

Own the Bone: Osteoporosis for the Orthopaedic Surgeon

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Disclosures

- Speakers Bureau for Eli Lilly
 - Osteoporosis education
 - Lecture honoraria <\$10,000/year

Why?

- Hip fractures:
 - Excellent job of orthopaedic surgical management
 - Inadequate job of treating underlying disease
 - Patients discharged without diagnosis or management of underlying osteoporosis
 - Fractures are undertreated medically
 - Assumption that primary MD is responsible
 - Only 16%-20% of hip fracture patients receive osteoporosis care

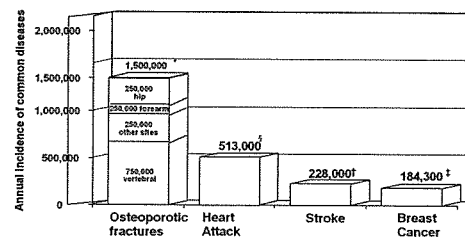
Why?

- Osteoporosis affects 45% of women aged 50 and older
- Osteoporotic fractures are 4 times more common than stroke
- Annual hip fractures
 - US: >300,000
 - Europe: >400,000
 - Incidence expected to double over the next 50 years

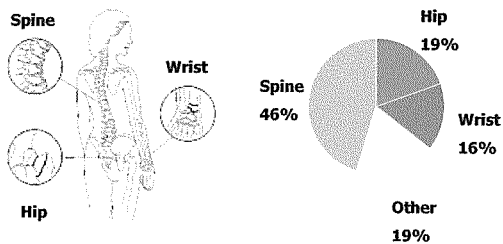
Why?

- Osteoporotic fractures pose a lifetime risk of death comparable to breast cancer
 - Cummings, Archives of Internal Medicine (1989)
- Osteoporotic fractures are a major risk factor for subsequent fractures
 - 10% have another fragility fracture within one year
 - 17%-21% have another fragility fracture within two years

Osteoporosis Fracture Incidence vs. Heart Attack, Stroke, Breast Cancer



Common Fracture Sites



Source: National Osteoporosis Foundation, 1997

FRAGILITY FRACTURE

Falls from standing height or less

Remember that if 50% of people have osteoporosis then 50% will fracture

NORMAL MAY NOT EQUAL IDEAL

What do I need to know?

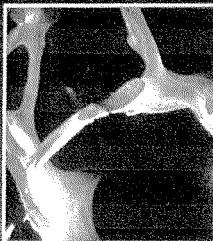
- What are the common causes of a fragility fracture
- What tests might I need to order
- What are the treatments for the various causes of a fragility fracture
- How can I help to realize which of my patients might be at risk for a fragility fracture

Osteoporosis Defined

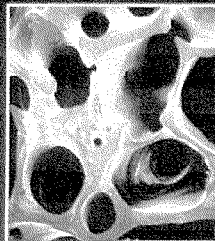
A metabolic bone disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk

OSTEOPOROTIC vs NORMAL BONE

Osteoporotic iliac crest



Normal iliac crest



Compston DW et al. J Bone Miner Res 1995;10:13

Bone Metabolism

- Integral part of endocrine system
- Constant remodeling
- Three cell types involved
 - Osteoblast
 - Osteoclast
 - Osteocyte

Osteoblast

- Mesenchymal cell origin
- Synthesize organic bone matrix
- Receptors
 - Estrogen
 - PTH
 - Vitamin D
- Produce
 - OPG
 - RANK Ligand
 - alkaline phosphatase

Osteocyte

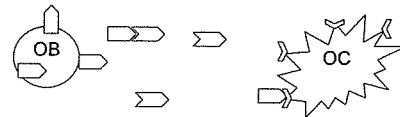
- From osteoblasts encased in matrix
- Connect with cytoplasmic processes
- No longer form bone
- Respond to mechanical signals and influence remodeling
 - sensing the bone microenvironment
 - stimulating systemic response

Osteoclast

- Monocyte precursor
- Recruitment/ development/activity signals
 - RANK ligand
 - M-CSF
- Resorb bone at ruffled membrane
 - Secrete protons/lysosomal enzymes

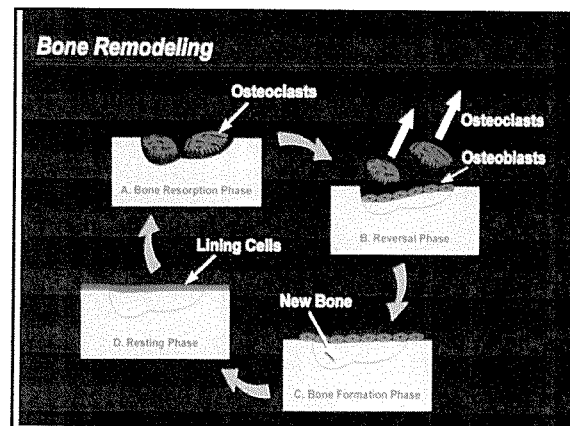
RANK/ RANK ligand

- RANK(⋈): receptor on osteoclast
- RANK-ligand(⊐): signal on surface of osteoblasts and secreted by them
- OPG(⊓): decoy receptor, inhibitor of RANK ligand



