Fractures: Epidemiology and Risk Factors

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Outline

• Fracture incidence and impact of fractures
• Major determinants of fracture incidence
  – Gender
  – Age
  – Race
  – Geography
• Clinical risk factors for fracture

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  – Age
  – Race
  – Geography
• Clinical risk factors for fracture

Osteoporotic fractures: Comparison with other diseases

1996 new cases, all ages

American Heart Association, 1996
American Cancer Society, 1996
Riggs BL & Melton LJ 3rd, Bone, 1995;17(suppl):S51-S65
Common sites of fracture

- Spine
- Hip
- Wrist

Cooper C et al. J Bone Miner Res 1992

5-year Risk of Fracture: Role of Age and Sex

- Men
- Women

Age Group, yr

5 year fracture risk

5-year Risk of Fracture: Role of Age and Sex

- Hip
- Vertebrae
- Wrist

Impact of Vertebral Fractures

- 20% excess mortality in 5 yrs after fracture
- Deformity & height loss
- Acute & chronic pain
- Pulmonary dysfunction
- Diminished quality of life: loss of self-esteem, sleep disorder, depression, loss of independence

Hip fractures are associated with increased morbidity and mortality

- One year after a hip fracture:
  - Death within one year: 20%
  - Permanent disability: 30%
  - Unable to walk independently: 40%
  - No longer able to live independently: 50%

- Direct costs: > $10 billion / yr
  - Cost of hip fracture > $80,000 per person

Cooper C. Am J Med. 1997;103(2A):12S-17S.
Prospects for the Future...

- Elderly represent fastest growing segment of population

World Population: 1990 and 2025

Rates of hip fracture vary dramatically by region and country

Worldwide Distribution of Hip Fractures in Women: 1990 to 2050
Vertebral fractures have more similar incidence worldwide than hip fractures

**Lifetime risks of clinical fractures**

50 year old white women (U.S.)

- Hip fracture: 17%
- Wrist fracture: 16%
- Vertebral fracture: 16%
- Any fracture: > 50%
- Breast cancer: 15%

*Refs: Melton; Black; Kanis

**Lifetime risks of fracture: Impact of gender**

<table>
<thead>
<tr>
<th>Fracture</th>
<th>Lifetime Risk at Age 50*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>Men (%)</td>
</tr>
<tr>
<td>Wrist</td>
<td>3</td>
</tr>
<tr>
<td>Clinical Vert Fx</td>
<td>5</td>
</tr>
<tr>
<td>Any</td>
<td>16%</td>
</tr>
</tbody>
</table>

*Among Caucasians

**Osteoporosis in Men**

- 1 in 5 to 6 men over age 50 will suffer osteoporotic fracture
- 30% of hip fractures worldwide are in men
- Mortality rates due to fracture higher in men than women
- Treatment rates following fracture are abysmal
Race and rate of hip fractures (age adjusted to U.S.)

<table>
<thead>
<tr>
<th>Race</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian (US)</td>
<td>968</td>
<td>396</td>
</tr>
<tr>
<td>Black (US)</td>
<td>214</td>
<td>179</td>
</tr>
<tr>
<td>Hispanic (US)</td>
<td>219</td>
<td>97</td>
</tr>
<tr>
<td>Asian</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US (California)</td>
<td>383</td>
<td>116</td>
</tr>
<tr>
<td>Japan</td>
<td>227</td>
<td>79</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>389</td>
<td>196</td>
</tr>
<tr>
<td>Beijing</td>
<td>97</td>
<td>101</td>
</tr>
</tbody>
</table>

Luz Villa, Osteoporosis, 2001. Rates per 100,000 person-years, age-adjusted

Clinical risk factors for fracture

Age is Independent of BMD as Risk Factor for Hip Fracture (more later, S. Harris)

Cooper C et al. J Bone Miner Res 1992

Kanis et al. 2004

5-fold increase in fracture probability from age 50 to 80 at same BMD
**Previous non-vertebral fracture predicts future fracture**

- History of *any* fracture: 1.5-3.0 fold greater risk of fracture

*True for*
- any fracture type
- even traumatic fractures
- especially strong for men
- Mostly independent of BMD

vanStaa, Osteop Int 2002;13:624-9

**Vertebral fractures indicate a very high risk of future fracture**

- 4x risk of more vert fxs
- 2x risk of other fractures  
  (vanStaa, Osteop Int 2002)
- Women with clinical diagnosis of vertebral fracture have 5-15% 5 yr hip fracture risk!

