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CME ARTICLE

Male osteoporosis: clinical approach and management in family practice

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You were surprised to find Mr Roger Lee struggling into your polyclinic consultation room. Although he is 85 years old, Roger has always been healthy and spirited. That morning, he had slipped on the wet floor of his toilet at home and was now experiencing severe, persistent pain on his lower back. You performed an X-ray, which showed a compression fracture at the 4th lumbar vertebra. Roger wished to know why his 'simple' fall would result in a fracture.

WHAT IS MALE OSTEOPOROSIS?

Osteoporosis in females has been widely discussed in the medical literature for many years. In recent years, female osteoporosis has been highlighted in the media, causing interest and concern among both female patients and members of the public. Therefore, family physicians are now more aware of the need to screen for this condition (e.g. using the Osteoporosis Self-Assessment Tool for Asians)[1,2] and to perform bone mass density tests for female patients at risk. Moreover, family physicians are starting to initiate therapy and follow up on female patients with osteoporosis (e.g. based on the predicted risk of fracture using FRAX®).[3] However, the clinical approach to osteoporosis in males and the available treatment modalities are less familiar to family physicians. As the incidence of male osteoporosis will likely increase due to the ageing population of Singapore, doctors and the general public will likewise place greater emphasis on this condition in the male population.

Osteoporosis is defined as a progressive systemic skeletal disease characterised by low bone mass with microarchitectural deterioration of bone tissue, consequently leading to an increase in bone fragility and susceptibility to fracture.[4] Bone density increases from birth and reaches a peak in both genders in the mid-twenties to early thirties. From age 50 years, bone density in males declines at about 0.2%–0.5% per year. Bone loss in men probably starts progressively and significantly from age 30 years, and continues throughout life.[5]

Low bone mineral density (BMD) was found to be an important predictor of fracture risk in both men and women.[6] BMD measurement is thus used to predict a person's risk for fracture. The most widely available and recognised method used locally to measure BMD is the dual-energy X-ray absorptiometry (DXA) test. The measurements taken are for the hip and spine, and reported as T- and Z-scores. BMD measurements of the femoral hip and total hip joint are the best predictors of hip fracture and other osteoporotic fractures.[7]

For both genders of the same age and BMD, no difference in the absolute risk for fractures is found. Therefore, in both genders, the diagnosis of osteoporosis is made using the World Health Organization (WHO) definition, based on a BMD hip T-score of –2.5 standard deviation (SD) or lower.[8]

HOW RELEVANT IS THIS TO MY PRACTICE?

The prevalence rate of osteoporosis in men aged 50 years and above has been reported to be 19%.[9] Of the estimated annual incidence of 9 million new osteoporotic fractures worldwide in the year 2000, 39% occurred in men, with the peak number occurring between those aged 50–59 years. Of these osteoporotic fractures in men, 30% were fractures of the hip, 20% the forearm, 42% vertebral, and 25% were humeral fractures.[10] In Singapore, the incidence of hip fractures in men has increased by 1.5 times since the 1960s.[11,12]

In men, the relative risk of subsequent fracture markedly increases (relative risk [RR] 3.47; 95% confidence interval [CI] 2.68–4.48) after a low-trauma fracture (i.e. caused by a fall from a standing height or lower) at any skeletal site.[13,14] Both low- and high-traumas (i.e. caused by falls from greater than standing height, or road accidents) have been associated with low BMD. In men, each 1-SD reduction in total hip BMD is associated with an increased risk of low-trauma fracture (relative hazard 1.69; 95% CI 1.49–1.91) and high-trauma fracture (relative hazard 1.54; 95% CI 1.20–1.96).[15]

More men than women die at one year after a hip fracture, with a mortality rate of up to 37.5% in men.[16] This mortality rate is comparable to that found in a local study (i.e. 32%) conducted at the Singapore General Hospital in 2007.[17] In terms of recovery after acute inpatient rehabilitation, men were found to have significantly worse functional outcomes than women.[18] Vertebral fractures are associated with height loss, reduced quality of life, respiratory dysfunction, increased risk of death, and subsequent hip and other fractures.[19]

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CLINICAL APPROACH TO MALE OSTEOPOROSIS

Risk factors

Male osteoporosis can either be primary (idiopathic) or secondary. The risk factors for fractures in men are presented in Table I. Up to 30%–60% of male osteoporosis are due to secondary causes,[20] with corticosteroid use, high alcohol intake and hypogonadism cited as the major causes (Table II).

