Management of “Osteoporosis”: What Do the Guidelines Say?

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Learning Goals

• Review guidelines for osteoporosis
• Consider these in light of pathophysiology
• Point out limitations of the guidelines
• Suggest a “fracture-centric” approach to patient care
Outline of Talk

• Why the Quotation Marks?
• Pathophysiology Review
• Diagnosis- Initial Bone Densitometry
• Non-Pharmacological Measures
• Medications
• Monitoring Therapy
• Summary and Questions
“Osteoporosis”

- The standard definition: “a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures”

- The operational definition: low bone mass (usually T-score < -2.5 by DXA, by WHO) as measured in the clinical setting
The Problem is Fracture, NOT Osteoporosis

• Osteoporosis in the absence of fractures has NO symptoms
• The WHO diagnostic criteria for osteoporosis are based on bone densitometry, NOT clinical outcomes
• While BMD is a useful tool in assessing fracture risk, there are other risk factors besides BMD
Fracture Incidence

• ~ 50% of Caucasian women will experience an osteoporotic fracture in their lifetime\textsuperscript{1,2}
• USA ~ 1.5 million osteoporotic fractures yearly
• Distribution\textsuperscript{1,2}
  – 700,000 Vertebrae
  – 250,000 Forearm
  – 250,000 Hip
  – 300,000 Other

Hip Fracture Outcomes

- 24% mortality within first year\textsuperscript{1}
- 50% of hip fracture sufferers unable to walk without assistance\textsuperscript{2}
- \sim 33% totally dependent\textsuperscript{3}
- 7.8% need long-term nursing home care for an average of 7.6 years\textsuperscript{4}

In vivo Loading

- Long bones are slightly curved and are loaded primarily by bending.
- There is tension on 1 side of the bone and compression on the other.
- Vertebrae are loaded primarily in compression.
Whole Bone Strength Components

- **Strength of the tissue**
  - Protein (primarily type 1 collagen)
  - Cross-linking
  - Mineralization

- **Size of the bone**
  - Cross-sectional area for compression
  - Moment of inertia for bending and torsion

- **Architecture of the trabeculae**
  - Orientation
  - Connectivity
Age Increases Hip Fracture Risk

Lightning Overview of Key Metabolic Issues

Ca, PTH, vitamin D
Whole Body Calcium Flux

- Bone: 
  - Ca\(^{2+}\) 1.0 kg
  - Ca\(^{2+}\) 0.5 g / Day

- Intestine: 
  - Ca\(^{2+}\) 1.0 g / Day
  - Ca\(^{2+}\) 0.2 g / Day
  - Ca\(^{2+}\) 0.8 g / Day

- ECF Ca\(^{2+}\)
  - Ca\(^{2+}\) 9.8 g / Day
  - Ca\(^{2+}\) 10.0 g / Day

- Kidney
  - Urine Ca\(^{2+}\) 0.2 g / Day
Integration of Flux

Low concentration of calcium in blood

Release of parathyroid hormone

- Efflux of calcium from bone
- Decreased loss of calcium in urine
- Enhanced absorption of calcium from intestine

Increased concentration of calcium in blood
Glucocorticoid Actions

- Glucocorticoids
  - Decreased Pituitary Hormone Secretion
    - Decreased IGF-1, E2, T
      - Decreased Ca Absorption
      - Increased IL-6
        - Decreased Muscle Mass
      - Decreased Matrix Production, Increased Resorption
Guidelines and Fracture Risk

- All guidelines include “fudge factor” for clinician’s assessment of fracture risk
- This is good, because it allows flexibility in justifying care and monitoring
- This is bad, because it limits utility of guidelines in individual, complex patients
- For the most part, risk factors are more heavily based on epidemiology than pathophysiology
“RED FLAGS” per US SG Report

• History of fractures related to mild or moderate trauma (e.g., a fall from standing height or less)
• Family history of bone disease
• Low body weight
• Weight loss of more than 1 percent per year in the elderly
• Late onset of sexual development
• Unusual cessation of menstrual periods
• Anorexia nervosa (often related to marked weight reduction)
• Athletic amenorrhea syndrome (related to intense physical activity)
• Patients being treated with drugs that affect bone metabolism (e.g., glucocorticoids)
• Patients with diseases linked to secondary osteoporosis
• High levels of serum calcium or alkaline phosphatase in otherwise healthy patients
• Hyperparathyroidism, hyperthyroidism, or treatment with high doses of thyroid hormone
• Height loss or progressive spinal curvature

http://www.surgeongeneral.gov/library/bonehealth/
Initial Bone Densitometry-Females

