Welcome to UVM ECHO: Osteoporosis in Men

Facilitators:
Jennifer J. Kelly, DO (course director)
Liz Cote
“Introduction” to ZOOM for ECHO

• Please mute microphone when not speaking
• Please use camera as much as possible
• Test both audio & video before joining
• Communicate clearly during clinic:
  • Can use “raise hand” feature to comment
  • Speak clearly
  • Use chat function for technical issues
• RECORDING OF SESSION TO BEGIN
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Osteoporosis in Men

Jennifer J. Kelly, DO, FACE, CCD
Director of the Metabolic Bone Program
Associate Professor of Medicine
Division of Endocrinology and Metabolism
University of Vermont Medical Center
Burlington, VT
Epidemiology

• Osteoporosis is a silent disorder characterized by reduced bone strength predisposing to increased fracture risk.

• Although osteoporosis affects women more often than men, approximately 20% of the 44 million Americans who have osteoporosis or low BMD are men.

• Between 30 and 40% of fractures due to osteoporosis occur in men; the lifetime risk of fracture for men aged 50 or older is between 13 and 30%.
Epidemiology

• Men with hip fractures have a mortality rate two to three times higher than women.

• Fractures in childhood and teenage years are more common in males, probably due to differences in lifestyle and trauma; most are at peripheral sites.

• Past middle age, fractures due to osteoporosis are more common in women. In later years, fracture risk rises exponentially in both sexes, but the increase occurs about a decade later in men than in women.

• Of the 3.5 million fractures in men worldwide annually, 14% were at the hip, 10% at the forearm, 16% at the vertebrae, 5% at the humerus, and 55% elsewhere.
Annual Incidence of Osteoporotic Fractures Higher Than Other Epidemic Diseases

- 44 million Americans have low bone mass, including 10 million with established osteoporosis. Of these, 80% are women.¹

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*New and recurrent cases. †New cases only.
Fractures

• The incidence of fractures due to osteoporosis varies with race/ethnicity and geography.

• The highest rates in men are in Northern Europe and North America. Lowest rates are in Blacks and Asians as well as in some parts of South America.

• The ratio of hip fractures between women and men also varies by geography. Although the female-to-male ratio among Caucasians is about 3–4:1, the ratio is much closer to 1:1 or even higher in Asia.
- In young and middle-age men, a secondary cause for bone loss is usually identified, with hypogonadism being the most common.

- Idiopathic osteoporosis (no known cause) can occur and is probably a result of genetic factors that have yet to be determined.
Osteoporosis in Men

Identified in 40-60% men with osteoporotic fractures:

- Hypogonadism
- Glucocorticoid therapy
- Gastrointestinal diseases
- Vitamin D deficiency
- Anticonvulsant use
- Alcohol abuse
### SOME CAUSES OF SECONDARY OSTEOPOROSIS IN ADULTS

<table>
<thead>
<tr>
<th>Endocrine Disease or Metabolic Causes</th>
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<th>Drugs</th>
<th>Disorders of Collagen Metabolism</th>
<th>Other</th>
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<td>Vitamin D deficiency</td>
<td>Glucocorticoids</td>
<td>Osteogenesis imperfecta</td>
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<td>Hypercalcemia</td>
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<td>Hyperthyroidism</td>
<td>Vit. B12 deficiency</td>
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<td>Hyperparathyroidism</td>
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<td>Depo-Provera</td>
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<td>Cushing’s syndrome</td>
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<td>Growth hormone deficiency</td>
<td>Anorexia nervosa</td>
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<td></td>
<td>Chronic liver disease</td>
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<td>Renal tubular acidosis</td>
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<td></td>
<td>Alcoholism</td>
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<td>Gaucher’s disease</td>
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<td>Mastocytosis</td>
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<td></td>
<td>Prolonged TPN</td>
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<td>Thalassemia</td>
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</tbody>
</table>

Adapted from Hodgson SF and Watts NB, AACE Guidelines on Osteoporosis, www.aace.com
Pathogenesis

- Before puberty, BMD measured with DXA is similar in boys and girls and increases slowly but progressively. At puberty, bone turnover increases dramatically, followed by a rapid increase in BMD.

