Osteoporosis Case Studies: Could this be you or Someone you Know?
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I have no financial interest or other conflict of interest in relation to this program/presentation.

Objectives
At the end of presentation, participant will be able to:

- Identify evidence-based clinical guidelines for diagnosis and treatment of osteoporosis.
- Describe a plan for osteoporosis workup which considers possible secondary causes of low bone mineral density.
- Discuss the use of a fracture risk assessment in clinical decision-making for osteoporosis treatment.
- Discuss role of DXA scan in continued monitoring.
Guidelines

- International Society for Clinical Densitometry (ISCD) 2013 Adult Official Positions.
- American Association of Clinical Endocrinologists (AACE) Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Postmenopausal Osteoporosis (2016)

Download to Your Desktop

www.nof.org/professionals/Clinicians_Guide.htm

Case Study One

Fracture Risk: A Tale of Two Women
“Will I end up like my mother?”

- 68 years old
- Healthy
- Positive family history
  - mother with a vertebral fracture at age 60, hip fracture at age 73 requiring nursing home placement.

Does this woman have osteoporosis?

<table>
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<tr>
<th>Region</th>
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<th>Z-score</th>
</tr>
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<tbody>
<tr>
<td>L1-L4</td>
<td>0.754</td>
<td>-2.0</td>
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<td>Total Hip</td>
<td>0.781</td>
<td>-1.3</td>
<td>-0.5</td>
</tr>
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WHO Criteria for Osteoporosis

**Bone mineral density criteria**
- T-score ≤ -2.5

**Presence of a fragility fracture**
- Also referred to as “low energy” or “low trauma” fractures
- Primary sites: Vertebra, hip, forearm, proximal humerus (pelvis, ribs)
The T-score: What does it mean?

**Relational Score**

**Normal:**  
\[ T \text{-score} \geq -1.0 \]  
- BMD not more than \( \pm 1 \) S.D. below the young normal

**Low Bone Mass (Osteopenia):**  
\[ T \text{-score} < -1 \text{ and } > -2.5 \]  
- A BMD between \(-1.0 - 2.5\) S.D. below the young normal

**Osteoporosis:**  
\[ T \text{-score} \leq -2.5 \]  
- A BMD \( 2.5 \) or more SD below the young normal

**Severe osteoporosis:**  
\[ T \leq -2.5 \]  
- and the presence of one or more fragility fractures

ISCD Official Positions (2013)

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“I want to do everything to keep my bones strong”

- 53 years old
- Healthy
- No family history of osteoporosis
- Menopause at 50
- No HRT due to sister with breast cancer.

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Does this woman have osteoporosis?

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No. Low Bone Mineral Density (Osteopenia)
Should these Women be Treated?

- One-time DXA – limited information
- Phenomenon of peak bone mass.
- Motivation to treat:
  - Prevention: Maintain BMD
  - Treat loss of BMD
  - Prevent Fractures in patients at high risk

Historical Risk Factors for Osteoporosis & Fractures

<table>
<thead>
<tr>
<th>Non-Modifiable</th>
<th>Modifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced age (&gt;50)</td>
<td>Smoking (active/passive)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>Excessive alcohol intake</td>
</tr>
<tr>
<td>Race: White, Asian</td>
<td>Low levels of physical activity</td>
</tr>
<tr>
<td>Family history of osteoporosis and parental history of a fracture.</td>
<td>Low calcium intake</td>
</tr>
<tr>
<td></td>
<td>Vitamin D insufficiency</td>
</tr>
<tr>
<td></td>
<td>Excessive thinness</td>
</tr>
</tbody>
</table>

NOF, 2013

Focus on Fracture Risks

- Low body weight
- Propensity for or high risk for falls
- Poor health
- Poor depth perception
- Previous fracture
- Benzodiazepine use
NOF Guidelines for Treatment

Postmenopausal women & men ≥ 50 with the following:
- A hip or vertebral fracture (or other fracture c/w low trauma)
- T-score < -2.5 at the femoral neck or spine
- T-score between -1 and -2.5 at the femoral neck or spine and 10 year fracture probability:
  - > 20% for major osteoporosis-related fracture or ≥ 3% for hip fracture
- Clinician’s judgment and/or patient preferences may indicate treatment for people with 10-year fracture probabilities above or below these levels

2013 Clinician’s Guide to Prevention & Treatment of Osteoporosis

Calculating Fracture Risk

FRAX®

- Web-based algorithm developed by the WHO to assist clinicians in identifying patients at high risk for fractures (reference databases for 32 countries)
- Helpful in the decision-making process regarding treatment for osteopenia as opposed to a T-score threshold alone.