- Central DXA (consensus for all females over 65 years of age)
- National Osteoporosis Foundation (2003):
  - Also if low trauma fracture, + FH, weight under 127 lb, current smoking, chronic GCs
  - 60-64 + weight under 154 lb and/or no HRT
  - Postmenopausal < 65 years with risk factors, premenopausal with disturbed menses
Initial Bone Densitometry-Males

- Males over age 70 (ISCD)
- Males receiving GCs or GNRH agonists (consensus)
- Issue less studied in males, so recommendations are less fully developed and less well documented
Initial Bone Densitometry-Other

- Low trauma fracture
- Drugs interfering with vitamin D or bone metabolism (eg anticonvulsants, GCs)
- Malabsorption
- Rheumatoid Arthritis
- Hyperparathyroidism
- Hyperthyroidism
- Therapy for fracture prevention contemplated

Above are consensus recommendations
High-Risk Population v All-Comers

• By virtue of your practice in subspecialty medicine, your patients’ risk of low trauma fracture is much higher than in general IM or other primary care setting
• Identifying patients at risk should initiate evaluation for fracture risk factors, focusing on secondary causes of fragility and correctable fracture risk factors

*Consider whether guidelines address your patients*
Nutrition + Lifestyle

• Recommendations apply to all age groups and risk strata, although details vary
• “Adequate” vitamin D
• “Adequate” dietary + supplemental calcium
• “Adequate” weight bearing exercise
• No smoking + ethanol in moderation
• Fall prevention

Above are consensus recommendations

http://www.surgeongeneral.gov/library/bonehealth/
Vitamin D

- 200 international units/day up to 50 years
- 400 international units/day 50 to 70 years
- 600 international units/day over 70 years
- Important limitations of RDA's
  - No distinction between D2 and D3
  - No accounting for latitude or skin pigmentation
  - No accounting for actual body stores

*RDB and many other boneheads: RDAs are not adequate*

Institute of Medicine, 2002
Calcium

• 210 mg/day up to 6 months
• 270 mg/day 6 to 12 months
• 800 mg/day 1 year to 8 years
• 1300 mg/day 9 years to 18 years
• 1000 mg/day 18 years to 50 years
• 1200 mg/day over 50 years
• 2500 mg/day maximum consumption
  (sometimes therapy of specific disorders requires higher consumption)

Institute of Medicine, 2002
Calcium- 2

• Preceding slide gives quantities of elemental calcium
• Supplements have varying % of elemental calcium
  – Carbonate 40%
  – Citrate 21%
  – Lactate 13%
  – Gluconate 9%
  – Glubionate 6.5%
Exercise

• Load bearing stimulates bone matrix formation
• Loads from muscle contraction exceed those from static weight bearing
• Gains in strength, balance, and coordination from exercise reduce fall risk
• For bone formation, high-impact is most helpful, but other considerations may lead to limitation of impact
Surgeon General’s Recommendations

Figure 7-2. General Recommendations for Physical Activity in Adults

- Balance training for fall prevention
- Strength training 2 to 3 times per week
- Weight bearing exercises such as walking
- 30 minutes or more of moderate physical activity on most, preferably all, days of the week


http://www.surgeongeneral.gov/library/bonehealth/
Falls Are A Big Deal

• One third of people over age 65 fall each year, with half of those falls being recurrent (i.e., the individual has fallen before).
• One in 10 falls results in a serious injury, such as a hip fracture. In fact, 90 percent of hip fractures result from falls.
• Falls account for 10 percent of visits to emergency room visits and 6 percent of urgent hospitalizations in the elderly.
• The risk of falling varies tremendously depending upon an individual’s risk factors. An elderly person with no risk factors has only a 10 percent chance of falling each year, compared to an 80 percent likelihood of falling for a person with four or more risk factors.

