Atypical Femur Fractures

Bennet Butler

Assistant Professor of Orthopedic Surgery

Northwestern Memorial Hospital

John H Stroger Hospital of Cook County

Atypical Femur Fracture (AFF) Overview

- **Low energy femoral shaft fractures with a characteristic appearance**
- **Caused by a combination of unfavorable femoral anatomy (varus, anterior bow) and impaired bone healing/remodeling**
- **Frequently (but not always) associated with bisphosphonate use**
- **Successful treatment requires a combination of medical and surgical management**
- **Relatively high rates of delayed/nonunion compared to standard femoral shaft fractures**
- **Disease process often manifests bilaterally… patients must be checked and monitored for developing AFF of the contralateral femur**

Presentation Overview

- **AFF Definition/Characteristics**
- **Pathogenesis**
- **Association with Bisphosphonates**
- **Diagnosis**
- **Treatment**
- **Surgical Considerations**
- **Prognosis**

ASBMR Definition of AFFs (1)

- **Femoral diaphyseal fracture w/ at least 4 of the following major criteria:**

1. **Minimal or no trauma**
2. **Fracture originates at lateral cortex and is substantially transverse in orientation**
3. **Complete fractures may be associated with a medial spike, incomplete fractures are lateral cortex only**
4. **Fracture is noncomminuted or minimally comminuted**
5. **Localized periosteal or endosteal thickening is present at the lateral cortex**

ASBMR Definition of AFFs

- **Minor criteria may or may not be present**

1. **Generalized increase in cortical thickness of femur**
2. **Prodromal symptoms (thigh or groin pain)**
3. **Bilateral incomplete or complete fractures**
4. **Delayed fracture healing**

Practical Definition

- **Low energy subtrochanteric or femoral shaft fracture frequently associated with bisphosphonate use with a characteristic set of features.**

  - **Lateral origin of fracture line**
  - **Localized cortical thickening or beaking at origin of fracture line**
  - **Transverse or short oblique fracture (possibly with a medial spike)**
  - **Minimal or no comminution**

AFF Radiological Features

- Subtrochanteric or femoral shaft fracture
- Localized lateral cortical thickening/beaking
- Fracture line propagates from lateral cortex
- Substantially transverse or short oblique
- Minimal or no comminution
- Possibly associated with a medial spike

Pathogenesis of AFFs

- **Insufficiency fracture caused by a combination of…**

1. **Unfavorable mechanical environment**

2. **Impaired bone remodeling**

****note-**

insufficiency fracture = normal forces, abnormal bone

stress fracture = abnormal forces, normal bone

Pathogenesis of AFFs

- **Insufficiency fracture caused by a combination of…**

1. **Unfavorable mechanical environment**

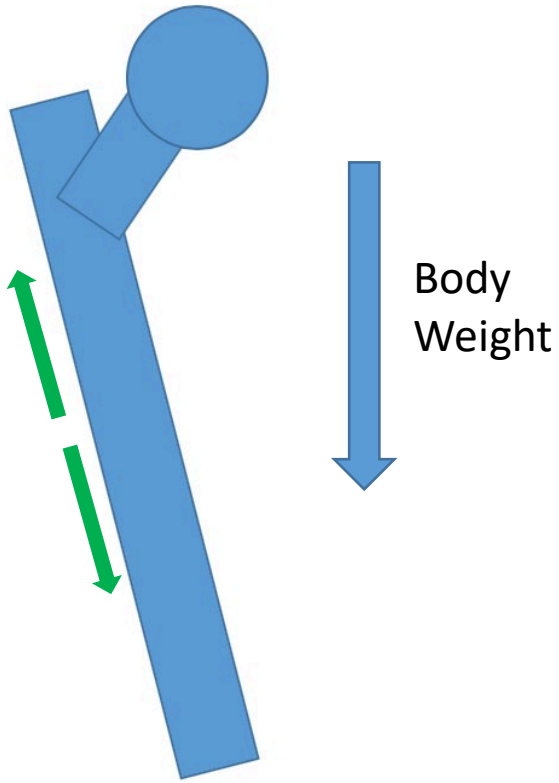
   -lateral femoral cortex experiences significant tensile stresses during normal weightbearing

   -in patients with relative femoral neck varus or anterolateral bowing these forces are increased

2. **Impaired bone remodeling**

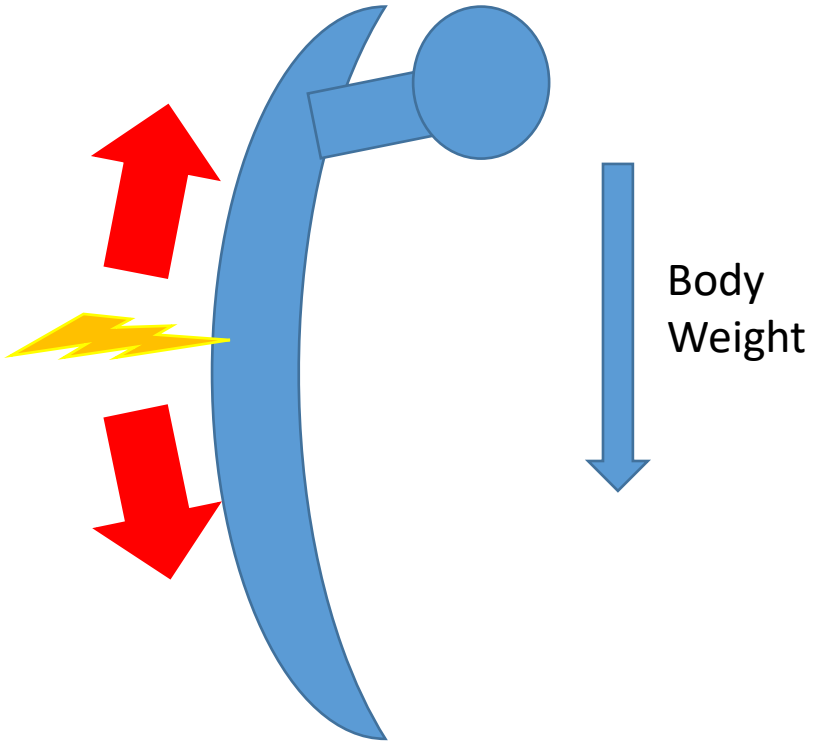
Pathogenesis of AFFs (Mechanical)

Normal Femur



Modest Tensile Forces
Along Lateral Cortex

Bowed/Varus Femur



Excessive Tensile Forces
Along Lateral Cortex

Pathogenesis of AFFs (2-5)

- **Evidence for mechanical contribution to AFF pathogenesis**
  - **Saita et al- location of AFF highly correlated with femorotibial angle (more varus = more distal fracture)**
  - **Sasaki et al- increased risk of AFF w/ increasing coronal plane femoral bowing**
  - **Hagen et al- increased risk of AFFs w/ increasing femoral neck varus**
  - **Oh et al- femoral neck varus associated with subtroch AFFs, femoral bowing associated with femoral shaft AFFs**