Screening and evaluation

Family physicians should screen and evaluate male patients with risk factors for osteoporosis. The clinical approach to the diagnosis of male osteoporosis is as follows:

- Screen male patients routinely for risk factors
- Look for clinical signs of secondary causes
- Perform a FRAX® calculation
- Perform a BMD test if the male patient is more than 70 years old, or younger with major risk factors.

FRAX®, the WHO fracture risk assessment tool, is used to predict the absolute ten-year fracture risk with or without BMD.[3] It includes key risk factors for osteoporosis such as:

- A prior fragility fracture
- Parental history of hip fracture
- Current tobacco smoking
- Long-term use of oral glucocorticoids

You screened Roger for any risk factors for male osteoporosis. Other than hypertension and hyperlipidaemia – both of which are well controlled – Roger has no other risk factors. His weight and height are 64 kg and 160 cm, respectively, and his body mass index (BMI) is 25 kg/m^2. He had no complaints of symptoms that suggested testosterone deficiency, and did not know whether his mother or sisters have osteoporosis or any sustained fractures. Roger is an avid walker who exercises daily for about one hour at the park.

Although Roger's BMD result was not available, you calculated his ten-year fracture risk based on his BMI, using an online FRAX calculator (available at: http://www.shef.ac.uk/FRAX/tool.jsp?locationValue=9). Since Roger had sustained a fracture, his ten-year probability of a major osteoporotic fracture and hip fracture was 14% and 8%, respectively. You advised Roger to measure his BMD, so as to further refine the estimation of his fracture risk. Roger was surprised to hear that he may have osteoporosis, as he thought that the condition occurs only in women. He agreed to undergo a BMD test.

One week later, the results of his BMD test showed the T-score of the hip was –3 SD. Based on the BMD result, you recalculated Roger's fracture risk. Now his ten-year probability of a major osteoporotic fracture and hip fracture has increased to 16% and 8.8%, respectively. Concerned, Roger enquired about his treatment options.

Table I. Risk factors for fractures in men.

• Past fractures from age 50 years
• Family history of minimal trauma fracture
• Physical inactivity
• Recent falls
• Sedative use
• Low body mass index
• Smoking

Table II. Secondary causes for osteoporosis in men.

• Corticosteroid use
• High alcohol intake
• Hypogonadism (primary or secondary)
• Low calcium intake
• Vitamin D deficiency or insufficiency
• Thyrotoxicosis
• Gastrointestinal disorders (e.g. coeliac disease, inflammatory bowel disease, liver disease)
• Malignancy
• Chemotherapy
• Gastric surgery
• Drugs (e.g. anticonvulsants, warfarin)
• Transplantation

- Rheumatoid arthritis
- Other causes of secondary osteoporosis
- Daily alcohol consumption of three or more units.

THERAPEUTICS

The main treatment options for male osteoporosis are bisphosphonates and teriparatide.

Bisphosphonates

Clinical trials conducted in the 2000s[21,22] concluded that bisphosphonates are the first-line treatment option for male osteoporosis. Commonly used bisphosphates are alendronate and risedronate, while the less commonly used ones include zoledronic acid and ibandronate.

