SESSION C2

Osteoporosis: Focus on Fractures

Susan Ott, MD

Session Description:

Osteoporotic fractures are a serious problem in older adults, and a leading cause of disability and loss of independence.

Learning Objectives:
Following my presentation, participants will be able to:
1. List the most important risk factors for an osteoporotic fracture.
2. Provide life-style advice that can help reduce fracture risk.
3. Discuss appropriate time to initiate prescription medications for osteoporosis treatment.
Osteoporosis: Focus on Fracture

Susan Ott, MD
October 2014

Objectives
• 1) Explain the difference between osteopenia and osteoporosis
• 2) List important risk factors for fractures
• 3) Describe the effects of bisphosphonates, raloxifene, estrogens, and other osteoporosis drugs on the risk of fractures

Lumbar Spine
Young Normal
Osteoporotic

Images courtesy of Ralph Müller, PhD, Switzerland

Bone density loss with aging

10 yr risk of an osteoporotic fracture
W.H.O. Risk Factors

<table>
<thead>
<tr>
<th>Risk Ratio</th>
<th>RR with BMD</th>
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<tbody>
<tr>
<td>BMI (20 vs 25)</td>
<td>1.95</td>
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<tr>
<td>Parental hip fracture</td>
<td>2.27</td>
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<tr>
<td>Glucocorticoids</td>
<td>2.31</td>
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<tr>
<td>Prior fragility fracture</td>
<td>1.85</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.84</td>
</tr>
<tr>
<td>High intake alcohol</td>
<td>1.68</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1.95</td>
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</table>

A 55-Year-Old Woman With Osteopenia

Who’s going to break her hip?

Which fractures are osteoporotic?

MAJOR: hip spine shoulder wrist

OTHER: ribs sternum, clavicle, scapula rest of humerus, radius, ulna pelvis rest of femur tibia & fibula above ankle

Body Mass Index

DeLaet, Osteoporosis Int 2005

Smoking

Kanis, Osteoporosis Int 2005
Secondary Osteoporosis

corticosteroids
anticonvulsants
gonadotropin releasing hormone agonists
aromatase inhibitors
depo-medroxyprogesterone acetate
SSRI’s
loop diuretics
excess thyroid
heparin
glitzones
anti-neoplastic agents
cyclosporin
methotrexate
proton-pump inhibitors
anti-retroviral therapy

Bone density by eGFR

data from NHANES

Vertebral fractures

- ignored on ~50% of radiology reports
- risk for a new fracture is 4 times higher than in a person with the same BMD without a fracture
- new fractures cause pain in about 40% of cases
- should be prescribed medication to strengthen bone!
If BMD at spine is low but hip is not:

- Check DEXA images to be sure study was done properly.
- Scoliosis can cause inaccurate DEXA results
- Check for vertebral fracture (if present, treat)
- If scans done correctly, then add 10% of the fracture risk to the FRAX score for every SD difference between spine and hip.

For example, if risk of fracture is 25% and spine is one SD lower than hip, the risk will be 25% + 2.5% = 27.5%

When to add medications

Donaldson, 2009, JBMR
Dawson-Hughes, 2009, OI

1,200 mg/day from all sources.
Don't give too much.
### LVA Morphometry

<table>
<thead>
<tr>
<th>Region</th>
<th>Avg. Ht. (^2) (cm)</th>
<th>Z-score</th>
<th>M/P Ratio (^2) (%)</th>
<th>Z-score</th>
<th>A/P Ratio (^2) (%)</th>
<th>Z-score</th>
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<td>96</td>
<td>0.8</td>
<td>105</td>
<td>1.7</td>
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<td>-1.2</td>
<td>102</td>
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<td>88</td>
<td>-0.5</td>
<td>89</td>
<td>-0.8</td>
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<td>L1</td>
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<td>88</td>
<td>-0.8</td>
<td>96</td>
<td>0.1</td>
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<td>91</td>
<td>-0.3</td>
<td>103</td>
<td>0.6</td>
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<td>L3</td>
<td>2.51</td>
<td>0.1</td>
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<td>0.6</td>
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<td>106</td>
<td>1.2</td>
<td>119</td>
<td>2.2</td>
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</table>

**COMMENTS:**
When to add medications

Intervention Threshold

Major Fracture - 10 year fracture probability

Hip - 10 year hip fracture probability

Age (years)

Treat
Lifestyle advice and reassure
Calcium supplements
1200mg/day calcium from food plus supplements