Bone Remodeling

- Osteoblasts drive the process via RANK/ RANK ligand signaling pathway
- Imbalance between bone resorption and bone formation



After Age 30 Bone Turnover

Usually Does Not

Replace

Full Bone Unit

The important players besides the cells

- Calcium
- Vitamin D
- Parathyroid hormone (PTH)
- Calcitonin

Calcium Regulation

- Intestines
 - Active absorb via calcium binding protein
- Kidney
 - mostly active reabsorption
- Bone
 - first source for calcium when needed
- Calcium balance
 - Renal excretion= intestinal absorption
 - Dietary intake requirement varies with age

Vitamin D

- Fat soluble steroid hormone
 - important in regulation of calcium metabolism
- Sources:
 - diet (vitamin D2 and D3)
 - Skin production (Vit D3)
- Hydroxylated
 - liver (@ 25th carbon)
 - kidney (@1st carbon)

Vitamin D

- Targets
 - Kidney
 - Increases calcium resorption
 - Intestines
 - regulates production of calcium binding protein
 - Bone
 - mobilization of calcium stores

Parathyroid Hormone

- Calcium sensing receptor on parathyroid cells
 - responds to low calcium levels
- Osteoblast receptors
 - initiates bone remodeling
 - Stimulate RANK ligand production
 - osteoclasts to resorb bone
- Kidney
 - Decreases PO_4 resorption
 - increased calcium resorption

Parathyroid Hormone

- Stimulate 1α hydroxylase
 - increase 1,25-Vit D levels
- Intestine
 - increase calcium binding protein production
 - greatest effect on calcium quantities
- PTHrP production by some cancers with similar effects

Calcitonin

- Produced by thyroid C-cells (parafollicular)
- Osteoclasts
 - Shrink
 - inhibit resorption of bone
 - lose ruffled border
- Decrease calcium/phosphate resorption in kidney

So how do we diagnose osteoporosis?

DXA Scan

- Currently the gold standard for diagnosis
- T score
 - Compares density relative to peak bone mass (Normal healthy 25 year old)
- Z score
 - Compares density to peers your same age
 - Use in people under age 25

DXA Scan



DXA Pros

Diagnostic
Low Radiation
Painless
Not Confining
Stay clothed!

DXA Cons

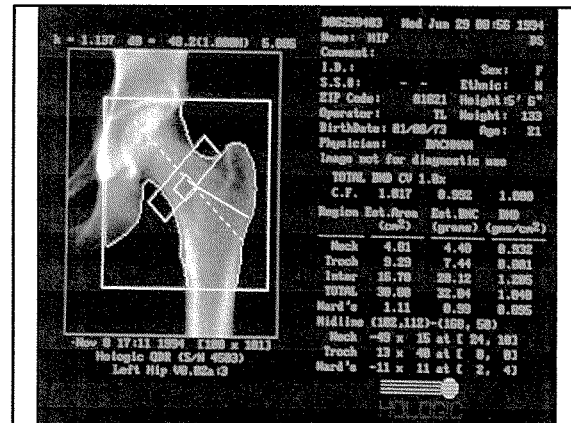
Cost?
Location?

Osteoporosis Diagnosis

- QCT (quantitative CT scan)
 - More radiation
 - very reader dependent
 - trabecular and cortical areas measured separately
 - Hydroxyapatite phantom for calculating density
 - Use in clinical trials
 - New interest in the use of peripheral QCT

Osteoporosis Diagnosis

- Ultrasound
 - May be a good tool for preliminary screening
 - Can only evaluate subcutaneous bones (calcaneus/tibia)
 - Fracture risk at hip/spine not correlate (only 70%)
 - Some evidence that overall risk of fracture correlates with poor measurements on ultrasound



WHO Definitions

- Bone mass measured at hip, spine, forearm
 - defined as standard deviations below peak bone mass
 - Lowest score defines level of disease
- -1 to -2.4= Osteopenic (mild to moderate bone deficiency)
- ≥ -2.5 = Osteoporotic
- Fragility fracture
 - Osteoporosis regardless of density score

Assessing Rate of Bone Loss

- Biochemical markers
 - Bone loss uses collagen cross-link products
 - N-telopeptide (urine)
 - Serum cross laps (blood)
 - Bone formation
 - Serum alkaline phosphatase (bone specific)
 - osteocalcin

High vs. Low Turnover Osteoporosis

- High Turnover
 - primary form that occurs at menopause
 - enhanced osteoclastic bone resorption
 - with more and deeper lacunae
 - osteoblasts unable to fully replace resorbed bone
 - high N-telopeptide
 - bone loss rate can be 2%-3% per year lasting 6-10 years

High vs. Low Turnover Osteoporosis

- Low Turnover
 - elderly
 - individuals with underlying genetic collagen disease
 - osteoclastic bone resorption normal or slightly decreased
 - failure of osteoblasts to form bone
 - NTX normal or even low
 - bone formation markers decreased levels