What is a Fragility Fracture?

What is Osteoporosis?

Common Misconceptions

Osteoporosis is an underlying cause of fragility fractures

Fragility fractures are due to multiple disease processes

Improving bone mineral density is the treatment for fragility fractures caused by decreased bone mineral density

All fragility fractures are caused by an imbalance in bone resorption and bone formation.

Osteoporosis

- Low bone mass
- Deterioration of bone tissue
- Disruption of bone architecture
- Increase in bone fragility
- Increased susceptibility to fracture

The Remodeling Cycle of Trabecular Bone

Resorption

Reversal

Resting

Formation
Bone Homeostasis

Osteoblasts: Bone Formation

Osteoclasts: Bone Resorption

OSTEOPOROSIS

Imbalance: bone resorption > bone formation

WHY?

Imbalance: bone formation > bone resorption

Paget’s disease

Epidemiology and outcomes of osteoporotic fractures

"No government acting alone can achieve health with justice. Instead, we need laws and policies at every level—local, national, and global—to achieve a world that is healthier and safer."
### How does this affect us?

- **90% of hip fractures are a result of a ground level fall.**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Risk of Falling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women age 46-49</td>
<td>1/5</td>
</tr>
<tr>
<td>Women age &gt; 85</td>
<td>1/2</td>
</tr>
<tr>
<td>Elderly Men</td>
<td>1/3</td>
</tr>
</tbody>
</table>

### Exponential Population Growth

- **Elderly population (>65 years of age)**
  - **Europe**
    - 1990: 68 million
    - 2050: 133 million
  - **Asia**
    - 1990: 145 million
    - 2050: 894 million

- **Projected # of hip fractures**
  - 1990: 1.7 million
  - 2050: 6.3 million
  - 2050: 8.2 million (age adjusted 1% rise in incidence)

### Fracture Outcome

- **Mortality**
- **Morbidity**
- **Cost**

### Mortality

- Hip fracture mortality > any other fracture mortality
- Greatest risk is immediately after injury
  - Decreases with time
  - Vertebral fracture mortality risk stays elevated >1 yr after
- What comes first?
  - Fracture
  - Chronic illness, poor health

### Morbidity

- Activities of daily living
  - 7% become dependent
  - 8% require in home nursing care
  - Hip fractures are largest burden
- Ambulatory status
  - 20% hip fractures do not ambulate at baseline
  - 40% depend on assistive devices
- Independent Living – lost by 50% hip fracture patients
WHO??

Assessment of Fracture Risk

All postmenopausal women AND men age 50 and older:

- Age, alcohol, body weight, falls, immobilization, low calcium/vit D intake, nicotine, prior non-traumatic fracture
- Family history of hip fracture
- Amenorrhea, Autoimmune diseases, Celiac, Diabetes, Eating disorders, ESRD, Gastric bypass, Hyperthyroidism, Hyperparathyroidism, IBD, Osteogenesis Imperfecta
- Anticoagulants, Anticonvulsants, Aromatase inhibitors, Chemotherapy, Depo-Provera, Glucocorticoids, Immunosuppressives, Lithium, Proton Pump Inhibitors

WHO Risk Assessment

- Age
- Gender
- Body mass index
- Prior osteoporotic fracture
- Parental history of hip fracture
- Alcohol intake (3 or more drinks per day)
- Current smoking
- Oral glucocorticoids ≥5mg/d pred for ≥3 months (ever)
- Rheumatoid arthritis
- Secondary osteoporosis
- Femoral Neck BMD
Indications for BMD Testing

- All women age 65 and older and men age 70 and older
- Younger postmenopausal women and men age 50 to 69 whom you have concern based on risk profile
- Perimenopausal women with a specific factor associated with increased fracture risk, i.e. low body weight, prior non-traumatic fracture or high risk medication
- Any adult with a history of fracture after age 50

Indications for BMD Testing

- Adults with a specific condition (e.g., RA) or taking a high risk medication associated with low bone mass or bone loss
- Anyone being considered for pharmacologic therapy for osteoporosis
- Anyone being treated for osteoporosis, to monitor treatment effect
- Anyone not receiving therapy in whom evidence of bone loss would lead to treatment
- Postmenopausal women discontinuing estrogen

Osteoporotic Fracture

- Pathologic fracture
- Fragility fracture
- “Fall from standing height”
- Increases risk for subsequent fracture

Initial Evaluation

- CBC
- Calcium
- Albumin
- Creatinine
- TSH
- PTH
- Alkaline Phosphatase
- 25-OH vitamin D level
- Serum Protein Electrophoresis
- +/- Testosterone in men
Treatment

- Weight-bearing and muscle strengthening exercises
- Fall prevention
- Nicotine cessation
- Decreased alcohol consumption
- Treatment of secondary causes

- Adequate Calcium and Vitamin D Intake
- Pharmacologic Therapies

Calcium and Vitamin D

- Lifelong calcium for achievement of peak bone mass
- No more than 3000 mg calcium per day
- At least 1000 IU of vitamin D₃ a day

- Achieve serum 25 OH vitamin D level of at least 30 ng/mL
- Achieve serum 25 OH vitamin D level of at least 40 ng/mL for adequate bone healing

Pharmacologic Therapy

- Pathologic Hip or Vertebral Fracture Irrespective of BMD
- T-score ≤ -2.5 at hip or spine after excluding secondary causes
- Osteopenia (T-score between -1.0 and -2.5) and a FRAX calculation of:
  - ≥ 3% hip fracture 10 year probability
  - ≥ 20% major osteoporosis related fracture 10 year probability

