Osteoporosis: An Overview of the Disease and Its Consequences

Harbour View Breast Cancer Support Group
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Osteoporosis in the Clinic: 3 Cases

**Ms. P**
- 60 years of age
- No prevalent fx
- Family history of fx
- Menopause at 47 years
- Has never had a BMD test

**Ms. Q**
- 82 years of age
- History of hip fx
- Widow, lives independently
- Alcohol >2 drinks per day
- Depression

**Ms. R**
- 72 years of age
- No documented vertebral fractures
- Height loss
- Inadequate calcium and vitamin D
- Sedentary lifestyle
Osteoporosis: Definition

NIH Definition:

“Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture”

Epidemiology of Osteoporosis in the US

44 million Americans, 80% of whom are women
- 10 million have established osteoporosis
- 34 million have osteopenia or low bone mass
- 1.5 million fractures occur per year in US

Osteoporosis is Common Among US Women

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- 1.5 million fractures occur per year in US

Risk Factors for Osteoporotic Fractures

Genetic/Nonmodifiable
- Age
- Female sex
- Asian or white ethnicity
- Previous fragility fracture
- Family history of hip fracture or osteoporosis
- Small frame

Potentially Modifiable
- Menopause-related estrogen deficiency
- Low body weight
- Calcium/vitamin D deficiency
- Inadequate physical activity
- Excessive alcohol intake
- Cigarette smoking
- Long-term glucocorticoids
Vertebral Fractures Have Significant Consequences for Patients, Including Dorsal Kyphosis

Vertebral Fractures

- Associated with
  - Acute and chronic pain
  - Kyphosis and height loss
  - Impaired function
  - Increased morbidity and mortality
  - Increased fracture risk

Hip and Other Non-Vertebral Fractures Have Significant Consequences

- Hip fracture associated with
  - Loss of ambulatory status in 30% of patients
  - Increased morbidity and mortality
  - Increased fracture risk
  - Major reason for admission to chronic care facilities

- Non-vertebral fractures
  - Pain
  - Increased risk of future fractures

Fracture Incidence Increases With Age: 5-Year Fracture Rates in Women and Men

1-Year Risk of Refracture in Patients With Incident Vertebral Fracture

Clinical Presentation of Osteoporosis

» Usually asymptomatic and undiagnosed

» Signs and symptoms
  - Low-trauma fractures of spine, wrist, or hip
  - Loss of height
  - Kyphosis (rounded back)
  - Acute or chronic back pain

» Diagnostic tests
  - Bone mineral density measurement
  - Spine x-ray or morphometry
# WHO Bone Density Criteria for Diagnosing Osteoporosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>BMD T-Score: Number of SD Below Mean in Healthy Young Women*</th>
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<tbody>
<tr>
<td>Normal</td>
<td>−1 or above</td>
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<tr>
<td>Low bone mass [osteopenia]</td>
<td>Between −1 and −2.5</td>
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<tr>
<td>Osteoporosis</td>
<td>−2.5 or less</td>
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<tr>
<td>Severe osteoporosis</td>
<td>−2.5 or less with fragility fractures</td>
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- Reduction by 1 SD equals a 10% to 12% decrease in BMD
- 1 SD change increases fracture risk by 1.5- to 2.0-fold

National Osteoporosis Foundation Guidelines

- Recommend BMD testing for
  - All women 65 years of age and older
  - Younger postmenopausal women with one or more risk factors (other than being white, postmenopausal, and female)
  - Postmenopausal women who present with fractures (to confirm the diagnosis and determine disease severity)
Nonpharmacologic Interventions

- Goal of nonpharmacologic interventions is to prevent future fractures through lifestyle change
  - Diet and dietary supplements
    - Calcium
    - Vitamin D
  - Exercise
  - Fall prevention
  - Smoking cessation
Decision to Treat Is Affected by Several Factors