- Androgens increase periosteal bone apposition, increasing the cross-sectional diameter of bone. Because BMD measured by DXA is directly related to bone size, part of the apparent pubertal BMD increase is due to a projection artifact from increasing bone size. Peak spine BMD as measured by DXA is generally reached by age 18 in males.

- As men and women age, bone resorption exceeds formation, leading to bone loss. BMD may begin to decline in men as early as age 30 to 40, decreasing slowly (about 0.5–1.0% annually), without the acceleration that is seen in women at menopause. In elderly persons, however, degenerative change often increases DXA-measured BMD in the spine.
Bone loss over time in men and women

- Peak bone mass
- Bone loss related to age
- Effects during growth
- Menopausal bone loss

Bone mass vs. Age (years)
## Treatment options in men

<table>
<thead>
<tr>
<th>Drug</th>
<th>Potential advantages</th>
<th>Potential disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral bisphosphonates</td>
<td>Inexpensive</td>
<td>Adherence and compliance</td>
</tr>
<tr>
<td></td>
<td>Long experience</td>
<td>Side effects: GERD, ONJ, AFF</td>
</tr>
<tr>
<td>Intravenous bisphosphonates</td>
<td>Long intervals between infusions</td>
<td>More expensive</td>
</tr>
<tr>
<td></td>
<td>Potential improved adherence</td>
<td>Side effects: ONJ, AFF</td>
</tr>
<tr>
<td>Denosumab</td>
<td>Convenient 6 month dosing</td>
<td>More expensive</td>
</tr>
<tr>
<td></td>
<td>Appears to increase BMD up to 6 years</td>
<td>Side effects: ONJ, AFF</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>Anabolic</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>No ONJ or AFF</td>
<td>Daily subcutaneous injection</td>
</tr>
</tbody>
</table>
Treatment

- For most men who are candidates for pharmacological therapy, generic alendronate will often be preferred because of: 1) extensive experience with its use; 2) lack of evidence that other agents are more effective or better tolerated; and 3) low cost.

- For men with upper or lower gastrointestinal problems, a nonoral therapy (e.g. zoledronic acid or teriparatide) may be preferred. In postmenopausal women, risedronate has been shown to reduce hip fracture risk and is a reasonable alternative for men at risk for hip fractures.
Treatment

- The effects of bisphosphonates and teriparatide on BMD and BTM appear to be similar in men and women. Of the FDA-approved agents used to treat osteoporosis in men, alendronate, risedronate, and zoledronic acid have been shown to reduce the risk of hip fractures in women with postmenopausal osteoporosis. Denosumab has been shown to increase BMD and reduce the incidence of vertebral fractures in men receiving ADT for non-metastatic prostate cancer.

- Once-yearly treatment with IV zoledronic acid reduced risk of recurrent fractures in more than 2100 subjects (~25% were men) who had undergone repair of a hip fracture within 90 d of treatment initiation. Teriparatide increases spine BMD more than alendronate.
Treatment

• For men at high risk of vertebral fracture, teriparatide may be preferred because it increases spine BMD more than alendronate, although it is more expensive.
• Teriparatide could also be considered for men who fail to tolerate or respond adequately to other agents.
• Bisphosphonate therapy should not be used in men with impaired kidney function (estimated glomerular filtration rate ≤30–35 ml/min).
Management of Hypogonadal Men at High risk for Fracture-Endocrine Society guidelines

• For men at high risk of fracture who are receiving testosterone therapy, we suggest adding an agent with proven antifracture efficacy (e.g. a bisphosphonate or teriparatide).

• We suggest testosterone therapy in lieu of a “bone drug” for men at borderline high risk for fracture who have serum testosterone levels below 200 ng/dl on more than one determination, if accompanied by signs or symptoms of androgen deficiency (e.g. low libido, unexplained chronic fatigue, loss of body hair, hot flushes, etc.) or “organic” hypogonadism (e.g. due to hypothalamic, pituitary, or specific testicular disorder).