Bisphosphonates increase the BMD at the femoral hip by about 2%–3% and at the lumbar vertebral spine by 4%–7% over two years.[22–25] They also reduce the risk of vertebral fractures by about 60%.[21,22] Only one trial has shown that risedronate reduced the risk of hip fractures (RR 0.19) despite falls in post-stroke hemiplegic men.[26] Other bisphosphonates, however, do not show this effect. Similarly, only risedronate has been shown to reduce the risk of non-vertebral fractures by 50%.[22]

The most common but usually avoidable side effect of bisphosphonates is gastro-oesophageal irritation. Rarely, osteonecrosis of the jaw may occur with the use of amino-bisphosphonates, but the risk is very low when they are used for the indication of osteoporosis (prevalence rate of 0.05%–0.10%).[27] There is, however, an increased risk of subtrochanteric, femoral shaft and atypical femur fractures with the use of bisphosphonates (RR 1.70; 95% CI 1.22–2.37).[28]

Teriparatide

Human parathyroid hormone is an 84-amino-acid peptide that plays a central role in the maintenance of calcium homeostasis. Most clinical trials have employed teriparatide, a 34-amino-acid peptide human parathyroid hormone (1–34), which has been commercially available in recent years.[29] Teriparatide can be used as an alternative for a period of two years, if the patient is unable to tolerate bisphosphonates. It can also be used in men with hypogonadism. Teriparatide increases BMD of the hip and spine by 2.9% and 13.5%, respectively,[30] and reduces the risk of moderate and severe vertebral fractures by 83%.[31]

Other medications

Testosterone increases the BMD of the spine.[32] However, no data regarding fracture risk reduction on testosterone supplementation is available. Thus, the clinical efficacy of testosterone on osteoporosis treatment in men can only be indirectly inferred.

Combination therapy

Combination therapy of teriparatide and alendronate has been shown to be less effective in increasing BMD of the lumbar spine and hip in men than treatment with teriparatide alone, but it was reported to be more effective than treatment with alendronate alone.[33] As alendronate is found to attenuate the stimulation of bone formation by teriparatide, the two drugs should not be used in combination.

REFERRAL TO A SPECIALIST

After a BMD test is performed, patients should be counselled regarding their risk for future osteoporotic fractures. The male patient with osteoporosis should be referred, especially if he is younger and has more severe disease, to a specialist centre such as an endocrinology, rheumatology or orthopaedic clinic.

TAKE HOME MESSAGES

1. Osteoporosis in men is becoming an increasingly common chronic condition, which can be prevented, screened, diagnosed and treated early.
2. Screening for osteoporosis should occur for men older than 70 years, or younger men with major risk factors for osteoporosis.
3. Secondary causes for male osteoporosis, the most common being hypogonadism, excessive oral corticosteroid use and excessive alcohol intake, should be excluded and removed, if present.
3. The ten-year fracture risk can be calculated using a FRAX® calculator.
4. Bisphosphonates such as alendronate and risedronate, which are the main drug treatment for men with osteoporosis, have been proven to increase BMD of the hip and vertebral spine and reduce the risk of vertebral fractures.
5. Risedronate has been shown to reduce the risk of hip fractures despite falls in stroke patients and the risk of non-vertebral fractures.

After hearing your summary of the treatment options, Roger requested for time to consider his decision concerning treatment. You counselled Roger about fall prevention at home, and prescribed him with a calcium and vitamin D supplement and an analgesic. You also advised him to return for follow-up if he experiences increased intensity of pain, or numbness or weakness of his legs. Lastly, you arranged for Roger to see an endocrinologist for further management at a hospital of his choice.

6. The most common adverse effect of bisphosphonates use is gastro-oesophageal irritation, which can be avoided in most patients who follow the appropriate advice.
7. Teriparatide can be used as an alternative to bisphosphonates if the latter is not tolerated. Teriparatide can also be used in men with hypogonadism.
8. Teriparatide increases BMD of the hip and spine, and reduces the risk of moderate and severe vertebral fractures.
9. Testosterone is not shown to reduce fracture risk, so it is not recommended for use.
10. Combination therapy of teriparatide and alendronate has been shown to be less effective in increasing BMD of the hip and spine than teriparatide alone. Alendronate also attenuates the stimulation of bone formation by teriparatide. Thus, the drugs should not be used in combination.
11. Men with osteoporosis, especially younger persons with more severe disease, should be referred to a specialist for further evaluation and management.

