Osteoporosis Update

Diabetes/Endocrinology Clinic

April 16, 2015
Osteoporosis-What’s the big deal?
Significance of Osteoporosis in Women

Osteoporotic Fractures:
- 1,456,000 total fractures
  - 223,000 hip fractures
  - 327,000 wrist fractures
  - 415,000 other sites
  - 103,000 pelvic fractures
  - 388,000 vertebral fractures

Compared to:
- 370,000² Heart Attack
- 425,000² Stroke
- 182,460³ Breast Cancer

1 Annual fracture incidence in women all ages
2 Annual estimate new & recurrent Ml ages 35+
3 Annual estimate new & recurrent stroke in women all ages
4 2008 new cases in situ & invasive breast cancer all ages

Cost of Osteoporosis

- Projected annual direct costs of osteoporosis: $25.3 billion by 2025\(^1\) and ~$50 billion by 2040\(^2\)
- Osteoporotic fractures account for:
  - ~$17 billion in direct medical costs\(^1\)
  - >400,000 hospital admissions\(^3\)
  - ~2.5 million physician visits\(^3\)
  - >180,000 nursing home admissions\(^3\)

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DXA measures BMD (quantity): Other Contributors to Bone Strength

Bone Density (Quantity 40%)

Bone Turnover (Quality 20%)

Bone Architecture (Quality 20%)

Bone Mineral Content (Quality 20%)

Remember Bone Density accounts for ONLY 40% of fracture risk
Bone dynamics

Bone Loss Following Menopause

- Women can lose up to 20 percent of their bone mass during the first 5 to 7 years following menopause.

- Annual bone loss of 3-5 percent occurs during the first 5 postmenopausal years compared to a nearly zero loss during years 6 through 8.

Fracture Risk with Aging

*white women

Vertebrae

Hip

Colles'

Annual Fracture Incidence, per 100,000

Age (years)

0 35 45 55 65 75 85+ 85+

Hip Fractures

- 15% of postmenopausal women will have hip fracture during their lifetime
- Up to 30% will require long-term nursing care
- Only 15% can walk unaided after 6 months
- Up to 25% excess mortality following hip fracture
Risk Factors for Osteoporosis and Fracture in White Postmenopausal Women.

Table 2. Risk Factors for Osteoporosis and Fracture in White Postmenopausal Women.\textsuperscript{11}

<table>
<thead>
<tr>
<th>Major risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal history of fracture as an adult</td>
</tr>
<tr>
<td>History of fragility fracture in a first-degree relative</td>
</tr>
<tr>
<td>Low body weight\textsuperscript{†}</td>
</tr>
<tr>
<td>Current smoking</td>
</tr>
<tr>
<td>Use of oral corticosteroid therapy (daily dose equivalent, ≥5 mg of prednisone) for more than 3 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired vision</td>
</tr>
<tr>
<td>Estrogen deficiency at an early age (before 45 years)</td>
</tr>
<tr>
<td>Dementia</td>
</tr>
<tr>
<td>Poor health or frailty</td>
</tr>
<tr>
<td>Recent falls</td>
</tr>
<tr>
<td>Low calcium intake (lifelong)</td>
</tr>
<tr>
<td>Low physical activity</td>
</tr>
<tr>
<td>Alcohol in amounts greater than two drinks per day</td>
</tr>
</tbody>
</table>

\textsuperscript{*} The information is from the National Osteoporosis Foundation.\textsuperscript{11}  
\textsuperscript{†} Low body weight is defined as a weight below 127 lb (58 kg), which is based on the lowest quartile for weight of the cohort in the Study of Osteoporotic Fractures, but the definition varies among populations.

Relative Risk of Hip Fracture According to Key Clinical Risk Factors after Adjustment for Age and Bone Mineral Density.

**Table 3. Relative Risk of Hip Fracture According to Key Clinical Risk Factors after Adjustment for Age and Bone Mineral Density.**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior fracture after age 50 yr</td>
<td>1.62 (1.30–2.01)</td>
</tr>
<tr>
<td>Body-mass index (20 vs. 25)</td>
<td>1.42 (1.23–1.65)</td>
</tr>
<tr>
<td>Previous or current use of systemic corticosteroids</td>
<td>2.25 (1.60–3.15)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1.73 (0.94–3.20)</td>
</tr>
<tr>
<td>Parental history of hip fracture</td>
<td>2.28 (1.48–3.51)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.60 (1.27–2.02)</td>
</tr>
<tr>
<td>Alcohol intake &gt;2 drinks daily</td>
<td>1.70 (1.20–2.42)</td>
</tr>
</tbody>
</table>

* Data are from Kanis et al.\(^{16}\) Body-mass index is the weight in kilograms divided by the square of the height in meters.