Pathogenesis of AFFs

- **Insufficiency fracture caused by a combination of…**

1. Unfavorable mechanical environment

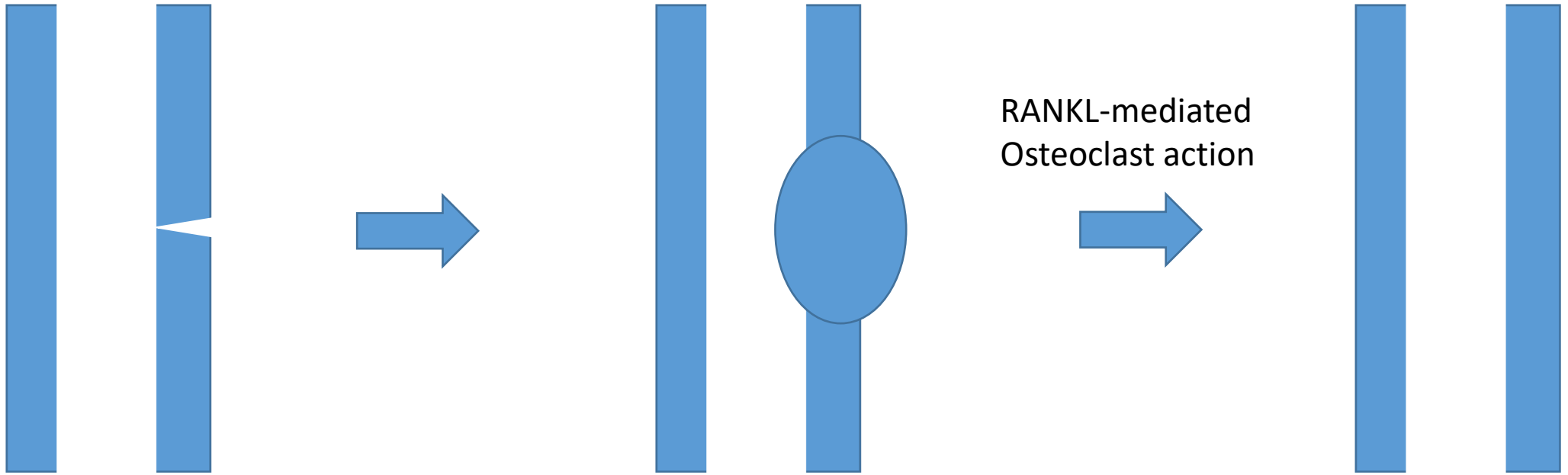
2. **Impaired bone remodeling**

   -under normal circumstances, stress formed microfractures are healed by callous formation followed by localized remodeling

   -patients with impaired bone remodeling are at risk for propagation of unhealed/partially healed microfractures in high stress regions

Pathogenesis of AFFs (Biological)

- **Normal Microfracture Repair**

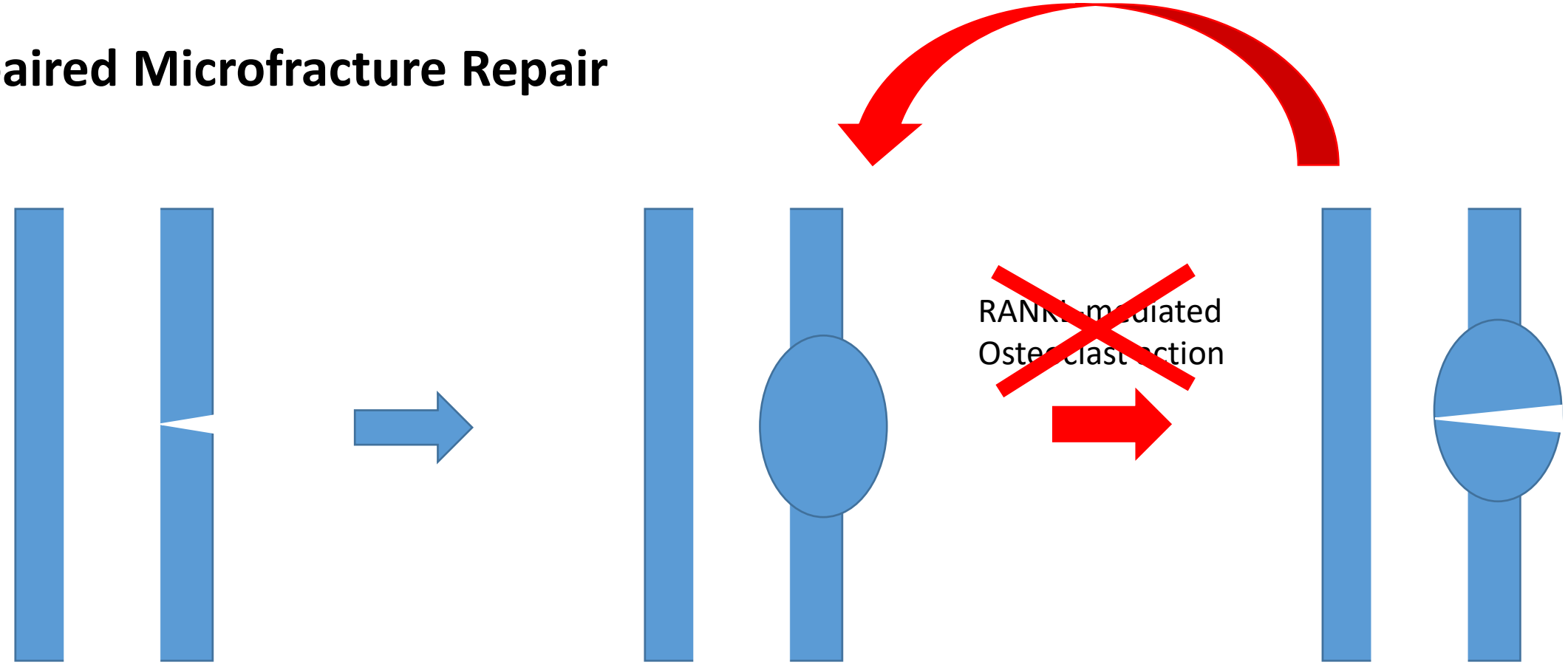


Callous formation for initial stabilization

Remodeling for final healing

Pathogenesis of AFFs

- **Impaired Microfracture Repair**



Callous formation for initial stabilization

Failure of remodeling, microfx reforms/propagates

Pathogenesis of AFFs (2-5)

- **Evidence of biological contribution to AFFs**
  - **many studies linking bisphosphonate use to AFFs (future slides)**
  - **case reports of AFFs associated with denosumab use (RANKL inhibitor) [6,7]**
  - **case reports of AFFs associated with various metabolic bone diseases (hypophosphatasia, x linked hypophosphatemic rickets) [8]**

Pathogenesis of AFFs (2-5)

- **Other risk factors for AFFs**
  - **Older age (9)**
  - **Female (9)**
  - **Asian or Hispanic race (9)**
    - **possibly related to increased anterolateral femoral bowing in these patient populations**
  - **Specific genetic mutations (GGPS1 mutations) (10)**

Bisphosphonates and AFFs

- **Bisphosphonates (BPs) are potent osteoclast (bone resorption, remodeling) inhibitors**

- **Common examples- alendronate, pamidronate, etidronate, ibandronate, zoledronate, risedronate**

- **Indications**
  - **First line treatment for osteoporosis**
    - **Decrease rate of wrist, hip and vertebral fractures in high risk populations by 30-60% [11]**
  - **Decrease bone pain/fracture risk in patients with lytic bone lesions (multiple myeloma, metastatic disease)**

Bisphosphonates and AFFs

- **Bisphosphonate use is a major risk factor for AFFs**
  - **AFFs first noted in medical literature in ~2007 in association with alendronate use (12)**
  - **Subsequent studies have demonstrated a population-wide increase in femoral shaft/subtroch fxs coinciding with onset of BP use (13)**