• If testosterone treatment does not alleviate symptoms of androgen deficiency after 3–6 months, it should be discontinued and other therapy considered.
Androgens and Estrogen

• Measurements of serum testosterone levels are useful to identify men who have androgen deficiency and who may be candidates for testosterone replacement.

• Low levels of both testosterone and estradiol are associated with bone loss and fractures in men, although the associations are weak.

• Low estradiol levels are more strongly associated with increased fracture risk and accelerated bone loss in older men.

• Measurement of estradiol levels in clinical situations in men is not recommended because of the lack of easily available, accurate assay methods (mass spectrometry) and the absence of validated clinical algorithms that incorporate estradiol measurements into treatment decisions.
ADT for Prostate Cancer

• Several small studies have examined rates of bone loss during the first year of GnRH agonist therapy in men with prostate cancer.

• In general, spine BMD declines by 3–4% in the first year. Decreases in hip BMD are more modest. Interestingly, BMD declined more rapidly in the radius than in the spine or hip.

• Fracture risk is increased in men receiving ADT.
Prostate cancer treatment with ADT

• A placebo-controlled trial showed the benefits of denosumab in men with early prostate cancer receiving ADT; after 36 months of treatment, denosumab increased spine, hip, and distal radius BMD and decreased the incidence of vertebral fractures by 62%; denosumab is approved by the FDA for treatment of men with non-metastatic prostate cancer receiving ADT.

• Denosumab in higher doses than used to treat osteoporosis has been shown to improve the outcome of men with advanced prostate cancer metastatic to bone (denosumab 60 mg SQ every 6 months is the dose for treatment of osteoporosis; 120 SQ monthly is the dose for treatment of bone metastases).
Prostate Cancer and ADT

- Clinical trials of zoledronic acid on BMD have shown benefits in men with prostate cancer receiving ADT and men with prostate cancer metastatic to bone. If treatment with zoledronic acid is not feasible due to prior side effects, cost, or other logistical issues, oral alendronate therapy is a reasonable alternative, based on a single randomized controlled trial in men with prostate cancer receiving ADT and on the more extensive data in men with primary osteoporosis and women with postmenopausal osteoporosis.
Facts and Statistics from the NOF

• Up to one in four men over age 50 will break a bone due to osteoporosis.

• Approximately two million American men already have osteoporosis. About 12 million more are at risk.

• Men older than 50 are more likely to break a bone due to osteoporosis than they are to get prostate cancer.

• Each year, about 80,000 men will break a hip.

• Men are more likely than women to die within a year after breaking a hip.

• Men can fracture bones in the spine or hip, but this usually happens at a later age than women.
It’s erroneous to think it’s a lady’s disease.
Screening in practice

• Do not need to go from zero to 100!

• Consider starting with screening likely candidates: thinner older men with any of the following: COPD, Type 1 DM, CHF, CVA, Parkinson's, chronic steroid use, smoker, alcoholism. Hypogonadism, prostate cancer treatment with ADT.

• Frailty and Fall risk important.
Questions prior to patient case?

- Can use raise hand option or chat for questions/comments.
- Also can unmute and chime in!
• RECORDING TO BE STOPPED FOR CASE PRESENTATION
Cases/HIPAA

- Names
- Address
- DOB
- Phone/Fax #
- Email address
- Social Security #
- Medical Record #

The discussion and materials included in this conference are confidential and privileged pursuant to 26VSA Section 1441-1443. This material is intended for use in improving patient care. It is privileged and strictly confidential and is to be used only for the evaluation and improvement of patient care.
Conclusion

• Volunteers to present cases (this is key to the Project ECHO model)
  • Please submit cases to Jennifer.Kelly@uvmhealth.org
• Please complete evaluation survey after each session
• Claim your CME at www.highmarksce.com/uvmmmed
• Please contact us with any questions, concerns, or suggestions
  Elizabeth.Cote@uvm.edu
  Jennifer.Kelly@uvmhealth.org