*Not in FRAX*

**Existing Vertebral Fracture Predictive of Future Vertebral Fracture Independent of BMD**

<table>
<thead>
<tr>
<th>Previous Vert Frx</th>
<th>No Vert Frx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low BMD</td>
<td>5.8</td>
</tr>
<tr>
<td>Mid BMD</td>
<td>3.4</td>
</tr>
<tr>
<td>High BMD</td>
<td>2.3</td>
</tr>
<tr>
<td>1 vert fx</td>
<td>1.7</td>
</tr>
<tr>
<td>&gt;1 vert fx</td>
<td>1.0</td>
</tr>
<tr>
<td>0 vert fx</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Ross 1991

**Effect of prevalent radiographic vertebral fracture on non-vertebral fracture risk**

<table>
<thead>
<tr>
<th>Femoral neck T-score</th>
<th>Absolute fracture risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2</td>
<td>No vert fx: 4.0, &gt;1 vert fx: 5.0</td>
</tr>
<tr>
<td>-3</td>
<td>No vert fx: 3.5, &gt;1 vert fx: 4.5</td>
</tr>
<tr>
<td>-4</td>
<td>No vert fx: 3.0, &gt;1 vert fx: 3.5</td>
</tr>
</tbody>
</table>

Siris et al, Osteop Int 2007
Family history of hip fracture is a strong risk factor for hip fracture

- 2-fold increased risk of hip fracture
- Regardless of hip BMD
- “My mother had a spine fracture” or “osteoporosis”: no increased risk.

Guess our risk of hip fracture

Higher weight is protective.
Lower weight is strong predictor of hip fracture and of low BMD

Low BMI is a strong risk factor for fracture

De Laet et al. 2005

Corticosteroids (more later, J. Graf)

Van Staa, Osteop Int 2002
**Rheumatoid arthritis**

Orstavik et al 2004

**Smoking**

- Smokers have a 1.4 to 2-fold increased risk of hip fracture.
- *Independent* of BMD.
- Due to poor health, weaker muscles & impaired balance

**Alcohol and risk of hip fracture**

- ≤ 2 drinks/day: no increased risk
- > 2 / day
  - 30-40% increased risk
  - 6-10/day in men: ~ 5 X risk
- Greater risk with beer than wine! (?)

Hoidrup Am J Epidemiol 1999;149:993

**Summary of Risk Factors for Fracture**

- Age, gender, race, geography
- BMD
- Previous fracture
- Parent fractured hip
- Body Mass Index (BMI) (weight/height^2)
- Current smoking
- Glucocorticoids
- Alcohol 3+ drinks/day
- Secondary osteoporosis (if BMD not included)
- Others
More Clinical Risk Factors for Fracture

- Parkinson’s: 2x higher risk (hip)
- Dementia: 2x higher risk (hip)
- Diabetes: 20 to 40% higher risk (hip)
- Early menopause (<47 yrs): 70% higher risk (all)
- Frequent falls: 80% higher risk (hip)
- Chair stand as a measure of physical function. Uses arms to stand: 70% higher risk (hip)
- Medications that are bad for the bone
  - Thyroid meds, TZD’s, aromatase inhibitors, and more..(later)

Very High risk groups

- Nursing homes
  - 4 to 6% hip fracture per year
- Post-stroke
  - Over 70 years: 3-5% annual hip fracture risk for women and ~2% per year for men

Surprising Non-Risk Factors

- Hair color/skin pigment
  - Common wisdom: Blonds/light skin higher risk
  - Truth: Blondes & brunettes & redheads seem to have same risk
- North-South gradient of risk
  - Common wisdom: Fracture risk increases as you go north
  - Truth: Lower hip fracture risk in north U.S.

Combining Risk Factors for Osteoporosis

- In heart disease, risk factors (e.g. BP, lipids, smoking) play independent role
  - Risk factor models and tools are in common clinical use
- For fractures, BMD doesn’t tell the whole story and that other risk factors play important (and independent) role
  - T-scores alone are problematic
- Develop systems for estimating risk based on multiple risk factors
Combining BMD with Clinical Risk Factors

WHO Risk Model (FRAX): Overview

- To be discussed by Dr. Harris
- Based on 10 year risk of hip or major clinical fracture
- Combine observational studies from around the world to define a set of robust risk factors. With and without BMD.
- Make country-specific risk-based diagnostic and treatment thresholds based on local considerations
- Other risk prediction equations have been proposed (Garvin, Qfracture, etc)

Summary

- Fractures are common (and will become more common), and are associated with significant morbidity, mortality and costs.
- Fracture risk is multifactorial
- Strong risk factors (besides BMD) include:
  - Older Age
  - Gender
  - History of fracture especially vertebral fracture
  - Maternal history of hip fracture
  - Low weight
- Methods for combining risk factors, together with BMD are now available

Thank you