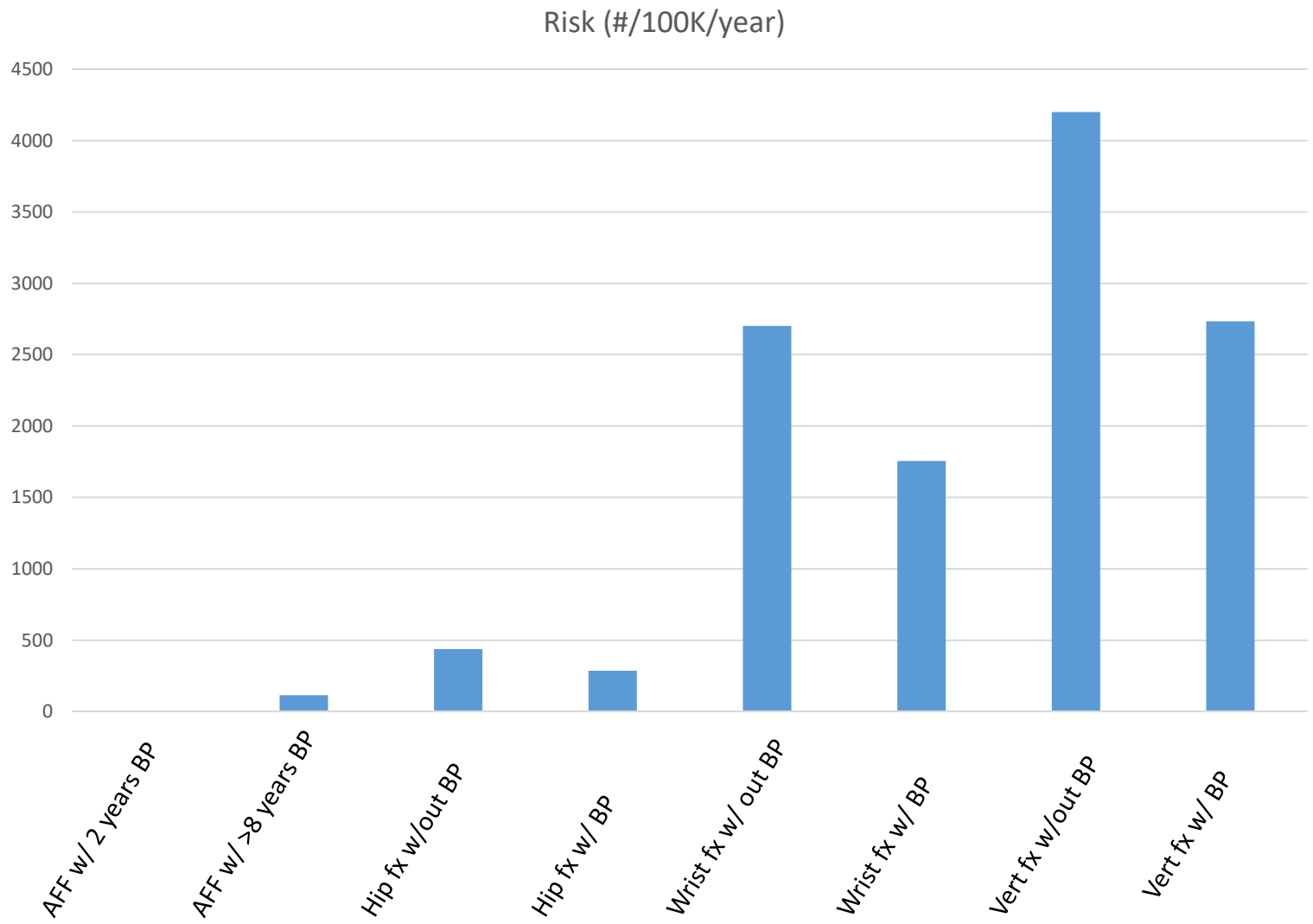
Bisphosphonates and AFFs

- **Relative risk of AFF with BP use: 2-128 (1)**
- **Absolute risk of AFF with BP use: 3.2-113/100K/year (1, 14)**
- **Risk increases with duration of use: 1.8/100K/year w/ 2 year use, 113/100K/year w/ >8 year use (14)**
- **Risk rapidly drops off after discontinuation of BPs: 70% decrease in risk 1 year after discontinuation (15)**
- ***In spite of a significant increase in relative risk of AFFs with BP use, absolute risk of sustaining an AFF remains low**

Balancing the Risks/Benefits of BPs (16)

- **Ultimately BPs prevent far more fractures than they create**

- **Concern about AFFs should not prevent their routine use when indicated**



Balancing the Risks/Benefits of BPs

- **Possibly a role for bisphosphonate holiday in patients at lower risk for fragility fractures**
  - **FLEX study- continuing alendronate after 5 years of use decreases bone loss, vert compression fractures, NOT other fractures (17)**
  - **HORIZON study- continuing zoledronic acid after 3 years of use decreases bone loss, vert compression fractures, NOT other fractures (18)**
- **Adler et al (16)- recommends discontinuation of BPs after 3-5 years if…**
  - **No fragility fractures before or during BP use**
  - **DEXA T score >-2.5**
  - **Low fracture risk (FRAX) score**

Diagnosis

- **History and Physical**
  - **Low or no energy trauma**
  - **Prodromal thigh/groin pain (33-50%, mean onset 6 mos prior to fx) [19-21]**
  - **Specific risk factors**
    - **Bisphosphonate use (especially long term use)**
    - **Denosumab use**
    - **Asian or Hispanic race**
    - **Female**
    - **Older age**

Diagnosis

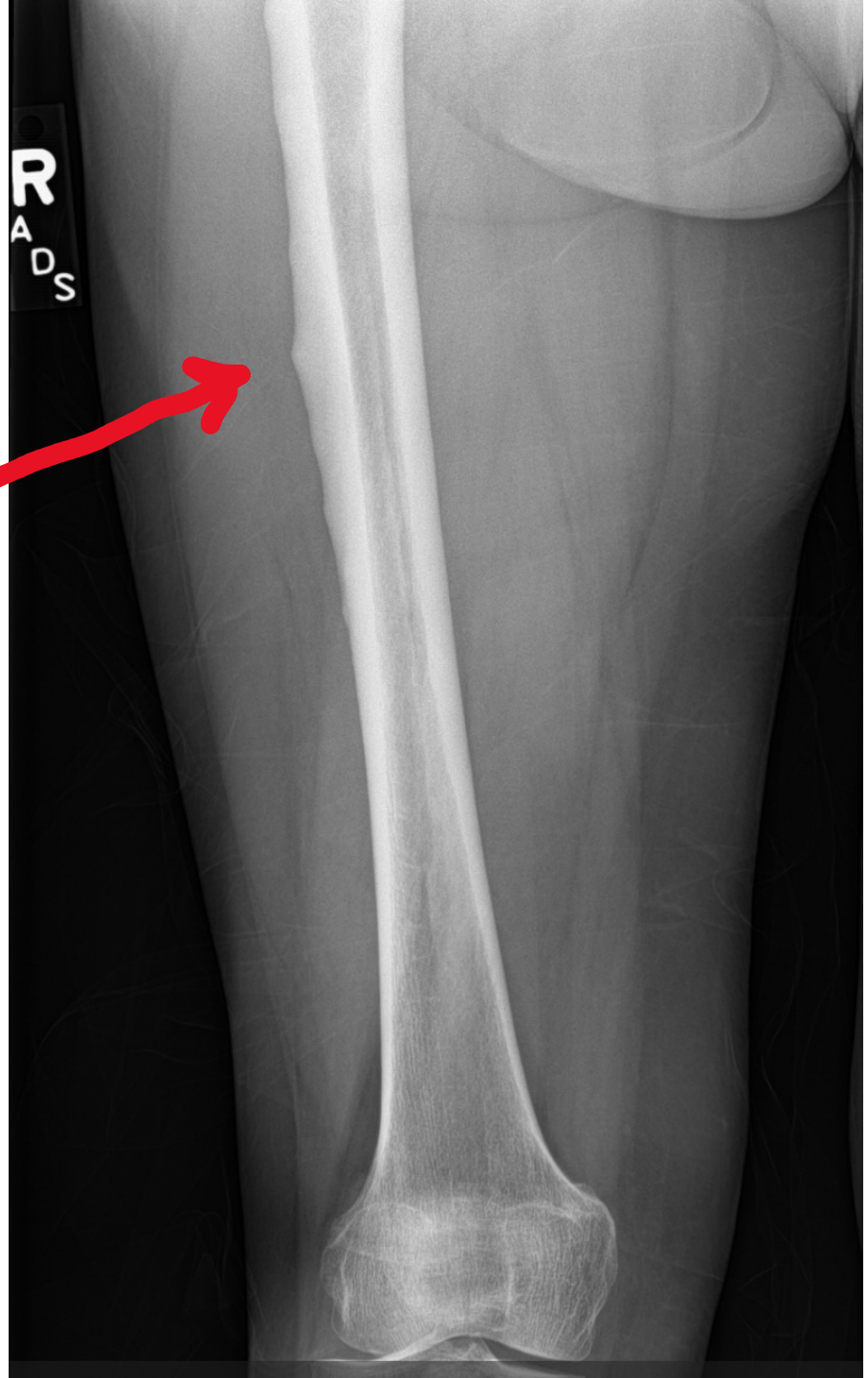
- **Diagnostic Imaging**
  - **Standard AP and lateral radiographs of femur**
    - **Generally sufficient to diagnose complete or incomplete AFFs**
    - **Characteristic features defined by ASBMR guidelines (1)**
  - **MRI**
    - **Occasionally needed to diagnose developing lateral cortical stress reaction/fractures in high risk patients (eg BP use) with prodromal pain but negative radiographs (22)**

