evolve over time, with initial development of a cortical "bump" that likely represents early periosteal thickening, and the eventual appearance of a transverse cortical lucency (fracture) in the region of periosteal thickening, which may or may not progress to a complete fracture. Until more evidence becomes available regarding the clinical significance of such areas of cortical thickening, the opinion of the task force is that such lesions, whether they are detected on dual-energy X-ray absorptiometry (DXA) scans or plain radiographs, should be further evaluated with higher-order imaging to determine whether a cortical lucency is associated with the periosteal thickening. Options for imaging include magnetic resonance imaging (MRI), which could detect a cortical fracture line and associated bone and marrow edema or hyperemia, indicative of a stress fracture. If MRI cannot be performed, computed tomography (CT) could detect the cortical fracture or lucency and associated new-bone formation. Radionuclide bone scan could detect focal bone and marrow hyperemia but with less specificity than MRI or CT. If higher-order imaging detects a cortical lucency, such a lesion could be considered an incomplete AFF. If no cortical lucency is present but marrow edema is present, then such lesions could be considered a stress reaction.

Suggested management of an incomplete AFF is summarized in the 2010 original task force report. For patients with a stress reaction, stress fracture, or incomplete or complete subtrochanteric or femoral shaft fracture, potent antiresorptive agents should be discontinued. Dietary calcium and vitamin D status should be assessed, and adequate supplementation prescribed. Prophylactic reconstruction nail fixation is recommended for incomplete fractures (with cortical lucency) accompanied by pain. If the patient has minimal pain, a trial of conservative therapy, in which weight-bearing is limited through the use of crutches or a walker, may be considered. However, if there is no symptomatic and radiographic improvement after 2 to 3 months of conservative therapy, prophylactic nail fixation should be strongly considered, because these patients may progress to a complete fracture. For patients with incomplete fractures and no pain, or those with periosteal thickening but no cortical lucency, limited weight-bearing may be continued and vigorous activity avoided. Reduced activity should be continued until there is no bone edema detected on MRI or no increased activity detected on bone scan.

Since the first task force report, there have been numerous anecdotal reports of medical therapy. Most reports extend early descriptions of using teriparatide (TPTD) in patients with AFFs. One study on the treatment of a 63-year-old woman with thigh pain and bilateral AFFs who had taken bisphosphonates (BPs) for 13 years. After 6 months of daily TPTD, her pain diminished, MRI revealed less edema around the fracture, and after 16 months, there was complete healing and relief of pain. Similarly, another research group described a 77-year-old woman whose AFF closed after only 1 month of TPTD. Interestingly, this latter group treated 2 other patients (women 63 and 77 years old) with strontium ranelate, with fracture closure after 2 and 3 months, respectively, of treatment. More recently, a third group described a 63-year-old woman treated with BPs for only 3 years who presented with thigh pain and a stress fracture. After 10 months of TPTD followed by 5 months of raloxifene, the fracture healed completely.

Another report provides information on a somewhat different case. A 70-year-old man with prostate cancer was treated with androgen deprivation therapy and 4 mg intravenous zoledronic acid monthly for 2 years. He complained of thigh pain and was found to have a transverse femoral shaft fracture. An orthopedic nailing procedure produced a further fracture. After 2 months of TPTD therapy, there was full healing.

Thus, discontinuation of BP therapy and TPTD treatment (and strontium ranelate in 2 cases) has been associated with fracture healing. Nonetheless, in a randomized, placebo-controlled study of women with distal radius fractures, the efficacy of TPTD was questioned because although 20 μg daily appeared to hasten fracture healing, 40 μg daily dosing did not. Moreover, the unpublished clinical experience of bone experts

is that only some patients appear to respond to TPTD. Variable response to TPTD was reflected in several reports of medical treatment of AFFs presented at the ASBMR Annual Meeting in 2012. One report described a 57-year-old Argentine woman who had been treated with alendronate for 7 years and sustained a non-healing FS fracture. Her pain improved after 10 days of TPTD and healing was complete after 3 months. However, another study reported that only 1 of 3 German patients with AFF responded to 2 years of TPTD. Similarly, another research group reported 13 Canadian women with BP-associated AFFs treated with TPTD. Three required surgery, 5 improved with TPTD, and the others did not improve or even worsened. In another study, bone biopsies were performed before and after TPTD treatment in 15 women with surgicallyâ€treated AFFs. TPTD increased mineral apposition rate and bone formation rate, as expected. All patients appeared to improve clinically.

