VERTEBRAL FRACTURE INITIATIVE
Part I

Overview of osteoporosis:
Epidemiology and clinical management

By Pawel Szulc and Mary Bouxsein
Definition of osteoporosis

A disease characterized by low bone mass and micro-architectural deterioration of bone tissue leading to reduced bone strength and a consequent increase in fracture risk.
OSTEOPOROSIS:
THE SIZE OF THE PROBLEM
Osteoporosis is a prevalent disease

- Estimated to affect 200 million women worldwide
  - 1/10 of women aged 60
  - 1/5 of women aged 70
  - 2/5 of women aged 80
  - 2/3 of women aged 90

  From European, North American, Japanese and Australian cohorts

- Worldwide, an osteoporotic fracture occurs every 3 seconds, a vertebral fracture every 22 seconds

- 20-25% Caucasian women and men over the age of 50 years have a prevalent vertebral fracture, 12% in Latin American women and men

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### Lifetime risk at the age of 50

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporotic fracture$^{1,2}$</td>
<td>46-53%</td>
<td>21-22%</td>
</tr>
<tr>
<td>Hip fracture$^{2,3}$</td>
<td>15-23%</td>
<td>5-11%</td>
</tr>
<tr>
<td>Radiographic vertebral fracture$^{4}$</td>
<td>27%</td>
<td>11%</td>
</tr>
<tr>
<td>Clinical vertebral fracture$^{2}$</td>
<td>15%</td>
<td>8%</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>10-13%</td>
<td></td>
</tr>
<tr>
<td>Prostate cancer</td>
<td></td>
<td>9-11%</td>
</tr>
</tbody>
</table>

NB: variable between countries

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Age-specific and sex-specific incidence of osteoporotic fractures

Comparison of osteoporotic fractures with other common diseases

Annual incidence in the United States - both sexes all ages

- Osteoporotic Fractures:
  - Hip: 300,000
  - Forearm: 400,000
  - Other sites: 800,000
  - Vertebral fractures (by X-ray): 550,000

- Heart Attack: 1,255,000

- Stroke: 795,000

- Breast Cancer: 186,500

Burge R et al. (2007) JBMR 22(3): 465
Increased burden of osteoporotic fractures worldwide

Estimated number of hip fractures (x1000)

- North America: 400 (1990), 800 (2050)
- Europe: 400 (1990), 800 (2050)
- Latin America: 100 (1990), 200 (2050)
- Asia: 1000 (1990), 4000 (2050)

Total hip fractures worldwide:
- 1990 = 1.66 million
- 2050 = 6.26 million

Adapted from Cooper C et al. (1992) Osteoporos Int 2: 285
OSTEOPOROSIS: MORTALITY & MORBIDITY
Similar mortality in patients with vertebral fractures and in those with hip fractures.
Relative risk of death following clinical osteoporotic fractures

Fracture Intervention Trial (FIT)*

*6459 postmenopausal women ages 55-81 years followed for an average of 3.8 years

Adapted from Cauley JA et al. (2000) Osteoporos Int 11: 556
Mortality rate increases with the number of prevalent vertebral fractures

$P$ for trend $< 0.001$

Adapted from Kado DM et al. (1999) Arch Intern Med 159: 1215
Vertebral fractures increase the risk of subsequent fragility fracture

- Women with vertebral fractures have a 5-fold increased risk of a new vertebral fracture and a 2-fold increased risk of hip fracture
  
  Black DM et al. (1999) J Bone Miner Res 14: 821
  Melton LJ 3rd et al. (1999) Osteoporos Int 10: 214

- Of women who suffer a vertebral fracture, 1 in 5 will suffer another vertebral fracture within a year
  
  Lindsay et al. (2001) JAMA 285(3): 320
Prior fracture increases the risk for future vertebral fracture, independent of BMD