- Current AACE position on treatment intervention
  - Women with postmenopausal osteoporosis
    - Women with low-trauma fractures and low BMD
    - Women with BMD T-scores of −2.5 and below
  - If risk factors are present, women with borderline-low BMD (T-scores of −1.5 and below)
  - Women in whom nonpharmacologic preventive measures are ineffective (bone loss continues or low trauma fractures occur)

- Individual clinician judgment is important

- Forthcoming guidelines are likely to be based on absolute fracture risk probability over 10 years rather than on BMD alone

AACE = American Academy of Clinical Endocrinologists

Classes of Pharmacologic Agents Currently Approved for the Treatment of Osteoporosis

▶ **Antiresorptive agents**
  - Bisphosphonates
    - Weekly oral alendronate
    - Weekly or monthly risedronate
    - Monthly oral or quarterly IV ibandronate
  - Calcitonin
  - Selective estrogen receptor modulators (SERMs)

▶ **Anabolic agents**
  - Parathyroid hormone

▶ **Estrogen therapy and hormone therapy**
  - (Indicated for prevention only)

Effects of Bisphosphonates

- ↓ Bone turnover
- ↑ BMD at lumbar spine and hip
- ↓ Risk of vertebral and hip fractures
- Sustained effects with continued treatment
- Best-studied class of agents used in osteoporosis
- Long-term safety record

Real-World Obstacles in the Management of Osteoporosis

- Insufficient rates of diagnosis
- Low awareness among physicians and patients of the imperative to treat
- Global challenge of adherence to therapy in chronic diseases, compromising effectiveness
- Poor adherence is two-fold problem
  - Low persistence: patient stops taking medication
  - Poor compliance: patient does not follow dosing instructions

Poor Compliance and Persistence Lead to Compromised Fracture Risk Reduction

N = 35,537

24 Month Fracture Risk (%)

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<th>Non-Persistent</th>
<th>Persistent</th>
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<td>29% Risk Reduction</td>
<td>10</td>
<td>7.7</td>
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<td>P &lt; .001</td>
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Refill Compliance and Fracture Protection Over 24 Months for Bisphosphonate-Treated Patients

For many clinicians, bisphosphonates are the standard of care in osteoporosis because of their rapid efficacy and long-term safety.

Poor adherence to daily, weekly, and monthly regimens of oral bisphosphonates results in compromised effectiveness.

A once-yearly IV bisphosphonate therapy can deliver real-world effectiveness by assuring adherence for the entire dosing interval.
Widespread use of hormonal manipulation in treatment of cancer greatly exacerbates problem

- Aromatase inhibitors in the treatment of breast cancer
- Weak LHRH agonists (Lupron) or orchiectomy in the treatment of prostate cancer
Effect of 2-year treatment with placebo or exemestane on bone mineral density (BMD) of the lumbar spine (A) and femoral neck (B)

The Problem with Aromatase Inhibitors

Changes from baseline bone mineral density (BMD) over time in the lumbar spine over time in patients treated for 36 months with anastrozole or tamoxifen {+/-} zoledronic acid.

Use of Bisphosphonates with Androgen Deprivation


(Not available in US)
Intravenous Reclast for Osteoporosis

- Most aggressive approach currently available
- Avoids side effects of oral bisphosphonates
- Cost competitive
- Once-a-year dosing very convenient
- Insurance reimbursement in a state of flux

- Available at Harbour View Women’s Center by special arrangement
- Requires prescreening for medical issues (dental health, adequacy of kidney function and vitamin D stores) by physician
Conclusions

- Osteoporosis is a major public health issue with significant morbidity, mortality, and health care costs.
- Prevalence increasing as population ages.
- Effective therapies are available, but treatment and adherence patterns are suboptimal in the real-world setting.
- Better diagnosis and longer-acting therapies with few adverse events that address obstacles to adherence may improve real-world outcomes.
For more information....

- Contact Laurie Jesz at 673-5861 or me...
- James J. Stark, MD, FACP at 397-4200...just across the street...

Or visit me on the web:
www.StarkOncology.com