Diagnosis

- **Best to diagnose AFFs before they happen!!**
  - **Obtain femoral XRs to rule out impending AFF in…**
    - **High risk patient (eg long term BP use) with thigh pain**
    - **Contralateral femur of patient with a known AFFs**
      - **Risk of contralateral AFF after initial AFF ~25% [20, 23]**

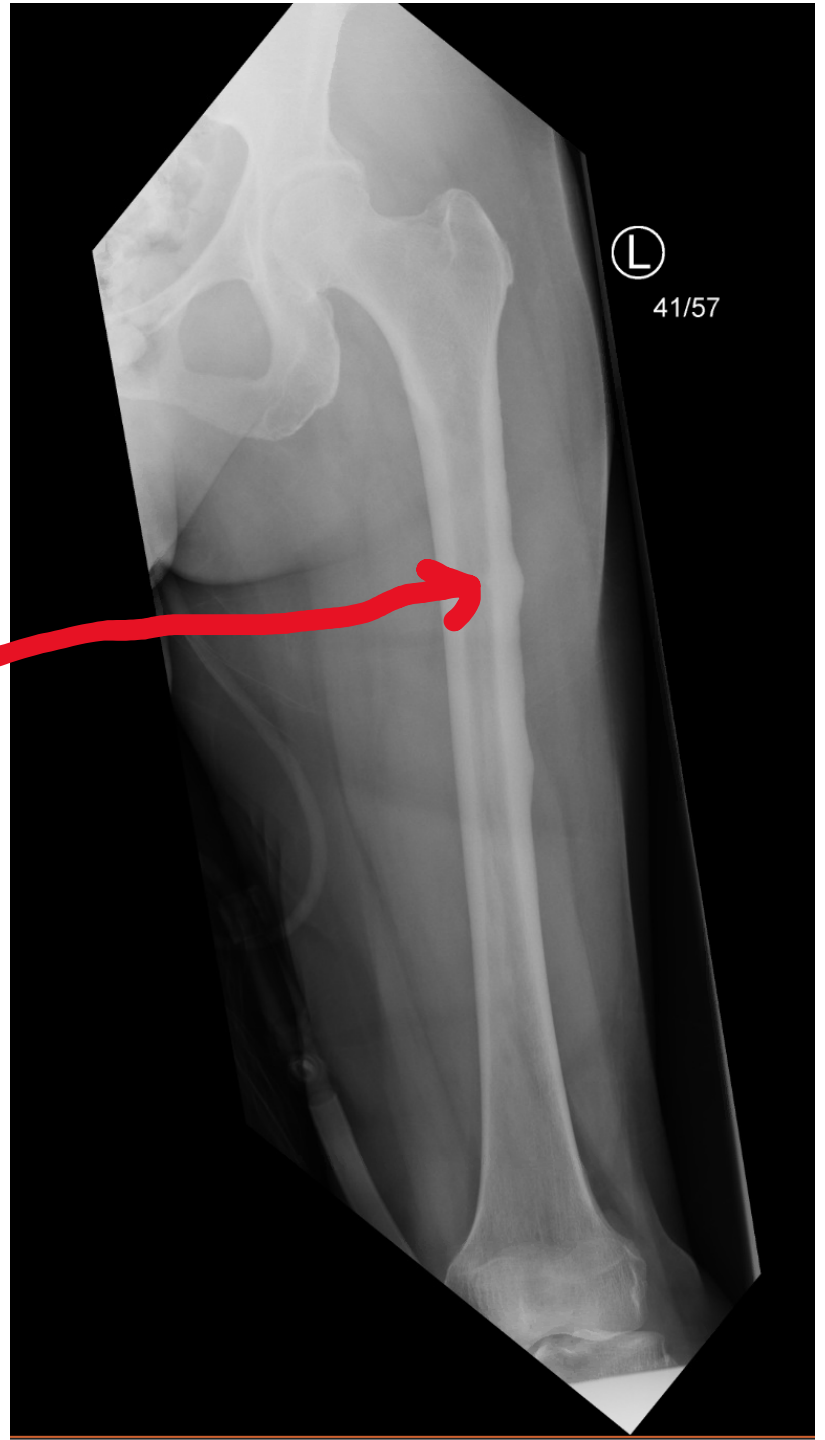
Diagnosis

- **Best to diagnose AFFs before they happen!!**
  - **XR of patient on BP therapy taken for thigh pain**
  - **Note beaking of lateral cortex**
  - **No action taken at time of imaging**
  - **Sustained complete AFF ~ 1 year after XR taken**



Diagnosis

- **Best to diagnose AFFs before they happen!!**
  - **XR of left femur of same patient following right sided complete AFF**
  - **Note beaking of lateral cortex**
  - **Patient noted to have left thigh pain**
  - **Treated with prophylactic nail**



Treatment

- **Complete AFF (22)**
  - **Intramedullary nail stabilization**
  - **Endocrine consult**
    - **Discontinuation of BPs (if currently using)**
    - **Vit D/Calcium supplementation**
    - **Consideration of alternative osteoporosis medications (eg teriparatide)**

Treatment

- **Developing or Incomplete AFF**
  - **Saleh et al (24)- w/ no radioluscent line in lateral cortex, 100% union with nonoperative management… w/ radioluscent line, 22% union w/ nonop management**
  - **Banffy et al (25)- w/ radioluscent line, 83% nonunion w/ nonop management**
  - **Egol et al (26)- incomplete AFFs, 100% union w/ prophylactic nailing, 18% union w/ nonoperative management**
  - **Jiang et al (27)- prophylactic fixation of contralateral femur in patients with AFF cost effective if "high risk" (Asian race, prodromal pain, varus proximal femur, femoral bowing, beaking, radioluscent line)**

Treatment

- **Developing or Incomplete AFF (22)**
  - **Lower risk patients- initial course of nonoperative management reasonable**
    - **Protected weight bearing**
    - **Endocrine consult- discontinue BPs, consider alternative osteoporosis medication, vit D/calciyum supplementation**
  - **Higher risk patient**
    - **Prophylactic IMN**
    - **Endocrine consult**
- **Surgeon should have low threshold for prophylactic fixation given relatively high rates of nonunion and progression to complete AFF with nonoperative management**

