

Atypical Femur Fractures

Atypical Femur Fracture (AFF) is a spontaneous or low-trauma, subtrochanteric/femur shaft fracture often complicated by delayed or nonunion (26-39%) and bilateral occurrence (28-44%).

1.8 per 100 000 person-years in pts on bisphosphonates under 2 years

113 per 100 000 person-years with more than 8 years duration

Bisphosphonates (BP) benefit to AFF risk ratio for 3-5 years of use.

Per 1 AFF caused by BPs ~1200 features would be prevented.

Higher risk groups- those on glucocorticoids and those with Asian ancestry (should be more closely monitored, especially after 3-5 years).

Limited evidence and guidelines on how to proceed after an AFF (lacking RCTs of drug use for treatment in patients with AFF), must balance risk of worsening or causing a contralateral AFF with chance of fragility fracture.

Recommend-

- Extensive monitoring with imaging of both upper legs during the first 1 or 2 years. (due to nonhealing and chance of contralateral AFF)
- To stop offending agent (bisphosphonate or denosumab) as continuation may worsen or lead to contralateral AFF (risk decreases by 70% per year from last use of antiresorptive drugs in those who haven't sustained an AFF, unknown if applicable to those with an AFF).
- After healing of bilateral, surgically managed AFFs bisphosphonates or denosumab may be continued.
- Continuation of bisphosphonates may lead to risk of atypical fractures at sites other than the femur, must balance this vs risk of osteoporotic fractures (likely lower).
- For surgically treated AFFs teriparatide may improve healing (RCT pending, 2022-NCT01896011).
- Observational data of 165 AFFs show 6 month healing in surgically treated incomplete AFF (n=9, 90%), complete AFF (n=44, 76%), compared to non-operated incomplete AFF (n=13, 43%) and complete AFF (n=34, 51%).
- Teriparatide- AFF reported in 165 patients, all associated with prior bisphosphonate exposure. Due to this it is considered a safer option in patients with AFF.
- Raloxifene- AFF reported in 8 patients, 1 without bisphosphonate exposure. May be a preferable option after teriparatide.
- Denosumab- AFF reported in 22 patients, 8 without prior bisphosphonate exposure.

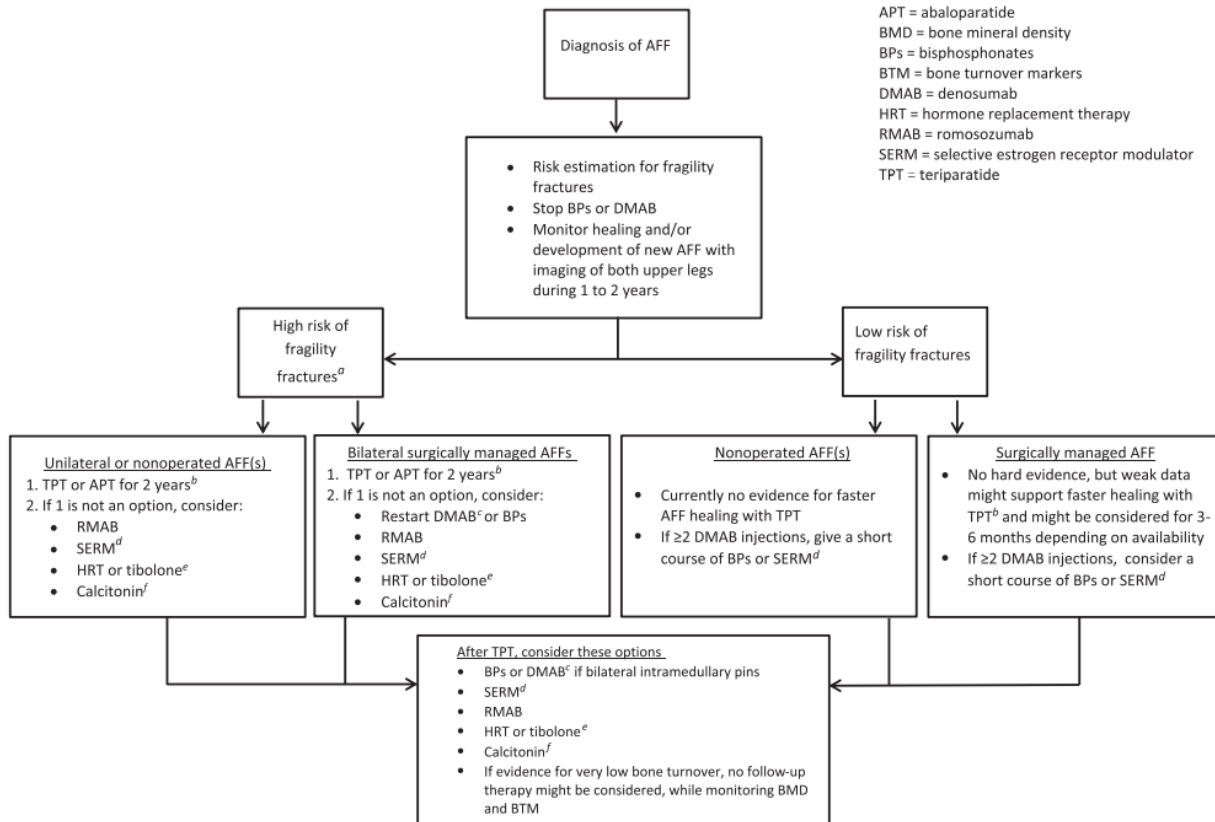


Figure 2. Decision tree with considerations for medical management after atypical femur fracture (AFF). ^aDefinition may vary across countries, eg, a hip BMD T-score ≤ -2.5 SD, older age (70–75 years), a recent fragility fracture, other strong risk factors for fracture, or a FRAX fracture risk score that is above country-specific thresholds (95). ^dRaloxifene or bazedoxifene are preferably prescribed in relatively young postmenopausal women who are at low risk of hip fractures and deep vein thrombosis (94), or in women in whom the use of teriparatide is contraindicated. ^eIn case of intolerance to SERMs, hormone replacement therapy or tibolone could be considered in women with a low risk of deep vein thrombosis and breast cancer, without a history of myocardial infarction or stroke (94). ^bSwitching denosumab to teriparatide may result in progressive BMD loss. ^cBe aware that antiresorptive therapy may be needed after stopping denosumab. ^fCalcitonin can be prescribed in patients who are not eligible for bisphosphonates, SERMs, hormone replacement therapy, tibolone, abaloparatide, or teriparatide.

References

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2. Black, D. M., Abrahamsen, B., Bouxsein, M. L., Einhorn, T., & Napoli, N. (2019). Atypical femur fractures: Review of epidemiology, relationship to bisphosphonates, prevention, and clinical management. *Endocrine Reviews*, 40(2), 333–368. <https://doi.org/10.1210/er.2018-00001>