**Risk of vertebral fractures (% per year)**

- Fracture: 5.8, 3.4, 2.3
- No Fracture: 1.7, 1.0, 0.2

**BMD Tertiles**
- Low
- Middle
- High

Adapted from Ross et al. (1991) Ann Int Med 114(11): 919
Prior vertebral fracture increases the risk of subsequent vertebral fracture

- RR=7.3 (4.4, 12.3) for ≥2 vertebral fractures at baseline
- RR=5.1 (3.1, 8.4) for ≥1 vertebral fracture at baseline
- RR=2.6 (1.4, 4.9) for 0 vertebral fractures at baseline

Adapted from Lindsay R et al. (2001) JAMA 285(3): 320
Incident vertebral fracture risk: effect of BMD and prevalent vertebral fractures

SQ score: worst grade of any fractured vertebra according to Genant semi-quantitative scale

Siris ES et al. (2007) Osteoporosis Int 18: 761
With kind permission from Springer Science+Business Media
Incident non-vertebral fracture risk: effect of BMD and prevalent vertebral fractures

SQ score: worst grade of any fractured vertebra according to Genant semi-quantitative scale

Siris ES et al. (2007) Osteoporosis Int 18: 761
With kind permission from Springer Science+Business Media
All types of vertebral fractures are associated with morbidity

![Bar chart showing the percentage of patients with limited activity and bed rest due to back pain across different types of fractures.]

- No incident fracture: Limited activity - 36.8%, Bed rest - 3.9%
- Radiographic fracture: Limited activity - 76.2%, Bed rest - 26.9%
- Clinical fracture: Limited activity - 93.2%, Bed rest - 52.7%

Adapted from Nevitt MC et al. (2000) Arch Intern Med 160: 77
Consequences of vertebral fractures

- Kyphosis
- Loss of height
- Bulging abdomen
- Acute and chronic back pain
- Breathing difficulties
- Depression
- Reflux and other GI symptoms
- Difficulty with activity of daily living (bending, rising, dressing, climbing stairs)
- Need to use a walking aid

REDUCED INDEPENDENCE AND QUALITY OF LIFE
Treatment of symptomatic vertebral fractures

- Bed rest (in the case of severe pain)
- Pharmacological treatment
  - analgesics
  - opioids
- Physical therapy
- Bracing
- Local steroid injections
- Vertebral augmentation
  - Vertebroplasty
  - Kyphoplasty
Summary

Vertebral Fractures

- Are the most common osteoporotic fracture
- Are associated with excess mortality
- Are associated with significant morbidity, even if they do not come to clinical attention
- Increase the risk of subsequent vertebral fractures by 5-fold and the risk of other fragility fractures (including hip) by 2 to 4-fold
COST OF OSTEOPOROSIS
Projected costs of osteoporotic fractures

Direct costs of vertebral fractures

Vertebral fractures:
6% of the total direct cost of osteoporotic fractures, costing 1 billion USD in the US in 2005

In Europe, the cost was 719 million EUR in 2005

Adapted from Burge R et al. (2007) J Bone Miner Res 22: 465
Vertebral fractures induce back pain and disability

Risk associated with incident vertebral fracture (Odd’s Ratio)
7223 women >65 yrs, 3.7 yrs follow-up

<table>
<thead>
<tr>
<th>Vertebral fracture at baseline</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back pain</td>
<td>2.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Back disability</td>
<td>1.8</td>
<td>4.1</td>
</tr>
<tr>
<td>≥ 1 day bed rest</td>
<td>4.9</td>
<td>7.5</td>
</tr>
<tr>
<td>≥ 7 days limited activity</td>
<td>2.7</td>
<td>7.4</td>
</tr>
</tbody>
</table>

Incident vertebral fracture + 1 to 2 days per year of bed rest + 10 days per year of limited activity

Adapted from Nevitt MC et al. (1998) Ann Intern Med 128: 793
Average hospital utilisation for osteoporotic fractures in the UK