Surgical Considerations

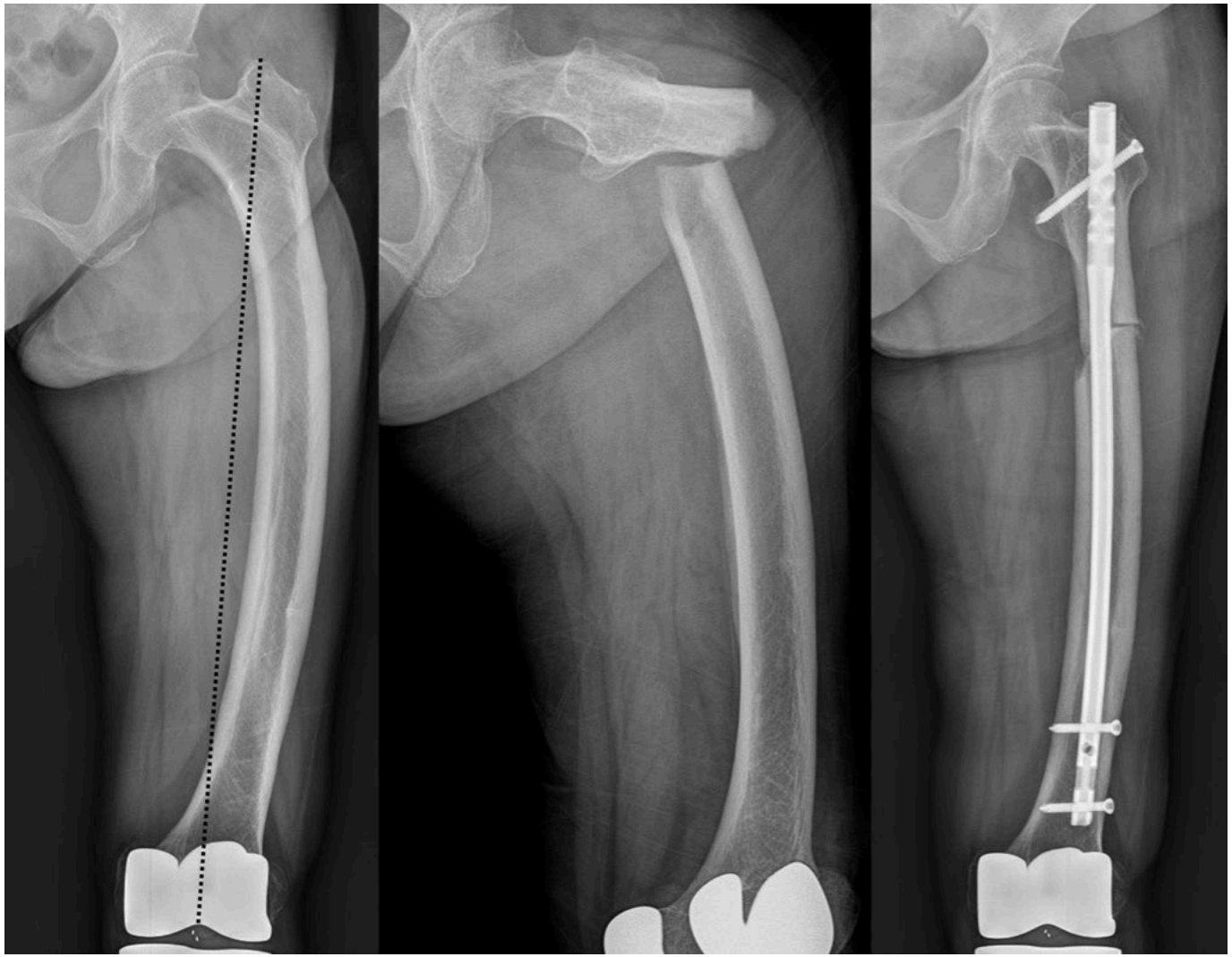
- **Operative fixation of AFFs frequently complicated by…**
  - **Anterolateral femoral bowing- risk of poor nail fit, mareduction, perforation**
  - **Localized lateral cortical thickening at fracture site- may deflect nail medially, creating varus malreduction**
  - **Poor bone quality- frequently sustained by patients with preexisting osteotoporosis and other comorbidities**
  - **High rates of delayed union- construct needs to survive a potentially long healing course**

Surgical Considerations

- **Anterolateral femoral bowing- risk of poor nail fit, malreduction, perforation**
    - **Choose nail with smallest possible radius of curvature (28)**

Surgical Considerations

- **Anterolateral femoral bowing-**
  - **Choose nail with smallest possible radius of curvature**
  - **Externally rotating nail may improve nail fit (29)**
    - **Converts normal anterior bow of nail into anterolateral bow, possibly improving nail fit**



Surgical Considerations

- **Anterolateral femoral bowing-**
  - **Choose nail with smallest possible radius of curvature**
  - **Consider externally rotating nail if needed**
  - **Medialize start point to avoid varus malreduction (30)**

Surgical Considerations

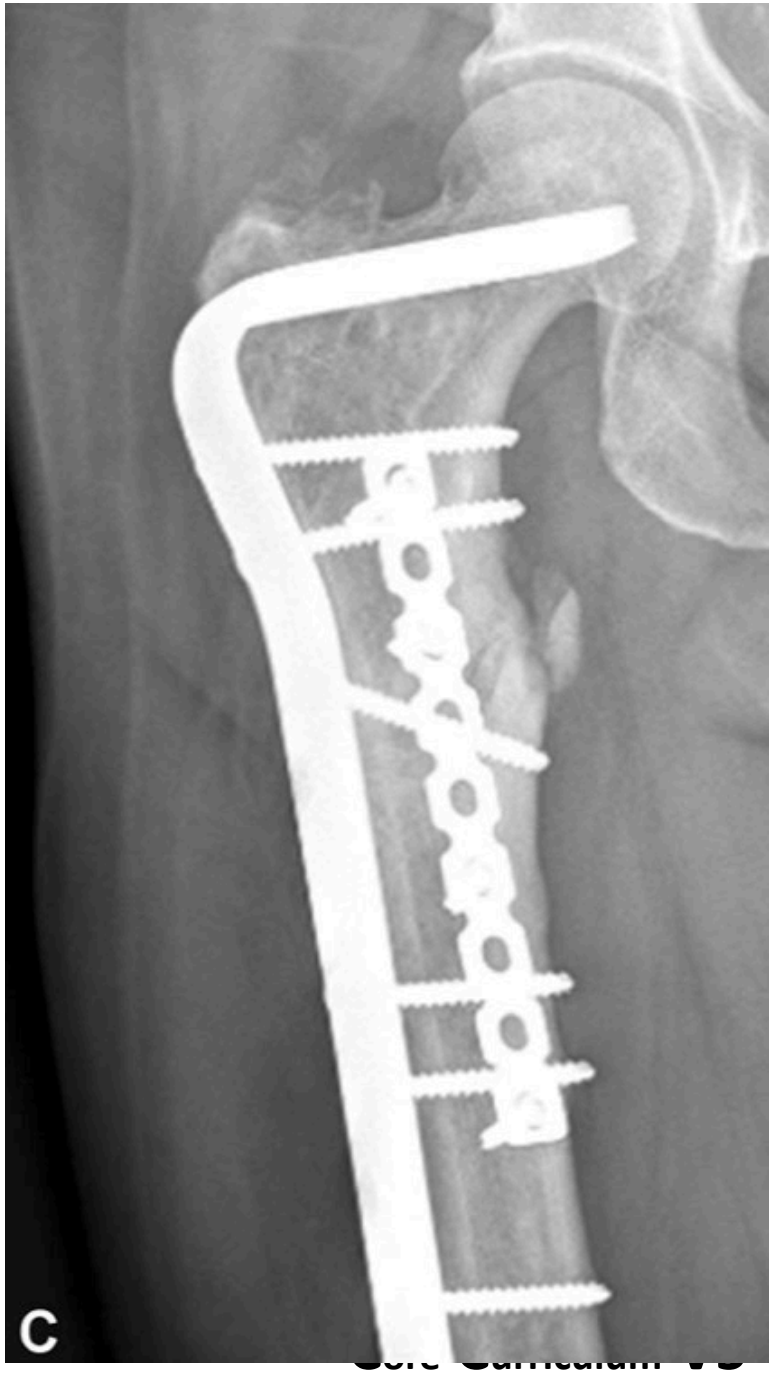
- **Anterolateral femoral bowing-**
  - **Choose nail with smallest possible radius of curvature**
  - **Consider externally rotating nail if needed**
  - **Medialize start point to avoid varus malreduction**
  - **Place blocking screws as necessary to fine tune nail path**

Surgical Considerations

- **Anterolateral femoral bowing-**
  - **Choose nail with smallest possible radius of curvature**
  - **Consider externally rotating nail if needed**
  - **Medialize start point to avoid varus malreduction**
  - **Place blocking screws as necessary to fine tune nail path**
  - **Carefully advance nail to ensure it will not perforate anteriorly**

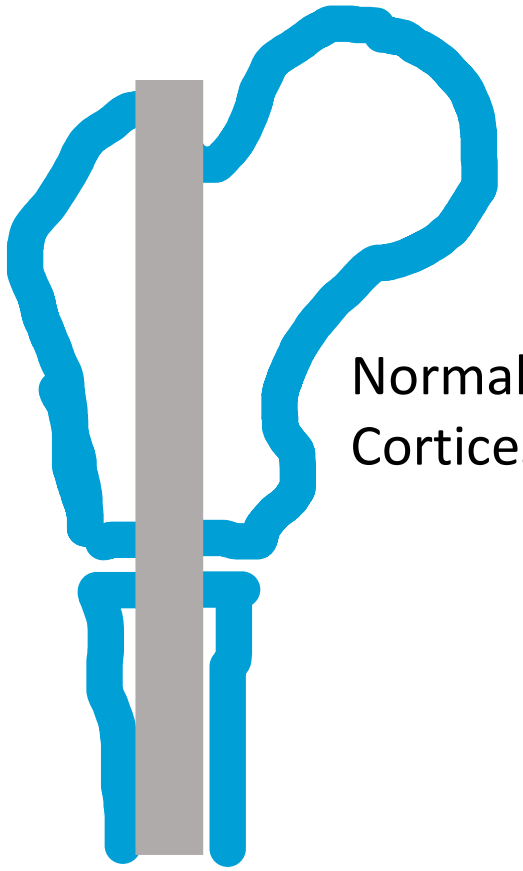
Surgical Considerations

- **Anterolateral femoral bowing-**
  - **Choose nail with smallest possible radius of curvature**
  - **Consider externally rotating nail if needed**
  - **Medialize start point to avoid varus malreduction**
  - **Place blocking screws as necessary to fine tune nail path**
  - **Carefully advance nail to ensure it will not perforate anteriorly**
  - **Plate femur if nailing impossible due to anatomy (31)**

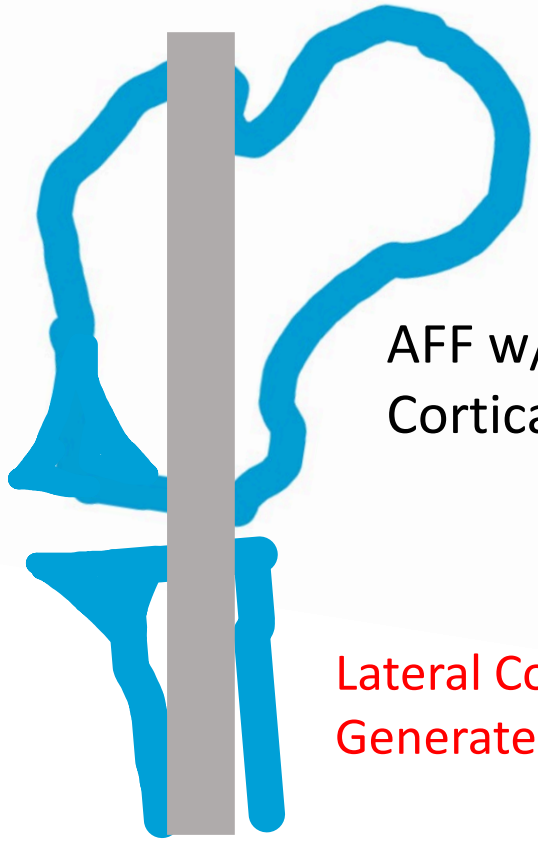


Surgical Considerations

- **Localized cortical thickening at fracture site- may deflect nail medially, generating varus malreduction**



Normal
Cortices



AFF w/ Lateral
Cortical Beaking

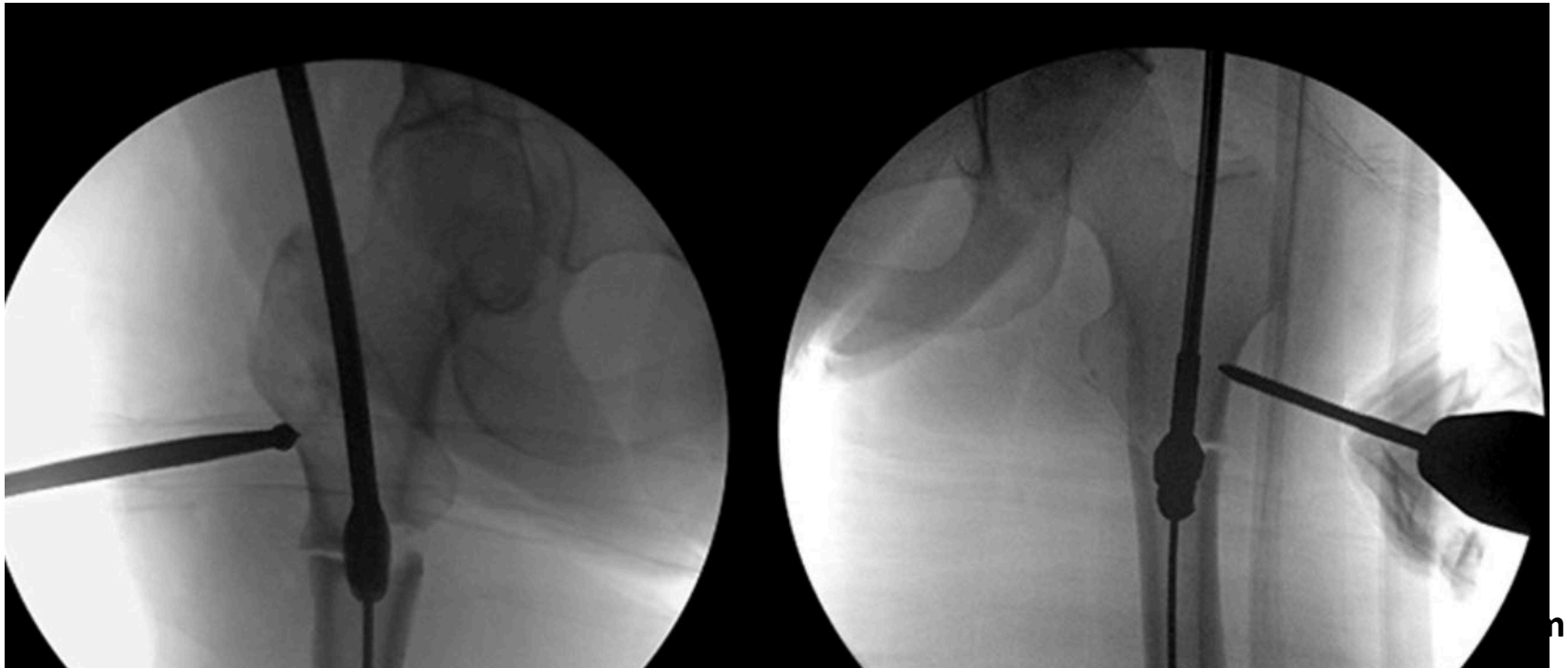
Lateral Cortical Thickening
Generates Varus Malreduction

