Elderly Osteoporosis - Beyond Bone Density and Drugs

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Introduction

It is very common for clinicians to encounter elderly patients with osteoporosis, or viewing it from another perspective, elderly persons at high risks of fragility fractures. Osteoporosis increases the risk of fractures in our elders, resulting in significant morbidities and mortalities. The hips, forearms and vertebrae are the common sites of osteoporotic fractures, of which hip fractures are of the most significant impact, especially in the short term. Despite a recent stabilising trend of age-specific incidences of hip fractures in Hong Kong, with the increasing size of our elderly population, the absolute number of hip fractures, with their impact, is expected to continue to increase.

Assessment – More Than Bone Mineral Density (BMD)

As other areas of Geriatric medicine, ‘osteoporosis’ assessments for elders include evaluations not only on bone health, but also comprehensive assessments of the full spectrum of bio-psycho-social domains. These may include, but not limited to, functional and fall risk assessment, cognitive assessment, and evaluation of personal and environmental contextual factors.

Initial investigations commonly utilised in the work-up of osteoporosis in elders are shown below. This also serves as an initial screening for common secondary causes of osteoporosis.
- Serum calcium and phosphate
- Complete blood count
- Creatinine / renal function test
- Alkaline phosphatase / Albumin / liver function test
- Thyroid-stimulating hormone
- Serum protein electrophoresis
- Lateral radiograph of lumbar and thoracic spine

Others:
- Vertebral fracture assessment
- Bone densitometry

Additional biochemical testing is carried out in selected patients based on clinical assessment. While bone turnover markers may have values in the assessment and management, they are not routinely checked in many local settings.

Bone mineral density (BMD) is an important predictor of bone strength. The most commonly used technique worldwide, including Hong Kong, is the dual-energy X-ray absorptiometry (DXA). The World Health Organization (WHO) established the definition of osteoporosis based on the BMD measurement by DXA. Osteoporosis is defined as BMD of 2.5 standard deviation (SD) or more below that of a “young normal” adult (i.e. T-score at or below -2.5).

It is important to note that the relationship between BMD and fracture risk is a continuous one, and there is no BMD threshold for osteoporotic fractures to occur. Elderly persons with normal BMD can develop osteoporotic fractures. This is similar to the occurrence of stroke in elders with normal blood pressure. On the other hand, a non-osteoporotic fracture can also occur in an elder (e.g. pathological fracture).

Diagnosis Does Not Equate to Drug Treatment

Although BMD helps to establish the presence of osteoporosis and an increased risk for fracture, most fractures occur in postmenopausal women and elderly men at moderate risk. This is one reason why BMD alone is not used as the sole decision factor for treatment. Other skeletal abnormalities, in addition to low BMD, can contribute to bone fragility. A variety of non-skeletal factors, such as age and liability of falls, also contribute to the fracture risks.

Recent attention has been put on clinical risk factors (CRF) that significantly contribute to the fracture risk which is independent of BMD measurements or age. These CRFs are of cumulative effects and, combined with BMD, provide a useful estimation of the fracture risks and help the subsequent management decisions.

To serve the purpose, the development of FRAX® algorithms integrates the weight of clinical risk factors, with or without information on BMD, and computes the 10-year probability of hip fracture or a major osteoporotic fracture. A major osteoporotic fracture is defined as a clinical spine, hip, forearm, and humerus fracture. The FRAX® tool can be assessed on-line on www.shef.ac.uk/FRAX. The model has also been calibrated for the use in Hong Kong.

FRAX® gives risk ratios for average doses or exposures for some CRFs despite a dose-response relationship between some factors and fracture risks, e.g. number of prior fractures, the use of alcohol and steroid. This should be remembered when interpreting the
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**Fall Risk Assessment and Interventions**

Falls do not lead only to fragility fractures, but also other serious outcomes including head and brain injuries. Even the fear of a fall can lead to negative health outcomes in the elderly population. The American Geriatrics Society (AGS) and British Geriatrics Society (BGS) recommended elders to be enquired for any history of falls (in the past year) and walking or balance difficulties. Elders with a positive history should undergo a gait and balance assessment. Recommended tests commonly used in Hong Kong include the Timed Up and Go test, Berg Balance Scale, and Tinetti Gait and Balance Scale. Elders who fail to perform satisfactorily on the above tests, together with those presenting with fall-related problems, reporting recent multiple falls, and those reporting walking or balance difficulties represent a higher risk group and should undergo more comprehensive multi-factorial fall assessments. Such assessments should include appropriate functional & environmental evaluations to be performed by clinicians with appropriate training and expertise, which are commonly available locally in Geriatrics Fall clinics.

To be effective in reducing falls, assessments have to be linked with appropriate interventions. For elders living in the community, effective interventions may include appropriate home modifications, exercises, minimising psychoactive drugs, rational reduction of medications; treatment of postural hypotension and foot problems, and the use of proper foot-wear. Dementia represents another higher risk group for falls and fractures, and be an unfavourable prognostic factor in hip fracture rehabilitation. Unfortunately, there are still insufficient evidences to make any valid recommendations on fall intervention strategies for demented elders.