Calculating Fracture Risk

FRAX®

- Utilizes risk factors, with or without BMD, to give 10 year absolute fracture risk of a major osteoporotic fracture and/or hip fracture.
- Developed to be utilized for both postmenopausal women and men ages 40 to 90 years, but NOF (2013) suggests focusing on postmenopausal women and men aged 50 and older

Calculating Fracture Risk

FRAX® WHO Fracture Risk Assessment Tool

Calculating Fracture Risk

FRAX® WHO Fracture Risk Assessment Tool

FRAX Limitations

- Site of BMD measurement utilized for FRAX is the femoral neck.
- For patients whose BMD is lower at the spine, fracture risk is underestimated.
- Does not include other known independent risk factors for fracture such as bone turnover, falls, BMD at skeletal sites other than the hip.
- It does not stratify glucocorticoid dose or duration.
- Underscores the importance of considering multiple factors when assessing fracture risk on a case by case basis.

ISCD, 2010; Watts, 2011
FRAX® Not for Everyone

Not indicated for patients:
- Already receiving osteoporosis drug therapy
- For whom treatment is clearly indicated
- Have T-scores better than -1.0

Excellent Resource by Dr. Nelson Watts
The fracture risk assessment tool (FRAX®): applications in clinical practice. Journal of Women's Health. 20 (4) 525-531
Case Study Two
Uncovering Secondary Causes

Patients at risk for osteoporosis commonly have undiagnosed coexisting conditions and/or are on medications that cause bone loss. This is important to include when considering screening. Potential contributing factors can be found in as many as 30% of women with osteoporosis.

Uncovering Secondary Causes

<table>
<thead>
<tr>
<th>Region</th>
<th>BMD g/cm²</th>
<th>T-score</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1-L4</td>
<td>0.576</td>
<td>-4.3</td>
<td>-1.9</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>0.465</td>
<td>3.5</td>
<td>-1.4</td>
</tr>
<tr>
<td>Total Hip</td>
<td>0.415</td>
<td>-4.3</td>
<td>-2.6</td>
</tr>
</tbody>
</table>

77 years old
- History of Vitamin D deficiency
- Anemia and Vitamin B12 deficiency
- History of myocardial infarction
- No fractures

- Started on teraparitide a couple of months ago by her internist

This is her first treatment for osteoporosis, but not her first DXA scan.
Medical History

- Hormone status
  - Normal or early menopause?
  - HRT?
  - Age at menarche?
- Eating disorder
- Calcium & Vitamin D intake

Fracture History

- Location, mechanism, age
- Current fracture symptoms
- Medications/
  Medical conditions /Medications which can be secondary causes of osteoporosis.

Vitamin D Deficiency

- Vitamin D plays major role in calcium absorption, bone health, muscle performance, balance and risk of falling.
- Vitamin D deficiency is a widespread and often overlooked cause of low bone mass.
- As many as 50% of postmenopausal women taking osteoporosis medication have less than optimum levels of 25-hydroxyvitamin D levels (30 nanograms per milliliter).

AACE, 2010

Secondary Causes

<table>
<thead>
<tr>
<th>Endocrine/Metabolic</th>
<th>GI/Nutrition</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
<td>Vitamin D deficiency</td>
<td>Antiepileptics</td>
</tr>
<tr>
<td>Diabetes: Type 1 &amp; 2 Growth hormone deficiency</td>
<td>Alcohol abuse</td>
<td>Aromatase inhibitors</td>
</tr>
<tr>
<td>Early menopause</td>
<td>Anorexia nervosa</td>
<td>Chemotherapy/immunosuppressants</td>
</tr>
<tr>
<td>Premature ovarian failure</td>
<td>Calcium deficiency</td>
<td>Glucocorticoids</td>
</tr>
<tr>
<td>Athletic amenorrhea</td>
<td>Chronic Liver Dx</td>
<td>Depo-Provera</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Malabsorption: Celiac disease</td>
<td>Heparin</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>Crohn's disease</td>
<td>Lithium</td>
</tr>
<tr>
<td></td>
<td>Gastric bypass</td>
<td>PPIs</td>
</tr>
<tr>
<td></td>
<td>Total parenteral nutrition</td>
<td>Thiazolidinedione</td>
</tr>
<tr>
<td></td>
<td></td>
<td>thyroid hormone</td>
</tr>
</tbody>
</table>

Adapted from: AACE Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Postmenopausal Osteoporosis (2010) and used with permission.
Secondary Causes

<table>
<thead>
<tr>
<th>Genetic Conditions</th>
<th>Other</th>
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<tbody>
<tr>
<td>Cystic Fibrosis</td>
<td>AIDS/HIV</td>
</tr>
<tr>
<td>Ehlers-Danlos syndrome</td>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>Homosystinuria</td>
<td>COPD</td>
</tr>
<tr>
<td>Gaucher's disease</td>
<td>Hypercalcium</td>
</tr>
<tr>
<td>Marfan's syndrome</td>
<td>Immobilization</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>Major depression</td>
</tr>
<tr>
<td>Osteogenesis imperfecta</td>
<td>Myeloma &amp; some cancers</td>
</tr>
<tr>
<td>Thalassemia/Hemophilia</td>
<td>Organ transplantation</td>
</tr>
<tr>
<td>Glycogen storage diseases</td>
<td>Renal sufficiency/failure</td>
</tr>
<tr>
<td>Hypophosphatasia</td>
<td>Systemic mastocytosis</td>
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Screening for Secondary Osteoporosis