Surgical Considerations

- **Localized cortical thickening at fracture site**
    - **Use awl or rigid reamer to drill through lateral cortical thickening (32)**

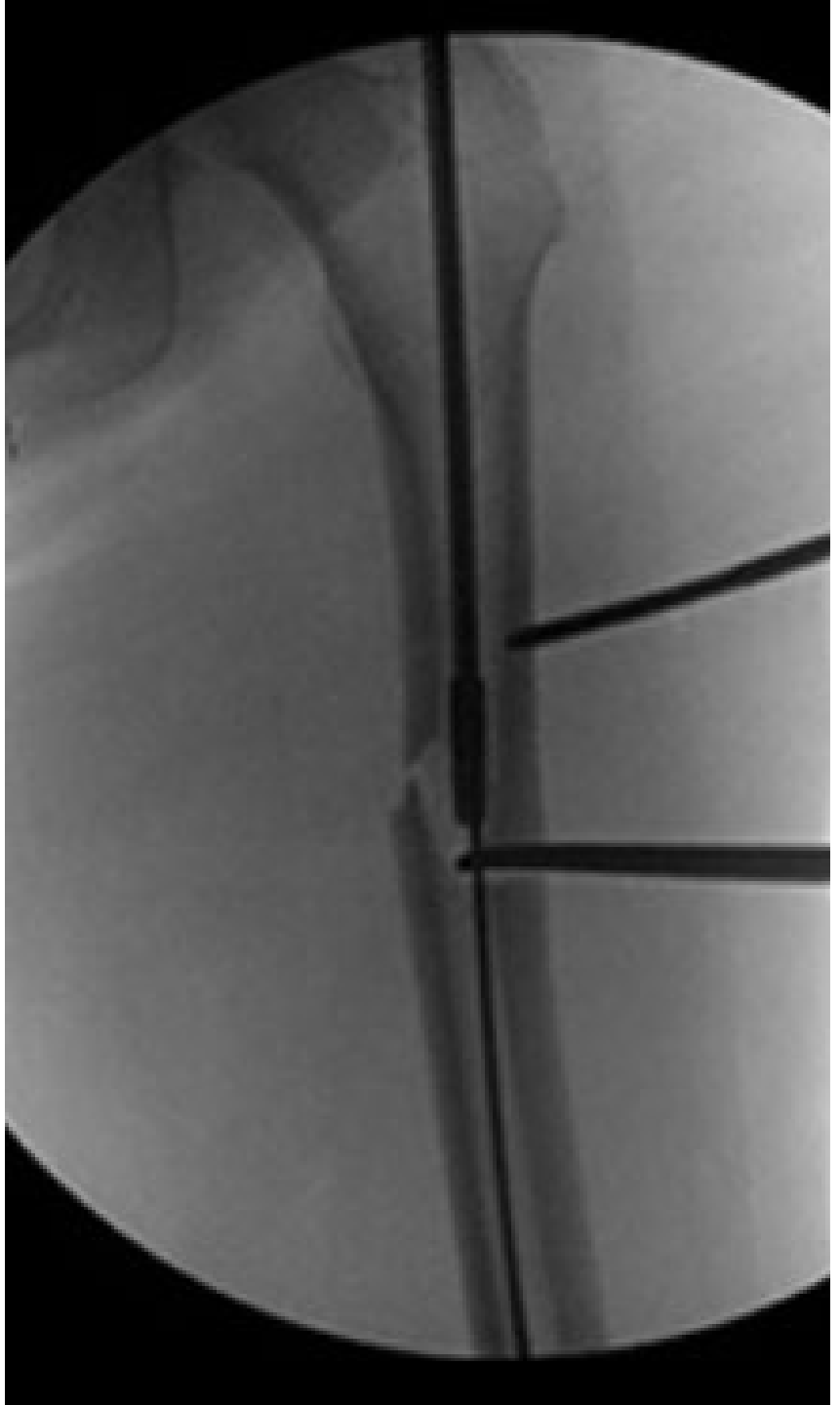
Surgical Considerations

- **Localized cortical thickening at fracture site**
  - **Use awl or rigid reamer to drill through lateral cortical thickening**
  - **Adduct proximal fragment with schanz pin or ball spike to allow reaming of lateral cortex (30)**



Surgical Considerations

- **Localized cortical thickening at fracture site**
  - **Use awl or rigid reamer to drill through lateral cortical thickening**
  - **Adduct proximal fragment with schanz pin or ball spike to allow reaming of lateral cortex (30)**
  - **Abduct guidewire with bone hook to allow reaming of lateral cortex (30)**



Surgical Considerations

- **Localized cortical thickening at fracture site**
  - **Use awl or rigid reamer to drill through lateral cortical thickening**
  - **Adduct proximal fragment with schanz pin or ball spike to allow reaming of lateral cortex**
  - **Abduct guidewire with bone hook to allow reaming of lateral cortex**
  - **Open approach to burr down lateral cortical thickening directly (32)**

Surgical Considerations

- **High rates of delayed union- construct needs to survive a potentially long healing course**
  - **Use multiple interlocks, blocking screws to increase longevity of construct**

Surgical Considerations

- **High rates of delayed union**
  - **Use multiple interlocks, blocking screws to increase longevity of construct**
  - **Recommend use of recon or cephalomedullary nails to improve proximal fixation/protect against potential femoral neck fracture**

Surgical Considerations

- **High rates of delayed union**
  - **Use multiple interlocks, blocking screws to increase longevity of construct**
  - **Recommend use of recon or cephalomedullary nails to improve proximal fixation/protect against potential femoral neck fracture**
  - **Further study needed to determine if bone grafting, LIPUS, BMP beneficial for AFF healing (33,34)**

Prognosis

- **Important to counsel patients regarding high rates delayed union, nonunion, and reoperation**
  - **Giusti et al- delayed/nonunion rate 39% (higher w/ continued BP use) (33)**
  - **Cho et al- delayed/nonunion rate 41% (avg time to union 10.7 mos) (34)**
  - **Lim et al- nonunion rate 30% (35)**

Atypical Femur Fracture (AFF) Summary

- **Low energy femoral shaft fractures with a characteristic appearance**
- **Caused by a combination of unfavorable femoral anatomy (varus, anterior bow) and impaired bone healing/remodeling**
- **Frequently (but not always) associated with bisphosphonate use**
- **Successful treatment requires a combination of medical and surgical management**
- **Relatively high rates of delayed/nonunion compared to standard femoral shaft fractures**
- **Disease process often manifests bilaterally… patients must be checked and monitored for developing AFF of the contralateral femur**

