Update on Osteoporosis

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Geisel School of Medicine
Disclosure

- I am an osteoporosis enthusiast
- I am not a nationally known speaker
- So no one gives me money to speak on this topic!
Objectives

- Review the tools used to make the diagnosis of OP and the pitfalls of this technology
- Learn some strategies for when bisphosphonates “fail”
- Learn where newer osteoporosis drugs fit into treatment
First case

- 65 year old woman comes to you because of a DXA scan showing a T-score of -2.6 in the lumbar spine.
- She wonders what she should do about this finding?
- What do you advise her?
She is on no risky meds
Good diet
No eating disorder, renal, liver, or thyroid disease
No FH or personal history of fracture
Lifetime non-smoker
1 glass wine per day
Normal labs
What labs are recommended?

- CBC
- Renal, liver function, calcium, phosphate, TP
- PTH
- TSH/T4
- Urine calcium?
- Vit D
Diagnosis of OP

- Based on T-score per WHO
- Central DXA
- Either femoral neck, total femur OR L1-4
- Only in postmenopausal women, men over 50
- In other groups, use the z-score to report “low bone mass for age”
- **A low impact/low energy fracture is considered evidence of OP regardless of DXA**
Advice for patient

- FRAX
- VFA – vertebral fracture assessment
- Urinary NTX (n-telopeptide)
FRAX

www.shef.ac.uk/FRAX/
### Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

**Country:** US (Caucasian)  
**Name / ID:**

**Questionnaire:**

1. Age (between 40-90 years) or Date of birth
   - **Age:** 72  
   - **Date of birth:** Y: 1937 M: 7 D: 28

2. Sex
   - Male  
   - Female

3. Weight (kg)
   - 67.13

4. Height (cm)
   - 170.18

5. Previous fracture
   - No  
   - Yes

6. Parent fractured hip
   - No  
   - Yes

7. Current smoking
   - No  
   - Yes

8. Glucocorticoids
   - No  
   - Yes

9. Rheumatoid arthritis
   - No  
   - Yes

10. Secondary osteoporosis
    - No  
    - Yes

11. Alcohol 3 or more units per day
    - No  
    - Yes

12. Femoral neck BMD (g/cm²)
    - Hologic  
    - .650  
    - **T-score:** -1.7

**BMI:** 23.2

The ten year probability of fracture (%)

- **Major osteoporotic:** 28
- **Hip fracture:** 14

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**Weight Conversion:**
- 148 pound = 67.13 kg

**Height Conversion:**
- 67 inch = 170.18 cm
Look at the study!!
Name: 
Patient ID: 
DOB: 
Sex: Female
Ethnicity: White
Height: 64.8 in
Weight: 119.8 lb
Menopause Age: 45
Age: 52

Scan Information:
Scan Date: February 07, 2003
Scan Type: L4 Lumbar Spine
Analysis: February 07, 2003 10:47 Version 11.2.3
Operator: TLS
Model: Delphi A (S/N 70512)

DXA Results Summary:

<table>
<thead>
<tr>
<th>Region</th>
<th>Area (cm²)</th>
<th>BMC (g/cm²)</th>
<th>BMD (g/cm²)</th>
<th>T-Score (%)</th>
<th>PR (%)</th>
<th>Z-Score (%)</th>
<th>AM (%)</th>
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<tbody>
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<td>Total</td>
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<td>0.970</td>
<td>-0.7</td>
<td>93</td>
<td>0.2</td>
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</table>

Total BMD CV 1.0%, ACF = 1.026, BCF = 1.015, TH = 1.031

Physician's Comment:
Reference curve and scores matched to White Female
Source: NHANES

Image not for diagnostic use
k = 1.146, d0 = 44.3
116 x 136
Take away message

- When things seem fishy, review the study not just the summary
- BMD isn’t everything, but it is a pretty good tool just know the limitations
- If there has been a fragility fracture, then the patient has OP regardless of DXA results
- Not all low T-scores are due to OP; consider multiple myeloma, marrow infiltration, osteogenesis imperfecta, osteomalacia and renal bone disease
If you decided to treat this patient, what agent works the best?

- Bisphosphonates: alendronate, risedronate, zoledronate, ibandronate
- Raloxifene
- Teriparatide
- Denosumab

What do you think?
All agents reduce fx over placebo in vertebral fx; all except raloxifene reduce non-vertebral fx.

For comparative effectiveness, there is no direct data, but a network meta-analysis shows no significant difference between the agents, except for raloxifene.