Basic Workup

- Complete Blood Count
- Comprehensive metabolic panel (alkphos & LFT's)
- Thyroid stimulating hormone
- Serum 25 (OH) D level
- Parathyroid hormone (PTH)
- 24-hour urinary calcium, creatinine, & sodium

Adapted from AACE Postmenopausal Osteoporosis Guidelines (2016)

Additional Testing for Select Patients

- Serum protein electrophoresis, serum immunofixation, and free light chains, urine protein electrophoresis (suspected myeloma)
- Tissue transglutaminase antibodies (anti-TTG)
- Tryptase
- Iron and ferritin levels
- Homocysteine
- Urinary histamine
- Iliac crest bone biopsy with double tetracycline labeling

Adapted from AACE Postmenopausal Osteoporosis Guidelines (2016)
Secondary Causes

History
- Menopause-age 50
- History of smoking- 3 pk/day x 20 years. Quit X 15 yrs
- + Calcium 600 mg daily, multiple vitamin
- Ergocalciferol 50,000 IU (Vitamin D2) weekly
- Chronic anemia requiring transfusions

ROS- Negative except for fatigue and SOB

Physical Exam
- Noncontributory
- No point tenderness

Secondary Causes

Diagnostic workup
- 25 OH Vitamin D- 11 ng/ml
- Hct- 27
- Hgb- 9.0
- Anti-TTG- >150
- No GI complaints c/w wheat allergy.
- Thoracic & Lumbar Spine
  - X-ray- no compression fractures

Impression/Diagnosis
- Osteoporosis in setting of malabsorption (probable celiac sprue)
- Final Diagnosis: Duodenal and small bowel biopsy:
  - Histologic features consistent with celiac sprue.

Secondary Causes?

History
- Menopause-age 54
- + Calcium & D3
- Low back pain

Physical Exam
- Point tenderness lumbar spine

Diagnostic workup
- Vitamin D- 44 ng/ml
- X-ray- T12 Compression fracture

History
- Lifelong lactose intolerance
- Just started Calcium & D3

Physical Exam:
- Noncontributory

Diagnostic workup
- 25 OH Vitamin D- 15 ng/ml

Note: Initial DXA does not document loss. Probably low peak bone mass due to suboptimal calcium intake, ? Low Vitamin D
Work up Results

- Low BMD on DXA: L1-L4 - 2.0, FN -2.0, Total hip - 1.3
- FRAX 10 year fracture risk: major - 20 and hip 3.6
- Meets risk criteria for treatment
- Workup - T-12 compression fracture. What is diagnosis now?

How does this change things?
- More drug options
- More aggressive drug therapy

Current FDA-approved Medications

- Bisphosphonates *
  - Oral: alendronate, ibandronate, risidronate,
  - Infusion: ibandronate, zoledronic acid (Reclast®)
- Estrogen agonist/antagonist: raloxifene (Evista®)*
- Estrogens and/or hormone therapy
- teriparitide (Forteo®) - anabolic agent
- Denosumab (Prolia®) - RANKL inhibitor

* Approved for treatment of low BMD, NOF, 2013

What about her?

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• Low BMD
  - FRAX: fracture risk
    - Vitamin D now 38
    - Calcium 1200 mg/day
    - Weight-bearing exercise
    - Recheck Vit D 1 yr
    - DXA in 2 yrs

Low BMD - FRAX: fracture risk
  - Vitamin D now 38
  - Calcium 1200 mg/day
  - Weight-bearing exercise
  - Recheck Vit D 1 yr
  - DXA in 2 yrs
Two Years Later......

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<th>Change</th>
</tr>
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<tbody>
<tr>
<td>L1-L4 0.56 gm/cm²</td>
<td>0.810</td>
<td>0.754*</td>
<td>-2.0 -2.1* Significant decrease of 7% compared to technically similar lumbar spine; 1.57% precision error (.040 gm/cm²) at 95% confidence interval</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>0.630</td>
<td>0.545*</td>
<td>-2.1 -2.2* No significant change compared to technically similar femoral neck. Precision error 2.39% at 95% confidence level (0.035 gm²)</td>
</tr>
<tr>
<td>Total Hip</td>
<td>0.816</td>
<td>0.790*</td>
<td>-1.0 -1.2* No significant change compared to technically similar total hip. Precision error 2.76% at 95% confidence level (0.034 gm²)</td>
</tr>
</tbody>
</table>

No guess work

- Significant loss at the lumbar spine since initial DXA two years ago. Patient motivated to prevent further BMD loss at spine. Stable at hip.
- HRT not an option due to sister’s breast cancer.
- Initiate raloxifene (Evista) 60 mg daily (SERM) which is protective against breast cancer.
- Recheck 25 OH Vitamin D
- Check Urine NTX or Serum Ctx for baseline. Repeat in 12 months.

www.toneyourbones.org
Please contact me
dlink@uab.edu

Questions?

References