Estrogen

- Inhibits osteoclastic activity
- May increase osteoblastic activity

- Estrogen (Premarin): Limited use due to side effects

- Selective Estrogen Receptor Modulators (SERMs):
  - Tamoxifen, Raloxifene (Evista)
  - Bind to estrogen receptor and block bone resorption
  - Poor compared to estrogen or bisphosphonates
**Calcitonin**
- Inhibits Osteoclastic Activity
- Miacalcin
- Safe in renal disease
- Not robust effect on bone density and fracture prevention
- Often used for pain from vertebral fracture

**Bisphosphonates**
- Inhibit Osteoclastic Activity
- Alendronate (Fosamax)
- Ibandronate (Boniva)
- Risedronate (Actonel)
- Zoledronic Acid (Reclast)
- Not used in renal failure

### Drug Common Dose Frequency Route Site of Fx Prevention

<table>
<thead>
<tr>
<th>Drug</th>
<th>Common Dose</th>
<th>Frequency</th>
<th>Route</th>
<th>Site of Fx Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>70 mg</td>
<td>Weekly</td>
<td>Oral</td>
<td>Hip, vertebral, nonvertebral</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>150 mg/3 mg</td>
<td>Monthly</td>
<td>Oral/IV</td>
<td>Vertebral</td>
</tr>
<tr>
<td>Risedronate</td>
<td>35 mg</td>
<td>Weekly</td>
<td>Oral</td>
<td>Hip, vertebral, nonvertebral</td>
</tr>
<tr>
<td>Zoledronic Acid</td>
<td>5 mg</td>
<td>Yearly</td>
<td>IV</td>
<td>Hip, vertebral, nonvertebral</td>
</tr>
</tbody>
</table>

**Contraindications**
- Esophageal abnormalities (oral agents)
- Inability to sit or stand for at least 30 mins (oral agents)
- Hypocalcemia
- Renal insufficiency (<30 to 35 mL/min)

**Side Effects and Considerations**
- Gastrointestinal side effects
- Long term skeletal retention
- Musculoskeletal pain
- Small risk for osteonecrosis of jaw
- Small risk for atypical femur fx (long term)

**Atypical Femur Fracture “Classification Criteria”**
- All Major Factors must be present:
  - Location anywhere along the femur, from just distal to the lesser trochanter to just proximal to the supracondylar flare
  - No or minimal trauma
  - Transverse or short oblique configuration
  - Non comminuted
  - Extend through both cortices and may be associated with a medial spike OR incomplete fracture that involves only the lateral cortex
Atypical Femur Fracture
“Classification Criteria”

- Minor (don’t need any of these, just additional data)
- Localized periosteal reaction of the lateral cortex including beaking or flaring
- Increase in cortical thickness of diaphysis
- Prodrome of dull pain in thigh or groin
- Bilateral fractures and symptoms
- Delayed healing
- Comorbidities including RA and vit D deficiency
- Use of steroids, bisphosphonates or proton pump inhibitors.

Denosumab (Prolia)

- RANK ligand (RANKL) inhibitor
- Prevents osteoclasts from maturing
- 60 mg Q 6 months, subcutaneous
- Hip, vertebral and nonvertebral fractures

- Hypocalcemia
- Chronic renal insufficiency (< 30 mL/min)

Parathyroid Hormone (PTH)

- Teriparatide (Forteo)
- Directly stimulates osteoblasts

- Postmenopausal female with severe osteoporosis (T -2.5 or greater and at least one fracture) who are unable to tolerate any of the available bisphosphonates
- OR who continue to fracture despite bisphosphonates
- OR postmenopausal females unable to tolerate bisphosphonates
- OR relative contraindications

Denosumab (Prolia)

- History of serious skin infections
- Concomitant immunosuppressive therapy or autoimmune disease
- Dermatitis
- Osteonecrosis of jaw

PTH

- 20 ug, daily, subcutaneous injection
- Vertebral and nonvertebral
- Paget’s disease
- Unexplained elevation of alk phos
- Hyperparathyroidism
- Preexisting hypercalcemia
- Prior bone malignancies or bone mets
- Prior radiation tx to skeleton

- Osteosarcoma has NOT been seen in humans receiving PTH for < 2 years
**Romosozumab**
- Monoclonal Anti-Sclerostin Antibody
- Sclerostin inhibits bone formation
- Increases bone formation and reduces bone resorption
- 210 mg SubQ Monthly
- Ongoing trials. Phase II shows increased BMD gains when compared to teriparatide

**Odanacatib**
- Cathepsin K inhibitor – inhibits bone matrix degradation, decreases resorption
- Cathepsin K degrades bone matrix
- Significant fracture risk reduction
- INCREASE STROKE RISK FDA HALTED

**Abaloparatide**
- Synthetic Analog of PTH related protein
- 80 mcg SubQ
- Similar to teriparatide (some phase III trials show better risk reduction of fracture)

**Monitoring Response to Therapy**

**Monitoring Therapy**
- Compliance
- Patients starting therapy: Follow-up DEXA at one year, if stable every two years
- Cr clearance at least Q one year

**Suboptimal Response**
- Having a Fracture
- BMD significant decrease
- Compliance
- Secondary causes of osteoporosis
- Inadequate GI absorption
- Inadequate vit D intake
Stopping Treatment

- After 4 to 5 years of treatment
- Reassess fracture risk
- Reassess fracture history
- Reassess medications
- Bone density STABLE

- Repeat DEXA one to two years after stopping therapy

Conclusions

- Silent Disease
- Significant Morbidity and Mortality
- Benefits Far Outweigh Risk in Majority of Cases

THANK YOU!