ADR – GI, esophageal cancer, atypical fx, ONJ, a-fib, myalgias/arthralgias (mild, uncommon or negative on re-evaluation).
Next case

- 75 yo lady with no prior testing or treatment for OP has a DXA scan showing a T-score of -2.6.
- She has no prior medical history and is on no medications.
- Her evaluation shows normal Calcium, Vit D, PTH, but a creatinine of 1.6 and a GRF of 28.
- How would you treat her?
Worth pointing out….

- Her risk is greater at the same T-score as the previous patient due to her age
- This will be apparent by FRAX testing
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<th>Age (years)</th>
<th>T-Score 0</th>
<th>T-Score -0.5</th>
<th>T-Score -1.0</th>
<th>T-Score -1.5</th>
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<th>T-Score -2.5</th>
<th>T-Score -3.0</th>
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<td>5.3</td>
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<tr>
<td>60</td>
<td>5.1</td>
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<tr>
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<td>24.5</td>
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</table>
Bisphosphonates

- Mainstay of treatment in OP
- Benefits outweigh risks
- Lots of administration options
- Reduces fracture risk by 50% even without change in BMD on treatment
- BUT cannot be used in renal insufficiency
Options

- Estrogen
- SERMs – selective estrogen modifiers
- Denosumab
Denosumab

- Monoclonal antibody against RANKL
- Interferes with the maturation and life of osteoclasts, thereby reducing bone turnover
- Given as an IV infusion twice a year.
- Inhibition stops when administration of the agent stops
- Also present on immune cells – so may increase infection
- May be good agent in those with inflammatory arthritis

NEJM 2009;36:756
Mechanism of action of denosumab

Factors stimulating bone resorption

RANKL

Osteoclast formation, activity, and survival stimulated

RANK

Osteoclasts

Osteoblasts

Denosumab binds to RANKL

Osteoclast formation, activity, and survival inhibited
Last case

- 70 yo woman on alendronate for 5 years
- Drug holiday recommended
- DXA shows progressive bone loss
What constitutes bisphosphonate failure?

- An increase or stability of BMD is considered **effective**
- If there is a >5% decrease in BMD
- If bone turnover markers remain high
- If there is a fracture
What should you do?

- Check for adherence to treatment including calcium and Vit D
- Consider malabsorption
- Switch to IV formulation
- Continue the medication and check in one year
- Switch to another agent
What are her options for treatment? Does she need to be treated?

- Switch to IV bisphosphonate
- Switch to denosumab
- Switch to teraperitide.
Teriparitide

- Is an osteoanabolic agent
- Given as a daily subcutaneous injection
- Increases BMD and decreases fracture risk
- Can cause hypercalcemia

- NEJM 2001; 344:1432
New agents in clinical trial

- Odanacatib – a selective cathepsin K inhibitor which inhibits bone resorption by osteoclasts but does not kill them, and increases bone formation (uncouples bone remodeling)

- Sclerostin inhibitors – blosozumab and romosozumab exert powerful anabolic effect on both cortical and trabecular bone

- Best Prac & Research Clin Endo & Meta 2014; 28:859
Osteoporosis tidbits

- Peak bone mass accrues earlier than thought
- 1/3 of vertebral fractures are asymptomatic
- Vertebral fractures increase mortality as does hip fracture
- 1% of falls leads to hip fractures
The quiz!

- What measurement on the DXA scan is used for follow up?
  - T-score
  - Z-score
  - BMD
  - Area
  - % change
What z-score should prompt an evaluation for secondary causes of OP?
- -2.0
- -1.5
- None
- Every
What are the FRAX thresholds for treatment?

- All fracture of >20%
- Hip fracture of >3%
- All fractures of >10%
- Hip fractures of >1%  
- All fracture of >30%
- Hip fracture of >5%
Who to screen?

- Women older than 65
- Women older than 50 with risk factors
- Anyone with fracture
- Men over age 70
Thank you!!

- Questions?
Scan Information:
Scan Date: November 12, 2005
ID: A11120501
Scan Type: x Lumbar Spine
Analysis: November 12, 2005 09:48 Version 12.4:3
Lumbar Spine
Operator:
Model: Discovery C (S/N 81202)
Comment:

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<tr>
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<td>105</td>
<td>1.9</td>
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</tbody>
</table>

Total BMD CV 1.0%, ACF = 1.000, BCF = 1.000, TH = 3.855
WHO Classification: Normal
Fracture Risk: Not Increased

Physician's Comment: