Osteoporosis is characterized by compromised bone strength, predisposing a person to an increased risk of fracture. The wrist, hip, and spine are the most common sites for fractures associated with osteoporosis. The economic and human costs of osteoporosis-related fractures are considerable. Although it is often considered a woman’s disease, osteoporosis is a significant source of morbidity and mortality in men. Available pharmacological treatments for osteoporosis include bisphosphonates, selective estrogen receptor modulators, calcitonin, parathyroid hormone, and hormone replacement therapy. Non-pharmacological interventions, such as nutritional counselling, exercise, and fall prevention, should also be considered in a fracture prevention plan.

Key words: osteoporosis, fragility fracture, bone, skeleton, bone density

Osteoporosis: Preventing the Deterioration of Bone

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Introduction

Osteoporosis has been defined as a skeletal disorder, characterized by compromised bone strength, predisposing a person to an increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality. The only clinical index of bone quality is a history of fragility fracture. A fragility fracture can be defined as a fracture that occurs in the absence of major trauma, such as during bending or as a result of a fall from standing height. The wrist, hip, and spine are the most common sites for fragility fractures. Age is one of the strongest independent predictors of hip fracture with a 1.5- to 9.5-fold increased risk of future fracture depending on the person’s age, as well as number and site of previous fractures. Age is one of the strongest independent predictors of hip fracture, as are bone mineral density, a prior fracture, or family history.

Epidemiology

In Canada, age-adjusted incidence rates for hip fracture in 1993/4 were 479 per 100,000 for women and 187 per 100,000 for men, and have been projected to increase four-fold by 2041. The annual cost of care associated with hip fracture in Canada has been estimated at $650 million. The one-year mortality rate after hip fracture has been reported to be up to 25%. For patients living in long-term care at the time of fracture, the mortality rate after hip fracture can be as high as 39%.

Hip fractures can have a dramatic impact on quality of life. A fear of falling may limit activity in individuals who have fractured, which can further impact physical function and mood. After a hip fracture, approximately 50% of community-living individuals do not regain their prefracture level of health and mobility, and many are dependent on assistive devices. One study revealed that 80% of women 75 years and older would prefer death than experience the loss of independence and reduced quality of life associated with a hip fracture and subsequent nursing home admission. Prevalent vertebral deformities were found in 23.5% of females and 21.5% of males in the Canadian Multi-Centre Osteoporosis Study. The clinical consequences of vertebral fracture include acute and chronic pain, reduced quality of life, functional impairment, and increased risk of future hip and vertebral fracture (Table 1). Only about 30% of vertebral fractures are diagnosed in clinical practice because a diagnosis depends on a report of pain or height loss that triggers the clinician to order a radiograph. Even then, many fractures are often not reported when present on x-ray.

Osteoporosis has often been considered a woman’s disease; however, it is a significant source of morbidity and mortality in men. In fact, the mortality rate associated with hip fractures is higher in men than in women. Several studies have documented that men were less likely than women to receive osteoporosis diagnoses or treatment after fragility fracture. A recent study demonstrated that fewer males than females are referred for bisphosphonate therapy, and males who are referred present with more severe osteoporosis, indicating that a
gender bias may exist with respect to osteoporosis management after fracture.\textsuperscript{21}

\textbf{Relationship with Bone Mass}
Bone mineral density (BMD) can be measured using densitometry and is a quantifiable predictor of fracture risk. Measurements of BMD can be expressed as T-scores (standard deviation units or SD units). The World Health Organization defines osteoporosis as having a BMD T-score at the spine, hip, or radius that is 2.5 SD or greater below the mean of a healthy young adult reference population.\textsuperscript{22} Although BMD is an important component in predicting fracture risk, other factors should also be considered: prior fragility fracture, age, family history of fragility fracture, and long-term glucocorticoid therapy (Table 2).\textsuperscript{3,23} The risk of fracture at a given BMD increases substantially with age.\textsuperscript{24} Spine BMD values can be falsely elevated with aging due to degenerative changes and/or calcification of the aorta.\textsuperscript{25}

\textbf{Prevention}

\textbf{Dietary Supplementation}
Adequate calcium and vitamin D are crucial for preventing bone loss. Between October and March, vitamin D production is minimal in northwestern Europe, the northern United States, and Canada due to inadequate UV exposure, so dietary and supplementary vitamin D becomes the primary source.\textsuperscript{26,27} Calcium and vitamin D supplementation in combination have been shown to significantly reduce hip fractures in older women.\textsuperscript{28} Adults over the age of 50 should consume 1500mg of calcium and 800IU of vitamin D daily. Among community-dwelling postmenopausal women presenting with acute hip fracture, 50\% were vitamin-D deficient (≤30nmol/L).\textsuperscript{29} A recent meta-analysis revealed that oral vitamin D supplementation using a dose of 700–800IU reduces the risk of nonvertebral fractures, but that supplementation with 400IU of vitamin D was not sufficient to prevent fracture.\textsuperscript{30} As well, vitamin D supplementation in the older patient can reduce falls by up to 20\%.\textsuperscript{31} A few recent studies did not provide support for the use of vitamin D for fracture prevention; however, poor adherence may have attenuated any treatment effects.\textsuperscript{31,32} It has been suggested that the active form of vitamin D, 1,25-hydroxyvitamin D, binds to a specific nuclear receptor in muscle, and that the reduction in fall risk associated with vitamin D intervention is attributable to improved muscle function.\textsuperscript{31} Given the prevalence of vitamin D deficiency in the older population,\textsuperscript{33,34} a minimum of 800IU of vitamin D in combination with calcium supplementation should be recommended to patients presenting with fragility fracture.\textsuperscript{3}

\textbf{Falls Prevention}
Fall prevention strategies in older adults may indirectly prevent fractures by reducing falls. Risk factor screening and intervention programs, muscle strengthening and balance training, and home hazard assessment and modification have been shown to reduce falls.\textsuperscript{35} Correction of vision may also reduce falls.\textsuperscript{35} Hip protectors have shown promise in reducing the rate of hip fractures in high-risk individuals living in long-term care, but there is insufficient evidence of their efficacy in community-living older adults.\textsuperscript{36,37} Poor adherence to the wearing of hip protectors may be a limitation.

\textbf{Exercise}
Another essential component of a fracture prevention program is exercise. In older adults, exercise can improve muscle strength, cardiovascular endurance, and functional capacity.\textsuperscript{38} Both impact exercises (e.g., walking, running, or aerobics) and

\begin{table}[h!]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
\textbf{Symptoms} & \textbf{Signs} & \textbf{Function} & \textbf{Future Risks} \\
\hline
Back pain & Height loss & Impaired activities of daily living (e.g., bathing and dressing) & Increased risk of future fracture \\
\hline
Sleep disturbance & Kyphosis & Difficulty fitting clothes due to kyphosis, protuberant abdomen & Increased mortality \\
\hline
Anxiety & Decreased lumbar lordosis & Difficulty bending, lifting, descending stairs, and cooking & \\
\hline
Depression & Protuberant abdomen & & \\
\hline
Decreased self-esteem & & Reduced lung function & \\
\hline
Fear of future fracture and falling & Weight loss & & \\
\hline
Reduced quality of life & & & \\
\hline
Early satiety & & & \\
\hline
\end{tabular}
\caption{Clinical Consequences Associated with Vertebral Fracture}
\end{table}

Source: Papaioannou A, et al., 2002.\textsuperscript{9}
Osteoporosis Prevention

### Table 2: Major and Minor Risk Factors for Osteoporosis

<table>
<thead>
<tr>
<th>Major Risk Factors for Osteoporosis</th>
<th>Minor Risk Factors for Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65 years</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Vertebral compression fracture</td>
<td>Past history of clinical hyperthyroidism</td>
</tr>
<tr>
<td>Fragility fracture after age 40</td>
<td>Chronic anticonvulsant therapy</td>
</tr>
<tr>
<td>Family history of osteoporotic fracture (especially maternal hip fracture)</td>
<td>Low dietary calcium intake</td>
</tr>
<tr>
<td>Systemic glucocorticoid therapy for &gt;3 months duration</td>
<td>Excessive alcohol or caffeine intake</td>
</tr>
<tr>
<td>Malabsorption syndrome</td>
<td>Weight &lt;57kg</td>
</tr>
<tr>
<td>Primary hyperparathyroidism</td>
<td>Weight loss &gt;10% of weight at age 25</td>
</tr>
<tr>
<td>Propensity to fall</td>
<td>Chronic heparin therapy</td>
</tr>
<tr>
<td>Osteopenia apparent on x-ray</td>
<td></td>
</tr>
<tr>
<td>Hypogonadism</td>
<td></td>
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<tr>
<td>Early menopause</td>
<td></td>
</tr>
</tbody>
</table>

Source: Brown JP, et al., 2002.\(^3\)

Hormone Therapy

Data from the Women’s Health Initiative revealed that estrogen-progesterin therapy reduced the risk for hip fracture and colorectal cancer in postmenopausal women; however, the risks of coronary heart disease events, breast cancer, pulmonary embolism, and stroke were increased.\(^6,46,49\)

Therefore, the risks associated with using HRT solely for the prevention and treatment of osteoporosis were felt to outweigh the benefits. Calcitonin is a naturally occurring hormone that is administered via a nasal spray. It has been shown to reduce pain associated with acute vertebral fracture, and has been shown to prevent vertebral fracture.\(^6,46\)

Teriparatide, the 1-34 component of parathyroid hormone, has an anabolic effect on bone and has been shown to increase spine BMD and reduce the incidence of new vertebral and nonvertebral fractures.\(^50\)

Conclusion

Given the increased risk of future fracture in individuals who have experienced a fragility fracture and the efficacy of pharmacological and nonpharmacological interventions for reducing fracture risk, it is critical to assess patients who are at risk of fracture and initiate appropriate treatment. Despite the availability of a number of therapeutic options, recent research has...

nonimpact exercises (e.g., resistance or strength training) had a positive impact on bone in postmenopausal women at the lumbar spine and femoral neck.\(^38\) The effect of weight-bearing exercise on bone was generally manifested as a prevention of bone loss rather than an increase in bone mass.\(^39-41\) A home-based exercise program can improve quality of life in older women with vertebral fractures.\(^42\)

Key elements of a rehabilitation program aimed at reducing falls and future fractures in individuals with vertebral fractures include strengthening of the back extensors and postural retraining.\(^43\) Older individuals wishing to begin an exercise program should do so under the supervision of a trained individual in order to ensure they are practicing the principles of safe movement.\(^44\) All exercise programs for older adults should include progressive resistance training two to three days per week, targeting major muscle groups of the trunk, upper extremities, and lower extremities each session with two to three sets of each exercise.\(^38\)

In addition, aerobic training can be incorporated with the goal of completing 20 minutes of moderate intensity (40–60% of heart rate reserve) activity at least three times per week. Balance training should also be incorporated. Exercise recommendations specific to patients with osteoporosis have been described. Forward bending and twisting movements should be avoided in individuals at risk of vertebral fracture.\(^44\) Oral protein and energy supplementation after hip fracture may reduce complications and unfavourable outcomes.\(^45\)

Pharmacological Therapy

Therapeutic options can reduce the risk of future fracture. Bisphosphonates are a class of drugs that target osteoclasts to inhibit bone resorption and have been shown to reduce the incidence of spine and nonspine fractures (including hip fractures) in individuals without a prior fracture by 30–50% over three years.\(^24,46,47\)

Raloxifene is a selective estrogen receptor modulator (SERM); it has estrogen agonist effects in bone and estrogen antagonist effects in the uterus and in breast tissue.\(^3\) Raloxifene has been shown to reduce fracture risk.\(^46\) The risk of venous thromboembolism associated with raloxifene has been reported to be similar to that of estrogen therapy. Data are limited on the use of raloxifene to prevent hip fracture, so in women at high risk bisphosphonates should be considered. Both bisphosphonates, such as alendronate and risendronate, and SERMs, such as raloxifene, are first-line therapeutic options for the prevention and treatment of osteoporosis in postmenopausal women; bisphosphonates are considered first-line osteoporosis therapy for women over the age of 75 and for men.\(^3\)
Osteoporosis Quick Reference Guide

Who should be assessed for osteoporosis?

**Major risk factors**
- Age ≥65 years
- Vertebral compression fracture
- Frailty fracture after age 40
- Family history of osteoporotic fracture (especially maternal hip fracture)
- Systemic glucocorticoid therapy >3 months
- Malabsorption syndrome
- Primary hyperparathyroidism
- Propensity to fall
- Osteopenia apparent on x-ray film
- Hypogonadism
- Early menopause (before age 45)

**Minor risk factors**
- Rheumatoid arthritis
- Past history of hyperthyroidism
- Chronic anticonvulsant therapy
- Low dietary calcium intake
- Smoker
- Excessive alcohol intake
- Excessive caffeine intake
- Weight < 57 kg
- Weight loss > 10% of weight at age 25
- Chronic heparin therapy

Note: Risk factors are additive and should not be considered independently of one another. Postmenopausal women and men over age 50 with at least one major or two minor risk factors should undergo testing for BMD.