2011 USPSTF Screening Recommendations

• Screen all women aged 65 or older
• Screen women < 65 years if:
  – 10-yr fracture risk is = or > than that of a 65-year-old white woman without additional risk factors
    (9.3% by FRAX® fracture risk assessment tool)
www.sheffield.ac.uk/FRAX/
WHO Diagnostic Categories of Bone Mineral Density.

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>A value for BMD or BMC that is within 1.0 SD of the reference mean for young adults</td>
</tr>
<tr>
<td>Low bone mass (osteopenia)</td>
<td>A value for BMD or BMC that is more than 1.0 but less than 2.5 SD below the mean for young adults</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>A value for BMD or BMC that is 2.5 SD or more below the mean for young adults</td>
</tr>
<tr>
<td>Severe osteoporosis (established osteoporosis)</td>
<td>A value for BMD or BMC that is 2.5 SD or more below the mean for young adults in combination with one or more fragility (low-trauma) fractures.</td>
</tr>
</tbody>
</table>

* The information is from the WHO. BMD denotes bone mineral density, and BMC bone mineral content.

Using T-scores vs. Z-scores

- **T-scores**
  - Number of standard deviations above or below the mean for a healthy 30 year old of the same ethnicity and gender

- **Z-scores**
  - Number of standard deviations above or below the mean for the patient’s age, ethnicity and gender
  - Low Z-score (less than -2.0) may indicate an increased risk for secondary osteoporosis
Using T-scores vs. Z-scores

T-scores
• WHO diagnostic classification in postmenopausal women and men age 50 and older
• WHO classification with T-score cannot be applied to healthy premenopausal women, men under age 50, and children

Z-scores
• For use in reporting BMD in healthy premenopausal women, men under age 50, and children
• Z-score -2.0 or less is defined as “below the expected range for age”
• Z-score above -2.0 is “within the expected range for age”
Prevention and Treatment Strategies

• Counsel on risk reduction
• Instruct on adequate daily intake of calcium and vitamin D
• Provide guidelines for regular weight-bearing and muscle strengthening exercise
• Provide strategies for fall prevention and balance training
• Counsel on avoiding tobacco smoking and excessive alcohol intake
Recommendations for Vitamin D Requirements

- **IOM (New 2011 guidelines)**
  - Children/adults $\leq$ 70: 600 IU/day
  - Adults $>$ 70: 800 IU/day

- **NOF**
  - Adults $<$ 50: 400-800 IU/day
  - Adults 50 and older: 800-1000 IU/day

- **American Academy of Pediatrics**
  - Children/adolescents: 400 IU/day
Tai Chi
Sensible Shoes
NOF Recommendations for Initiation of Therapy

Initiate therapy to reduce fracture risk in postmenopausal women and men age 50 and older:

• If the individual has a hip or vertebral fracture or

continued
NOF Recommendations for Initiation of Therapy (con’t)

If the T-score is:

- ≤ -2.5 in spine or total hip or femoral neck after evaluation to exclude secondary causes, or

- between -1.0 and -2.5 and 10-yr probability of hip fracture ≥ 3 percent or a 10-yr probability of any major osteoporosis-related fracture ≥ 20 percent based on US-adapted FRAX®
Table. Pharmacological Therapies for Osteoporosis

<table>
<thead>
<tr>
<th>Agent</th>
<th>Route and Frequency of Administration</th>
<th>BMD Response</th>
<th>Fracture Risk Reduction in Postmenopausal Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Spine</td>
<td>Hip</td>
</tr>
<tr>
<td>Alendronate</td>
<td>PO, daily or weekly</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>PO, daily or monthly; IV infusion, q3mo</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Risedronate</td>
<td>PO, daily or weekly</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>IV, yearly</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>Intranasal spray, daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen/hormone replacement</td>
<td>PO, daily; transdermal patch, twice weekly</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>PO, daily</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>SC injection, daily</td>
<td>++++</td>
<td>+</td>
</tr>
</tbody>
</table>

BMD, bone mineral density; +, modest response; ++, moderate response; ++++, good response; ++++, very good response.
Figure 1: Denosumab and Its Role in the Inhibition of Osteoclast Formation, Function, and Survival

- Pre-Fusion Osteoclast
- RANKL
- Multinucleated Osteoclast
- Activated Osteoclast

Macrophages

Osteoblasts

Bone Formation

Bone Formation, Function, and Survival Inhibited

Denosumab bound to RANKL (blocking its interaction with RANK)

Bone Resorption Inhibited
Regional variation in vertebroplasty