Fractures:
Epidemiology and Risk Factors

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Disclosures
A. Schwartz
Consulting: Merck

Outline

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

Epidemiology of Osteoporotic Fractures

• 1.5 million fractures in US annually
• 44 million individuals in US at risk for fracture
  – Treatable hypertension: 30 -50 million
  – High cholesterol: 40 million
• At age 50, a woman’s lifetime risk of fracture exceeds combined risk of breast, ovarian & uterine cancer
  – 1/3 women will have a fracture
• At age 50, a man’s lifetime risk of fracture exceeds risk of prostate cancer
  – 1/5 men will have a fracture

Surgeon General’s Report on Bone Health, 14 October 2004
Osteoporosis in Men, International Osteoporosis Foundation, Oct 2004

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44 million individuals in US at risk for fracture
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Common sites of fracture

Spine
Hip
Wrist

Overall incidence of fractures

Annual incidence (rate/1000)

Men
Women

Johansen et al, 1997

Overall incidence of fractures

Men
Women

0 20 40 60 80 0

Johansen et al, 1997

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

Men Women

Hip Vertebrae Wrist

Hip Vertebrae Wrist

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

Cooper C et al. J Bone Miner Res 1992

Hip fractures are associated with increased morbidity and mortality

One year after a hip fracture:

Patients (%)

Death within one year Permanent disability Unable to walk independently No longer able to live independently

20% 30% 40% 50%

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

Hip fractures are associated with increased morbidity and mortality

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

Cooper C. Am J Med. 1997;103(2A):12S-17S
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, distorted body image, dependence on narcotic analgesics, sleep disorder, depression, loss of independence

Prospects for the Future ...

- Elderly represent fastest growing segment of population
- By 2020, one-half of US citizens older than 50 will be at risk for fractures from osteoporosis

World Population: 1990 and 2025

Worldwide Distribution of Hip Fractures in Women: 1990 to 2050
Rates of hip fracture vary dramatically by region and country

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nigeria</td>
<td>1</td>
</tr>
<tr>
<td>Japan</td>
<td>108</td>
</tr>
<tr>
<td>Oxford</td>
<td>142</td>
</tr>
<tr>
<td>Minnesota</td>
<td>320</td>
</tr>
<tr>
<td>Sweden</td>
<td>378</td>
</tr>
<tr>
<td>Norway</td>
<td>421</td>
</tr>
</tbody>
</table>

Geographic Variation — Lifetime Risk of Hip Fracture at Age 50 yrs

Less variation in prevalence of ‘vertebral fractures’ by standard definitions

<table>
<thead>
<tr>
<th>Region</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>27</td>
</tr>
<tr>
<td>Taiwan</td>
<td>21</td>
</tr>
<tr>
<td>Minnesota</td>
<td>15</td>
</tr>
</tbody>
</table>

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>Men (%)</th>
<th>Women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Wrist</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>Clinical Vert Fx</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Any</td>
<td>16%</td>
<td>&gt; 50%</td>
</tr>
</tbody>
</table>

* Among Caucasians

### Osteoporosis in Men

- 1/5 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

### Outline

- Fracture incidence and impact of fractures
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  - Gender
  - Age
  - Race
  - Geography
- Clinical risk factors for fracture
Age and BMD Are Independent Risk Factors for Hip Fracture (more later, S. Harris)

- > 5-fold increase in fracture probability from age 50 to 80

Kanis et al, 2004

Combining BMD with Clinical Risk Factors

Cummings et al., NEJM 332(12):767-773, 1995

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
- In osteoporosis, growing realization that 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

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
Risk factors in WHO FRAX calculator

- Age, gender, race, geography
- BMD
- Previous fracture
- Parent fractured hip
- Body Mass Index (BMI) (weight/height²)
- Current smoking
- Glucocorticoids
- Rheumatoid arthritis
- Alcohol 3+ drinks/day
- Secondary osteoporosis (if BMD not included)

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!

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

Ross 1991

Existing Vertebral Fracture Predictive of Future Vertebral Fracture Independent of BMD

Siris et al, Osteop Int 2007
**Previous non-vertebral fracture predicts future fracture**

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

*True for*
- any fracture type (ankle, finger)
- even traumatic fractures
- especially strong for men
- Mostly independent of BMD

vanStaa, Osteop Int 2002;13:624-9

**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

De Laet et al. 2005

**Low BMI is a strong risk factor for fracture**

- Lower BMI is a strong risk factor for fracture
**Corticosteroids**  
*(more later, J. Graf)*

- 6-10% loss of spine BMD in 6-12 months of $\geq 10$ mg prednisolone / day
- Strong ($r=-0.6$) correlation between cumulative dose and deficit in spine BMD
- Clinical guidelines recommend bisphosphonate therapy to prevent bone loss

[Van Staa, Osteop Int 2002](#)

**Rheumatoid arthritis**

![Graph showing correlation between cumulative dose and deficit in spine BMD](#)

[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

![Skull with a cigarette](#)

**Alcohol and risk of hip fracture**

- $\leq 2$ 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](#)
Risk Factors – Not in FRAX

There are strong clinical risk factors for fracture that are not in FRAX.

Highest 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

Clinical Risk Factors for Fracture

- Parkinson’s: 2x higher risk (hip)
- Dementia: 2x higher risk (hip)
- Diabetes: 80% 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)

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.
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