Who should be tested for osteoporosis?

- **Height loss**—Kyphosis
  - **Spine radiography**
  - **History of low-trauma fracture confirmed by radiography?**
    - **Age**
      - <65 yr
      - ≥65 yr
    - **Clinical and risk factor evaluation**
      - With one major or two minor risk factors
        - **Stop (reassess at age 65)**
        - **Measure BMD by central DXA††**
          - **Normal††**
          - **Osteopenia††**
          - **Osteoporosis††**

- **Long-term moderate to high-dose glucocorticoids?†**
  - **Measure BMD if available**
  - **Evaluate for treatment**
  - **Repeat BMD to evaluate treatment response (at 1–2 yrs)**
  - **Consider repeat BMD testing at 2–3 yrs to monitor changing risk**

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*4cm historical height loss; 2cm prospective height loss. †Low to moderate: 2.5–7.5mg prednisone/day; moderate to high: >7.5mg prednisone/day. ††Central DXA = spine and hip.
†BMD classification as defined by the World Health Organization: Normal (T-score between +2.5 and –1.0 inclusive); Osteopenia (T-score between –1.0 and –2.5); Osteoporosis (T-score ≤ –2.5); Severe osteoporosis (T-score ≤ –2.5 plus fragility fracture).

### Osteoporosis Quick Reference Guide

#### Who is at high risk for fracture?

- Low BMD
- Prior fragility fracture after age 40
- Age
- Family history of osteoporosis

*With a prior fragility fracture after age 40, the risk of fracture increases by 1.5–9.5 times, depending on age at assessment and number and site of previous fractures.

#### Who should undergo fracture risk assessment and be treated for osteoporosis?

- Long-term glucocorticoids
- Fragility fracture after age 40
- Nontraumatic vertebral compression deformities
- Clinical risk factors (one major or two minor)
- Low BMD by DXA (T-score at or below −2.5)

Start bisphosphonate therapy

- Obtain BMD by DXA for follow-up

+ Low BMD by DXA (T-score below −1.5)

Consider therapy

Repeat BMD by DXA after one or two years

* ≥ 7.5mg prednisone for more than three months. †We have arbitrarily chosen T-score below −1.5; nontraumatic vertebral compression deformities; personal history of fragility fracture after age 40; clinical risk factors.

#### What is the best treatment for osteoporosis in postmenopausal women?

- Calcium: 1500mg/day
- Vitamin D: 800 IU/day
- Physical activity: ≥30 min at least three times a week

**1st CHOICE**

- Without fragility fracture:
  - Vasomotor symptoms
  - YES
  - HRT
- With fragility fracture:
  - Alendronate
  - Risedronate
  -Raloxifene

**2nd CHOICE**

- Alendronate
- Risedronate
- Raloxifene
- Calcitonin
- Etidronate
- HRT

*Mainly vertebral fracture. Only alendronate and risedronate and, recently, continuous estrogen-progesterone have been shown to decrease hip fracture risk.

*Permission from the Osteoporosis Society of Canada.*
suggested that osteoporosis management following fragility fracture is inadequate.\textsuperscript{51,52} It is important for physicians and patients to understand that a fragility fracture is not an acute injury but actually a manifestation of osteoporosis. Osteoporosis disease management needs to be integrated into standard postfracture care, such that older adults who present with fragility fracture should trigger a process of osteoporosis diagnosis and treatment in order to reduce the risk of another fracture in the future.

Dr. Giangregorio declares no competing financial interests. Dr. Papaioannou is or has been a consultant or on the speaker’s bureau for the following: Sanofi Aventis, Eli Lilly Canada Inc., Merck Frosst Canada, Novartis Pharmaceuticals Canada Inc., and Proctor and Gamble Pharmaceuticals. Dr. Adachi has been involved in clinical trials with Amgen, Eli Lilly, Glaxo Smith Kline, Merck Frosst, Novartis, NPS-Allelix, Pfizer, Procter & Gamble, Roche, Sanofi Aventis, and Wyeth, and has been a consultant to Astra Zenea, Eli Lilly, Glaxo Smith Kline, Merck Frosst, Novartis, Pfizer, Procter & Gamble, Roche, Sanofi Aventis, Servier, and Wyeth.

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