Finally, a study of 14 consecutive patients with AFFs was reported from Australia. Nine patients chose surgical or nonoperative management, and 5 opted for TPTD. High-resolution peripheral CT of the radius and tibia were performed before and 6 months after starting TPTD. Only 1 of the non-TPTD group had fracture healing (after 1 year). In the TPTD group, union occurred in 2 patients with the fracture line no longer visible. Two patients became pain-free and the remaining 3 patients had improvement in pain scores. Images, assessed by a novel software analysis, revealed less densely mineralized bone with TPTD treatment. In addition, bone turnover markers increased in the TPTD group.

In the absence of a randomized, placeboâ€controlled trial, no definite conclusion can be reached regarding the efficacy of TPTD treatment of patients with AFF. From the lowâ€quality evidence available, the recommendations of the ASBMR task force for medical management remain reasonable: discontinuation of BPs, adequate calcium and vitamin D, and consideration of TPTD for those who appear not to heal on conservative therapy.

Summary and Conclusions

AFFs are characterized by unique radiographic (transverse fracture line, periosteal callus formation at the fracture site, little or no comminution) and clinical features (prodromal pain, bilaterality) that resemble stress fractures or reactions. Based upon new information, the task force revised the original case definition to highlight the unusual radiographic features that distinguish AFFs from ordinary osteoporotic femoral diaphyseal fractures and to provide more precise guidance on what is meant by transverse orientation. In addition, the requirement that fractures be noncomminuted was relaxed to include those with minimal comminution, the periosteal and/or endosteal stress reaction at the fracture site was moved from the minor to the major features, and the association with specific diseases and drug exposures was removed from the minor criteria, in the spirit that these associations should be sought rather than part of the case definition.

The epidemiological evidence for a relationship between BP use and atypical subtrochanteric and femoral shaft fractures has become more compelling. AFFs appear to be more common in patients who have been exposed to long-term BPs, usually for more than 3 years (median treatment 7 years), but every series includes patients who have not been treated with BPs, suggesting that the "background rate" of AFF in osteoporosis patients is not zero. Moreover, the risk for AFFs may decline after BPs are stopped. The majority of studies have found a significant association with glucocorticoid use or duration. Although the relative risks of AFFs are very high in patients on BPs, ranging from 2.1 to 128, their absolute risk is extremely low, ranging from 3.2 to 50 cases per 100,000 personâ€years. Thus, these fractures are rare, particularly when considered against the incidence of common osteoporotic fractures of all types and of ordinary femoral neck and intertrochanteric fractures, all of which have been proven to decrease with BP therapy. However, longâ€term use may be associated with higher risk (>100 per 100,000 person-years). In conclusion, AFFs remain of concern and more information is urgently needed, both to assist in identifying patients at particular risk and to guide decision-making about duration of BP therapy.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Atypical subtrochanteric and diaphyseal femoral fractures

Note: The diagnosis of atypical femur fracture (AFF) specifically excludes high-trauma fractures, fractures of the femoral neck, intertrochanteric fractures with spiral subtrochanteric extension, pathological fractures associated with primary or metastatic bone tumors, and periprosthetic fractures.

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Orthopedic Surgery

Radiology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To review the major reports that had been published since the original report in 2010, focusing on those that addressed three major aspects of atypical femur fractures (AFF): their epidemiology, pathogenesis, and medical management
- To assess whether the information in those reports provided data that could be used to refine the original case definition of AFF

Target Population

Patients with known or suspected atypical subtrochanteric and diaphyseal femoral fractures

Interventions and Practices Considered

Diagnosis/Evaluation

1. Evaluation of fractures features (major and minor features associated with atypical femoral fracture [AFF])
2. Dual-energy X-ray absorptiometry (DXA) scans or plain radiographs
3. Magnetic resonance imaging (MRI)
4. Computed tomography (CT)

Treatment/Management

1. Discontinuation of potent antiresorptive agents (bisphosphonates [BPs])
2. Dietary calcium and vitamin D assessment and supplementation
3. Prophylactic reconstruction nail fixation for incomplete fractures accompanied by pain
4. Limited weight-bearing (crutches or a walker)
5. Teriparatide (TPTD)