Fall Risk Factors

- Age
- Arthritis
- Depression
- Orthostasis
- Poor cognition
- Poor vision, gait, or balance
- Need for home health care
- Use of four or more medications

Treatment

- Low Trauma Fracture with low bone mass (consensus)
- Postmenopausal, BMD T-score < -2.0 (NOF)
- Postmenopausal, BMD T-score < -1.5 and risk factors (NOF)
- Postmenopausal, BMD T-score < -2.5 (AACE)
- Postmenopausal, BMD T-score < -1.0 and continued bone loss with nutritional + lifestyle measures (AACE)
Treatment- 2

- Use bisphosphonates, raloxifene, HRT, teriparatide (consensus)
- Calcitonin (NOF + AACE, ACR as second-line agent)
  - Most boneheads would agree with ACR position, also add newer bisphosphonates
- Support based on methodologically sound trials showing fracture reduction
Chronic GCs - ACR -(2001)

- Densitometry and basic lab evaluation at initiation of therapy
- Lifestyle modification, fall prevention education
- Ca + D (800 IU/day)
- Consider HRT if postmenopausal female, offer BCPs or cyclic ER/PR to premenopausal with menstrual irregularity
- Bisphosphonates: use ½ usual dose of alendronate in men, premenopausal women or postmenopausal women receiving HRT

Chronic GC’s- ACR- 2

• Calcitonin- 2\textsuperscript{nd} line agent
• Fluoride, teriparatide- not recommended
• Follow-up DXA
  – Minimum every 2 years
  – Up to every 6 months
• Premenopausal females receiving bisphosphonates should also use effective contraception

\textit{RDB opinion: Dose adjustment is arbitrary and unfounded}

Renal Bone Disease

- There is a wide spectrum of bone disease seen in patients with CKD. They require different management, based on pathophysiology.
- Major guidelines for CKD are KDOQI (2003), which are limited by being based primarily on expert opinion rather than strong evidence (evidence supported points asterisked on following slides).
Renal Osteodystrophy

Calcium, Vitamin D, Aluminum

Adynamic
Normal
Mild
Osteitis Fibrosa

Osteomalacia
Mixed Lesion
Osteomalacia + HPT

PTH
K/DOQI Recommendations-1

• GFR <60 mL/min/1.73 m² should be evaluated, monitored annually stage III, quarterly IV and V (Ca, P, PTH), with target of normal Ca, P, Ca x P < 55, and
  – III: Ca normal, P 2.7-4.6, PTH 35-70
  – IV: Ca normal, P 2.7-4.6, PTH 70-110
  – V: Ca ideally < 9.5 and at least <10.2, P 3.5-5.5, PTH 150-300*

• DXA

http://www.kidney.org/professionals/kdoqi/guidelines_bone
K/DOQI Recommendations-2

- Bone Bx in selected cases only, but it remains gold standard in diagnosis of renal bone disease
- Restrict dietary P and use binders as necessary (P or PTH above target)*
- Restrict Ca to 2000 mg (less than general population, max 1500 mg from P binders)
- D supplementation to 25-OH-D ≥ 30 (III + IV)
- Active D therapy in stage V and PTH > 300, or PTH > target and 25-OH D adequate in III + IV

http://www.kidney.org/professionals/kdoqi/guidelines_bone
K/DOQI Recommendations- 3

- Suspicion of adynamic or Al bone disease is usual reason for bone bx
- Adynamic bone disease should be treated by allowing PTH to rise
- Osteomalacia should be treated by increasing D, and if necessary P
- Parathyroidectomy if PTH > 800 and/or Ca and P over target, refractory to medical rx

http://www.kidney.org/professionals/kdoqi/guidelines_bone
Summary and Editorial Comment

• Guidelines are overlapping - many areas of agreement among publishers, but some differences in details
• Guidelines, particularly those of Surgeon General, NOF, and AACE, are geared for primary care setting and focus largely on identifying patients at risk of fracture
• Subspecialists in geriatrics, rheumatology, nephrology, pulmonology, transplant medicine, and endocrinology see a patient population that is highly skewed toward increased risk.
Summary and Editorial Comment

• If patient is referred to any of you, a comprehensive bone disease evaluation is warranted, per Dr. Hansen’s lecture earlier this month or my upcoming geriatrics core lecture on fragility fracture

• Many areas of disagreement, incomplete evidence, and conflicts between incompatible goals exist
The bottom line

If you want 6 opinions, ask 4 subspecialists what they think.

Thanks for your attention.