ABSTRACT In Singapore, male osteoporosis is gaining greater importance due to our ageing population. Family physicians should screen for osteoporosis in elderly men and men with risk factors or secondary causes for the condition. A bone mineral density (BMD) test is used for diagnosis. FRAX® can be used to predict the absolute ten-year fracture risk. Management includes reduction of risk factors or secondary causes, fall prevention, appropriate physical activity and a diet adequate in calcium and vitamin D. Referrals to specialists for evaluation and therapy can be considered, particularly for younger men with more severe disease. Current first-line drug treatment includes bisphosphonates and teriparatide. Testosterone increases BMD of the spine, but data on fracture risk reduction is unavailable. Public and physician education with the involvement of health authorities can create greater awareness of this silent condition, which can lead to complications, morbidity and death, if left untreated.

Keywords: bone mineral density, family physicians, fracture, FRAX, male osteoporosis

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

(Code SMJ 201407A)

		True	False
1.	Osteoporosis only occurs in postmenopausal females.	☐	☐
2.	Bone density increases from birth and peaks in both genders in the mid-20s to early 30s.	☐	☐
3.	Low bone mineral density (BMD) was found to be an important predictor of fracture risk in women, but not in men.	☐	☐
4.	Locally, the most widely available and recognised method for measuring BMD is the dual-energy X-ray absorptiometry test.	☐	☐
5.	BMD measurement of the femoral hip and total hip joint, reported as T- and Z-scores, are the best predictors of hip fracture and other osteoporotic fractures.	☐	☐
6.	The World Health Organization definition for the diagnosis of osteoporosis, based on a BMD hip T-score of ≤ – 2.5 standard deviation, applies only to elderly females.	☐	☐
7.	More men than women die at one year after a hip fracture, with the mortality rate of men reported to be up to 37.5%.	☐	☐
8.	Risk factors for fractures in men include past fractures from age 50 years, physical inactivity, recent falls and sedative use.	☐	☐
9.	Secondary causes for male osteoporosis include hypogonadism, use of corticosteroids and high alcohol intake.	☐	☐
10.	Screening for osteoporosis should occur for men older than 70 years and younger men with major risk factors for osteoporosis.	☐	☐
11.	The ten-year fracture risk, which can be calculated using the online FRAX® calculator, is applicable for both males and females.	☐	☐
12.	The main treatment options for male osteoporosis are bisphosphonates (e.g. alendronate and risedronate) and teriparatide.	☐	☐
13.	Bisphosphonates increase the BMD at the femoral hip by about 2%–3% and at the lumbar vertebral spine by 4%–7% over two years but they have negligible efficacy in reducing the risk of vertebral fractures.	☐	☐
14.	The most common side effect of bisphosphonates is gastro-oesophageal irritation.	☐	☐
15.	Only risedronate has been shown to reduce the risk of hip fractures despite falls in stroke patients as well as the risk of non-vertebral fractures.	☐	☐
16.	Teriparatide, a human parathyroid hormone, is 34-amino-acid that affects the maintenance of calcium homeostasis.	☐	☐
17.	Teriparatide can be used as an alternative in patients who are unable to tolerate bisphosphonates, but it cannot be used in men with hypogonadism.	☐	☐
18.	Teriparatide can be used for about two years, and reduces the incidence of moderate or severe vertebral fractures by 83%.	☐	☐
19.	Testosterone had been shown in trials to increase the BMD of the spine, with longitudinal data on fracture risk reduction.	☐	☐
20.	The male patient with osteoporosis should be referred, especially if he is younger and has more severe disease, to a specialist centre such as an endocrinology, rheumatology or orthopaedic clinic.	☐	☐

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