References

1. Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM, et al. 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;29(1):1–23.
2. Saita Y, Ishijima M, Mogami A, Kubota M, Kaketa T, Miyagawa K, Nagura N, Wada T, Sato T, Fukasaku S, Gen H, Obayashi O, Nemoto M, Kaneko K. Association between the fracture site and the mechanical axis of lower extremities in patients with atypical femoral fracture. J Bone Miner Res. 2012; 27(Suppl 1).
3. Sasaki S, Miyakoshi N, Hongo M, Kasukawa Y, Shimada Y. Low-energy diaphyseal femoral fractures associated with bisphosphonate use and severe curved femur: a case series. J Bone Miner Metab. 2012; 30:561–7.
4. Hagen JE, Miller AN, Ott SM, Gardner M, Morshed S, et al. Association of atypical femoral fractures with bisphosphonate use by patients with varus hip geometry. J Bone Joint Surg Am. 2014 Nov 19;96(22):1905-9.
5. Oh Y, Fujita K, Wakabayashi Y, Kurosa Y, Okawa A. Location of atypical femoral fracture can be determined by tensile stress distribution influenced by femoral bowing and neck-shaft angle: A CT-based nonlinear finite element analysis modeal for the assessment of femoral shaft loading stress. Injury. 2017 Dec;48(12):2736-43.
6. Paparodis R, Buehring B, Pelley EM, Binkley N. A case of an unusual subtrochanteric fracture in a patient receiving denosumab. Endocr Pract. 2013;19(3):e64–e68.
7. Schilcher J, Aspenberg P. Atypical fracture of the femur in a patient using denosumab--a case report. Acta Orthop. 2014;85(1):6–7.
8. Al-Ashqar M, Panteli M, Chakrabarty G, Giannoudis PV. Atypical fractures: An issue of concern or a myth? Injury. 2018 Mar;49(3):649-55.
9. Marcano A, Taormina D, Egol KA, Peck V, Tejwani NC. Are race and sex associated with the occurrence of atypical femoral fractures? Clin Orthop Relat Res. 2014 Mar;472(3):1020-7.
10. Roca-Ayats N, Balcells S, Garcia-Giralt N, et al. GGPS1 mutation and atypical femoral fractures with bisphosphonates. N Engl J Med. 2017 May 4;376(18):1794-5.
11. Cummings SR, Thompson DE, Applegate WB, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: Results from the fracture intervention trial. JAMA. 1998. 280. 2077-82.
12. Goh SK, Yang KY, Koh JS, Wong MK, Chua SY, Chua DT, Howe TS. Subtrochanteric insufficiency fractures in patients on alendronate therapy: a caution. J Bone Joint Surg Br. 2007; 89:349–53.
13. Wang Z, Bhattacharyya T. Trends in incidence of subtrochanteric fragility fractures and bisphosphonate use among the US elderly 1996–2007. J Bone Miner Res. 2011; 26:553–60.
14. Dell RM, Adams AL, Greene DF, Funahashi TT, Silverman SL, Eisemon EO, et al. Incidence of atypical nontraumatic diaphyseal fractures of the femur. J Bone Miner Res. 2012;27(12):2544–2550.
15. Schilcher J, Michaëlsson K, Aspenberg P. Bisphosphonate use and atypical fractures of the femoral shaft. N Engl J Med. 2011;364(18):1728–1737.
16. Adler et al. Managing osteoporosis patients after long-term bisphosphonate treatment. J Bone Miner Res. 2016 Jan;31(1):16-35.
17. Black DM, Schwartz AV, Ensrud KE, Cauley JA, Levis S, Quandt SA, et al. FLEX Research Group. 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(24):2927–2938.
18. 18. Black DM, Reid IR, Boonen S, Bucci-Rechtweg C, Cauley JA, Cosman F, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT) J Bone Miner Res. 2012;7(2):243–254.

References

19. Black JD, Kancheria VK, De Long WG Jr. A review of atypical femoral fractures from a tertiary care teaching hospital: An alarming trend? J Orthop Trauma. 2016 Apr;30(4):182-8.

20. Bogdan Y, Tornetta P 3rd, Einhorn TA, Guy P et al. Healing time and complications in operatively treated atypical femur fractures associated with bisphosphonate use: A multicenter retrospective cohort. J Orthop Trauma. 2016 Apr;30(4):177-81.

21. Egol KA, Park JH, Rosenberg ZS, Peck V, Tejwani NC. Healing delayed but generally reliable after bisphosphonate-associated complete femur fractures treated with IM nails. Clin Orthop Relat Res. 2014 Sep;472(9):2728-34.

22. Blood T, Feller RJ, Cohen E, Born CT, Hayda R. Atypical fractures of the femur: Evaluation and treatment. JBJS Reviews. 2015 Mar 3;3:3.

23. Dell RM, Greene D, Tran D. Stopping bisphosphonate treatment decreases the risk of having a second atypical femur fracture. Paper presented at: American Academy of Orthopaedic Surgeons (AAOS) Annual Meeting; 2012 Feb 7–11; San Francisco, CA, USA.

24. Saleh A, Hegde VW, Potty AG, Schneider R, Cornell CN, Lane JM. Management strategy for symptomatic bisphophonate-associated incomplete atypical femoral fractures. HSS J. 2012 Jul;8(2):103-10.

25. Banffy MB, Vraha SM, Ready JE, Abraham JA. Nonoperative versus prophylactic treatment of bisphosphonate-associated femoral stress fractures. Clin Orthop Relat Res. 2011 Jul;469(7):2028-34.

26. Egol KA, Park JH, Prensky CZ, Rosenberg ZS, Peck V, Tejwani NC. Surgical treatment improves clinical and functional outcomes for patients who sustain incomplete bisphosphonate-related femur fractures. J Orthop Trauma. 2013 Jun;27(6):331-5.

27. Jiang SY, Kaufman DJ, Chien BY, Longoria M, Shachter R, Bishop JA. Prophylactic fixation can be cost-effective in preventing a contralateral bisphosphonate-associated femur fracture. Clin Orthop Relat Res. 2019 Mar;477(3):580-90.

28. Park JH, Lee Y, Shon HC, Kim JW. Surgical tips of intramedullary nailing in severely bowed femurs in atypical femur fractures: Simulation with 3D printed model. Injury. 2016 Jun;47(6):1318-24.

29. Park YC, Song HK, Zheng XL, Yang KH. Intramedullary nailing for atypical femoral fracutre with excessive anterolateral nowing. J Bone Joint Surg Am. 2017 May 3;99(9):726-35.

30. Berkes MB, Shaw JC, Warner SJ, Achor TS. Medialized trochanteric start point and focused lateral endosteal beak reaming to optimize success of intramedullary nailing in atypical femur fractures: A technical trick and case series. J Orthop Trauma. 2019 Aug;33(8):e313-7.

31. Rollick NC, Bear J, Diamond O, Wellman DS, Helfet DL. Orthogonal plating with a 95-degree blade plate for salvage of unsuccessful cephalomedullary nailing of atypic femur fractures: A technical trick. J Orthop Trauma. 2019 Jun;33(6):e246-50.

32. Githens M, Garner MR, Firoozabadi R. Surgical management of atypical femur fractures associated with bisphosphonate therapy. J Am Acad Orthop Surg. 2018 Dec 15;26(24):864-71.

33. Giusti A, Neveen A, Papapoulos SE. Atypical fractures of the femur and bisphosphonate therapy: A systematic review of case/case series studies. Bone. 2010 Aug;47(2):169-80.

34. Cho JW, Oh CW, Leung F, Park KC, Wong MK et al. Healing of atypical subtrochanteric femur fractures after cephalomedullary nailing: Which factors predict union? J Orthop Trauma. 2017 Mar;31(3):138-45.

35. Lim HS, Kim CK, Park YS, Moon YW, Lim SJ, Kim SM. Factors associated with increased healing time in complete femoral fractures after long term bisphosphonate therapy. J Bone Joint Surg Am. 2016 Dec 7;98(23):1978-87.