Major Outcomes Considered

- Incidence rates for atypical femur fractures (AFFs)
- Age-adjusted subtrochanteric and femoral shaft (ST/FS) fracture rates
- Risk of AFF or ST/FS fracture with bisphosphonate (BP) use
- Age-adjusted hospitalization rates
- Rates of rehospitalization
- Incidence of comorbid conditions (e.g., vitamin D deficiency, rheumatoid arthritis, hypophosphatasia)
- Localized periosteal reaction of the lateral cortex
- Generalized increase in cortical thickness of the diaphysis
- Prodromal symptoms such as dull or aching pain in the groin or thigh
- Bilateral fractures and symptoms
- Fracture healing
- Use of pharmaceutical agents (e.g., BPs, glucocorticoids, proton pump inhibitors)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The task force co-chairs searched the medical literature for publications on atypical femur fractures that addressed epidemiology, pathogenesis, and medical management. Databases searched include: MEDLINE and EMBASE. The final document included reports published January 1, 1990 to March 10, 2013. In addition, they reviewed abstracts from the 2011 and 2012 Annual Meetings of the American Society for Bone and Mineral Research (ASBMR).

Included were prospective or retrospective cohort studies, case-control studies, case series, studies that relied on International Classification of Diseases (ICD) codes, and those with radiographic review of fractures to identify atypical features. Only studies published in English were considered.

Case reports were not included in the analysis, except for those related to medical management. Other exclusion criteria were periprosthetic and high trauma fractures and fractures associated with local malignancy, animal studies, review articles, and editorials.

Search terms used: Diphosphonate (this term includes alendronate, clodronate, etidronate) OR Bisphosphonates OR ibandronate OR pamidronate OR zoledronic acid OR Denosumab AND [femoral fractures OR femur fracture OR hip fractures OR diaphyseal AND femoral fracture OR atypical AND femoral fractures] AND [subtrochanteric OR diaphyseal OR midshaft OR atypical].

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Epidemiologic data were extracted from each report and summarized in tabular form.

Studies of subtrochanteric and femoral shaft fracture incidence and their relationship to BP therapy fall into two general categories. In the first, subtrochanteric and femoral shaft (ST/FS) fractures are identified using large registry or database approaches with International Classification of Diseases, 9th edition (ICDâ€9) codes but there is no radiographic adjudication to ascertain whether the fractures have atypical features. In the second category of studies, radiographs are reviewed and the fractures categorized according to whether or not they meet consensus criteria for atypical femur fractures (AFFs).

Studies of AFFs with radiograph adjudication are described in order of publication in Table 2 of the original guideline document, which includes the criteria used to designate atypia.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Since publication of the first task force report in 2010, several studies have been published on the epidemiology of and risk factors for atypical femoral fractures (AFFs) and their relationship to bisphosphonate (BP) therapy. Certain studies have raised concerns about limitations of the American Society for Bone and Mineral Research (ASBMR) case definition and new data have emerged on the medical management of these fractures. Therefore, the ASBMR reconvened the task force at the 2012 Annual Meeting of the ASBMR.

A subcommittee of the task force held several conference calls on the case definition. Dr. Shane (epidemiology), Dr. Burr (pathogenesis), and Dr. Adler (medical management) wrote the first draft of the document, which was reviewed in detail by the task force members, and their revisions and concerns were addressed. The revised case definition was approved by formal vote, with 25 of 26 members voting to approve. The final report was also approved unanimously by formal vote.

Among the issues addressed by the task force was the case definition, which has been revised to more clearly delineate the features that distinguish atypical femur fractures (AFFs) from ordinary osteoporotic femur fractures. New epidemiologic studies, many of which incorporate radiographic review and provide new information on AFF incidence and association with bisphosphonates (BPs), and new data on the pathogenesis and management of AFFs were reviewed and summarized in the original guideline document. This document should be considered an update and companion to the first report, because much of the information in the first report has not been included here but is still valid and useful.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Timely identification and adequate treatment of atypical subtrochanteric and diaphyseal femoral fractures

Potential Harms

Not stated

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM, Cosman F, Curtis JR, Dell R, Dempster DW, Ebeling PR, Einhorn TA, Genant HK, Geusens P, Klaushofer K, Lane JM, McKiernan F, McKinney R, Ng A, Nieves J, O'Keefe R, Papapoulos S, Howe TS, van der Meulen MC, Weinstein RS, Whyte MP. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a Task Force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2014 Jan;29(1):1-23. [107 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2010 Nov (revised 2014 Jan)

Guideline Developer(s)

American Society for Bone and Mineral Research - Professional Association

Source(s) of Funding

Most of the American Society for Bone and Mineral Research (ASBMR) revenue comes from membership dues, fees paid to attend the Society's annual meeting, and subscriptions to ASBMR publications. Like many scientific, professional, and medical organizations, ASBMR also accepts grants from pharmaceutical companies, the federal government, and other entities to support its mission. ASBMR receives corporate support in the form of unrestricted educational grants from pharmaceutical companies, rental of exhibit space at its annual meeting, and paid advertisements in its journal.

Guideline Committee

American Society for Bone and Mineral Research (ASBMR) Atypical Femoral Fractures Task Force

Composition of Group That Authored the Guideline

Task Force Members: Elizabeth Shane (*Co-chair*); David Burr (*Co-chair*); Bo Abrahamsen; Robert A Adler; Thomas D Brown; Angela M Cheung; Felicia Cosman; Jeffrey R Curtis; Richard Dell; David W Dempster; Peter R Ebeling; Thomas A Einhorn; Harry K Genant; Piet Geusens; Klaus Klaushofer; Joseph M Lane; Fergus McKiernan; Ross McKinney; Alvin Ng; Jeri Nieves; Regis O'Keefe; Socrates Papapoulos; Tet Sen Howe; Marjolein CH van der Meulen; Robert S Weinstein; Michael P Whyte

Financial Disclosures/Conflicts of Interest

Disclosures

The American Society for Bone and Mineral Research (ASBMR) is well served by the fact that many of those responsible for policy development

and implementation have diverse interests and are involved in a variety of activities outside of the Society. Accordingly, the ASBMR requires all ASBMR Officers, Councilors, Committee Chairs, Editors-in-Chief, Associate Editors, and certain other appointed representatives to disclose any real or apparent conflicts of interest (including investments or positions in companies involved in the bone and mineral metabolism field), as well as any duality of interests (including affiliations, organizational interests, and/or positions held in entities relevant to the bone and mineral metabolism field and/or the ASBMR).

The committees, task forces, and editorial boards of the ASBMR and its publications carry out the work of the Society on behalf of the membership. The distinct functions of the committees, task forces, and editorial boards are intended to address the broad mission of the ASBMR: to promote excellence in research and education, to integrate basic and clinical science in the field of bone and mineral metabolism, and to facilitate the translation of research into clinical practice and the betterment of human health. Chairs and members of committees, task forces, and editorial boards must assure that they act in these roles in a manner free from commercial bias and that they resolve any conflict or duality of interest or disclose them and then recuse themselves from related deliberations and voting. A table providing a summary of disclosures from each task force member is available in the original guideline document.

ASBMR Disclosures

To ensure that the Society adheres to the highest ethical practices, ASBMR has an ethics committee, consults with experts in health care ethics, and periodically reviews its practices with regard to managing potential conflict of interest.

Although task force members were required to disclose their potential conflicts of interest and their disclosures are published with this document, ASBMR recognizes that this might not go far enough to demonstrate to some that the final output of the task force is free of all bias. In an effort to address this concern, an ethicist knowledgeable about the musculoskeletal system who does not work directly on bone or bisphosphonates (BPs) or with pharmaceutical companies who make or market BPs is a member of the task force and provided ethical oversight to the work of the task force. The ethicist has verified and attested to witness no commercial bias.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Shane E, Burr D, Ebeling PR, Abrahamsen B, Adler RA, Brown TD, Cheung AM, Cosman F, Curtis JR, Dell R, Dempster D, Einhorn TA, Genant HK, Geusens P, Klaushofer K, Koval K, Lane JM, McKiernan F, McKinney R, Ng A, Nieves J, O'Keefe R, Papapoulos S, Sen HT, van der Meulen MC, Weinstein RS, Whyte M, American Society for Bone and Mineral Research. 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 Nov;25(11):2267-94. [177 references]

Guideline Availability

Electronic copies: Available from the Journal of Bone and Mineral Research Web site .

Availability of Companion Documents

The following is available:

- Shane E, Burr D, Ebeling PR, Abrahamsen B, Adler RA, Brown TD, Cheung AM, Cosman F, Curtis JR, Dell R, Dempster D, Einhorn TA, Genant HK, Geusens P, Klaushofer K, Koval K, Lane JM, McKiernan F, McKinney R, Ng A, Nieves J, O'Keefe R, Papapoulos S, Sen HT, van der Meulen MC, Weinstein RS, Whyte M, American Society for Bone and Mineral Research. 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 Nov;25(11):2267-94. Electronic copies: Available from the Journal of Bone and Mineral Research Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on November 6, 2012. The information was verified by the guideline developer on December 5, 2012. This summary was updated by ECRI Institute on September 23, 2014.

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.