*percentage of patients requiring hospitalization after fracture

Average bed days during hospitalisation

- Hip: 25
- Pelvis: 25
- Spine: 15
- Wrist: 5

For patients aged >65:

- Stroke: 30
- Kidney/Urinary infection: 25
- Heart failure: 15
- Angina: 5

References:
UNDER-DIAGNOSIS OF VERTEBRAL FRACTURES:
A MISSED OPPORTUNITY
Under-diagnosed vertebral fractures

934 hospitalised women with a lateral chest X-ray

459 elderly patients

Fracture identified by study radiologists
Fracture noted in radiology report
Fracture noted in medical record
Received osteoporosis treatment

Fracture identified by study radiologists
Fracture noted in radiology report
Received osteoporosis treatment

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1 Gehlbach SH et al. (2000) Osteoporos Int 11: 577

2 Majumdar SR et al. (2005) Arch Intern Med 165: 905
Under-diagnosis of vertebral fractures is a worldwide problem

- Vertebral fractures are under-diagnosed in all geographic regions

  Missed diagnosis of vertebral fracture

  - North America: 45.2%
  - Latin America: 46.5%
  - Europe/South Africa/Australia: 29.5%
  - Global rate: 34.0%

- Attributable both to poor identification of vertebral fractures and, when a fracture is identified, use of ambiguous terminology in the patient’s medical record that does not clearly state vertebral fracture.

Delmas PD et al. (2005) J Bone Min Res 20:557
Awareness and treatment of vertebral fractures is low despite...

- Known disability associated with vertebral fractures
- Excess mortality associated with vertebral fractures
- Every year, over 1 billion USD spent in the US and over 750 million EUR in Europe for treating vertebral fractures alone (direct costs)
- Validated radiologic techniques for diagnosis
- **Effective and safe treatments**
- Evidence based guidelines for diagnosis and management of osteoporosis, including vertebral fractures
Effective therapies are widely available and can reduce vertebral fractures by 30% to 70%.
Effect of osteoporosis drugs on new vertebral fractures

- RLX 60 (MORE)*
- RLX 60 (MORE)**
- ALN 5/10 (FIT1)*
- ALN 5/10 (FIT2)**
- RIS 5 (VERT - NA)*
- RIS 5 (VERT - MN)*
  - IBANDRONATE (daily)
  - IBANDRONATE (intermittently)
- ZOLEDRONATE (Horizon)
- ZOLEDRONATE*** (Horizon)
- DENOSUMAB (FREEDOM)
  - CT 200 (PROOF)*
  - Teriparatide 20μg
  - Parathyroid hormone 1-84
- Strontium ranelate (SOTI)*
- Strontium ran. (SOTI+TROPOS)**

RR ± 95% CI

* with previous vertebral fracture
** without previous vertebral fracture
*** with hip fracture

Updated and adapted from Delmas PD (2002) Lancet 359: 2018
Conclusions

- Vertebral fractures are a common complication of osteoporosis and markedly increase the likelihood of subsequent fractures.

- Mild and moderate vertebral fractures are often not being recognised and reported, leading to under-diagnosis and under-treatment.

- Lateral spine radiographs or by lateral DXA imaging are the best ways to confirm the presence of vertebral fractures in clinical practice.

- Early radiographic diagnosis followed by appropriate therapy will help prevent subsequent fractures.

- Effective therapies are widely available and can reduce vertebral, hip and other fragility fractures by 30% to 70%.
Action is needed by radiologists and other clinicians to ensure:

- Recognition of vertebral fractures using radiography, DXA-VFA or other imaging techniques
- Reporting as **FRACTURED** to avoid ambiguity
- These actions will help patients receive effective treatment and prevent subsequent fractures
RECOGNITION & REPORTING OF VERTEBRAL FRACTURES

Part II
Recognition and Reporting of Vertebral Fractures

Part III
DXA-based Vertebral Fracture Assessment