These reliable brands are equally effective

Nutrition
- Adequate protein (fish, poultry, meat, dairy, nuts)
  1.0 – 1.2 g/kg body weight/ day
- Plenty of fruits and vegetables
- Avoid cod liver oil and magnesium supplements
- Underweight people should add high-calorie foods like olive oil, bread, pasta with cheese sauce, oil-based salad dressings, peanut butter, carrot cake and chocolate

Vitamin D
- Vitamin D:
  - Cholecalciferol (D$_3$) a little better than ergocalciferol (D$_2$
  600 IU/day younger than 70
  800 IU/day older than 70
- Blood levels of vitamin D should be between 20 and 50 ng/dl
  (= 50 to 125 nmol/l)

Tai-chi helps reduce falls
- Best to do weight-training exercises AND resistance-training exercises

Prevent Falls!
The usual stain for looking at bone sections results in green for mineralized bone and red-orange for osteoid. Here there will be a crack in the bone, following by “origination” of the BMU, and then resorption and then formation. After the bone has refilled the cavity, mineralization continues to increase, represented by the darker shades of green.

Bone remodeling showing multiple BMU’s

This is about 1.5mm of cancellous bone showing normal turnover. Remember that some BMU’s are going in and out of the plane of the section.

Bone remodeling at menopause

The resorption lasts a little longer and formation is also increased. Watch for perforations and micro-fractures.
Perimenopausal Bone Loss

Bone loss over 1 year at menopause

Bone loss over 2 years at menopause

Bone remodeling with raloxifene treatment

After 6 months, the medicine is given (stars). The effect is subtle but notice the LACK of perforations.
Bone remodeling with bisphosphonate treatment

After 6 months, the medicine is given (blue dots). They deposit in the bone and inhibit resorption.

Bone remodeling with PTH treatment

After 6 months, the medicine is given (chain of amino acids). The duration is short because that is when the study ended.

Tetracycline labels after 6 months

Estrogen

- Most effective for the skeleton, but . . .
- Increases risk of thrombophlebitis (oral dosing)
- When given without progesterone, does not increase risk of coronary artery disease or breast cancer, but does increase risk of endometrial cancer
- I think it is a good choice for women within first decade after menopause who have osteopenia, who also get more benefits from relief of menopausal symptoms
My Approach
1) For patients with low or moderate fracture risk, provide life-style advice
2) For women within 5 years of menopause consider estrogen if they have bone density that is below average.
3) For women with moderate to high fracture risk who are older than 60, consider raloxifene. Calcitonin is a 2nd choice.
4) For patients with a fragility fracture or hip bone density lower than T-score of -2.5, add a treatment drug such as bisphosphonate, denosumab, teriparatide or raloxifene, depending on the severity and other diseases.

Estrogen vs Alendronate

N = 1609
Women younger than 60

Non-vertebral fracture incidence

Nelson, Arch Intern Med 2002

Raloxifene
- Antagonistic to estrogen in breast
- May make hot flashes worse
- Not effective in premenopausal women
- No effect on uterus
- Acts like estrogen on bone
- Decreases LDL cholesterol like estrogen
- Increases blood clotting like estrogen
Bisphosphonates

- Indicated for patients with vertebral compression fractures or hip fractures or a bone density in the hip lower than -2.5
- Poor oral absorption: take on empty stomach and don’t eat for ½ hour
- Esophageal irritation: take with ½ glass of water and do not lie down or bend over for ½ hour
- Can be given as IV infusion that is effective for at least 2 years.

Results of FIT study

N = 6000
Women 55-80 with low BMD
Duration:
3 yrs (Fx present)
4 yrs (Fx absent)

Alendronate effects according to BMD

Risk of a clinical fracture in FIT2 study

Incidence of atypical femur fracture

Incidence per 100,000/yr

Duration bisphosphonate use, yrs

Dell, JBMR, 2012
Denosumab

Contra-indications

* Hypocalcemia
* Pregnancy or lactation
* Chronic Kidney Disease stage 4-5 (eGFR less than 30)
* Patients at risk for serious infections
* Patients with serious chronic liver disease (no studies)
* Children

Intermittent PTH

- recombinant PTH 1-34 (teriparatide) approved for treatment of osteoporosis
- high doses caused osteosarcoma in 50% of laboratory rats, but not in primates or humans
- anabolic effect diminishes with time after about a year
- expensive, requires daily injection

- until more long-term data available, I suggest this drug should be limited to those with severe disease who have become worse on other therapy