**Physical Activities and Exercises**

Physical activities and exercises, in particular weight-bearing exercises, are effective in increasing BMD at the lumbar spine and hip in postmenopausal women. Exercise programmes targeting at strength, gait and balance, such as Tai Chi, can also reduce falls. The American College of Sports Medicine (ACSM) recommended that fall-related exercise programmes for elders should include weight-bearing endurance and resistance activities aiming at preserving bone mass, and also activities designed to improve balance and prevent falls. Taking account into the high prevalence of co-morbid medical conditions in the elderly, exercise prescriptions and programmes should be individualised taking into consideration of one’s own physical capabilities and health profile. Regular reviews and adjustments of exercise progression are also needed. For osteoporotic elders, several forms of exercises are best avoided. These include twisting movements (e.g. golf swing), dynamic abdominal exercises (e.g. sit-ups), and excessive trunk flexion. Exercises involving abrupt, explosive or high-impact loading should also be avoided. While elders should be encouraged to remain active, formal exercise training programs in elders, especially for those with multiple co-morbidities, could best be prescribed and monitored by qualified professionals like geriatric, rehabilitation, or exercise specialists, if available. Despite the focus of this article on osteoporosis, falls and fractures, it is important to note that physical activities and exercises offer benefits more than just bones and fractures. Readers interested in exercise prescriptions for the elderly may refer to the related recommendations by ACSM and the American Heart Association (AHA).

**Calcium and Vitamin D**

Adequate daily calcium and vitamin D intake is safe, inexpensive and promotes bone health. The commonly recommended daily calcium intake ranged from 1000 to 1200mg. There are controversies about the efficacy of calcium in fracture reduction and the potential risks of higher-dose supplementation on renal stones or cardiovascular diseases. It is also important to pay attention to the possible worsening of constipation as a result of the calcium tablet intake. This is a common and troublesome issue to elders, but is easily overlooked by clinicians.

Apart from osteoporosis, vitamin D supplement in a dose of 700-1000 IU daily may reduce the risk of elderly falls. The commonly recommended daily vitamin D intake ranged from 800-1000IU. A daily intake of vitamin D up to 2,000 IU/day was regarded as safe by the National Osteoporosis Foundation (NOF) and Osteoporosis Canada.

**Anti-osteoporosis Agents - Considerations Beyond Efficacies**

National Osteoporosis Foundation (NOF) recommended that postmenopausal women and men aged ≥50 with the followings to be considered for drug treatment:

1. A hip or vertebral (clinical or morphometric) fracture
2. A DXA hip (femoral neck) or spine T-score ≤ -2.5
3. Low bone mass and a WHO 10-year probability of a hip fracture ≥3% or major osteoporosis-related fracture ≥20%.

The above recommendations are not rules. Clinical decisions on drug treatment also need to take account into patient factors, including personal preferences, co-morbidities, limitations of FRAX in application to individuals, risk factors not captured by FRAX (e.g. falls), the cost-benefit and compliance considerations of various modes of fracture prevention (which includes but not limited to anti-osteoporosis drug treatment), and also the willingness to pay by the concerned society. Decisions to treat therefore have to be made on a case-by-case basis.

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**FRAX® result** and clinical judgement should be employed for lower or higher exposures. For prior fractures, FRAX® includes not only symptomatic but also (subclinical) morphometric vertebral fractures detected during radiological evaluation. Vertebral fractures can be identified on lateral radiographs or via vertebral fracture assessment (VFA). VFA is a low radiation imaging of the spine now available on some bone densitometers and allows concurrent detection of significant vertebral fractures while measuring BMD.

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Current FDA-approved agents for postmenopausal osteoporosis include bisphosphonates (alendronate, ibandronate, risedronate and zoledronic acid), calcitonin, oestrogens (oestrogen and/or hormone therapy), raloxifene and teriparatide. Strontium ranelate was also approved for treatment of postmenopausal osteoporosis in some European countries. Alendronate, risedronate, zoledronic acid, and teriparatide are approved for osteoporosis for elderly men in the USA.

In clinical settings, apart from considerations on anti-fracture efficacies, drug cost, practical intake and compliance considerations also dictate the choice of agents. While readers may refer to various guidelines for the relative efficacies of different agents, the following discussions will try to highlight some practical considerations related to our elders.

Bisphosphonates: -Bisphosphonates may be given in oral form or by injection/infusion. Instead of daily intake, oral bisphosphonates are nowadays commonly taken once weekly or monthly. Side effects of oral bisphosphonates include gastrointestinal problems such as dysphagia, oesophagitis and gastric ulcer. Oral bisphosphonates only work in an empty stomach. Patients are therefore commonly instructed to take oral bisphosphonates as the first thing waking up in the morning, with an empty stomach and followed immediately by 200-250ml of plain water. For at least 30-60 minutes (depending on the bisphosphonates chosen) after medication intake, patients should remain upright (sitting or standing) and should not eat, drink other fluid or take any other medications. The complexity of intake instructions commonly imposes challenges to elderly patients and their care-takers, and results in compliance issues that clinicians must be aware of. Ibandronate and zoledronic acid can also be given less frequently in non-oral preparations (slow intravenous injection/infusion depending on the drug used). Renal function and calcium levels are to be checked before injection and the two IV bisphosphonates are contraindicated in patients with uncorrected hypocalcaemia. Patients receiving IV zoledronic acid infusion are given paracetamol to reduce common fever. There are concerns on bisphosphate-related osteonecrosis of the jaw (BRONJ), atrial fibrillation and atypical fractures. These concerns are routinely included in the author’s discussion with patients/families before treatment. It is also the author’s practice to advise patients to undergo dental check-up, partly as a practice to promote good elderly dental care and partly on the possible concern on BRONJ.

Oestrogen agonist/antagonist or Selective Oestrogen-Receptor Modulators (SERMs) – Raloxifene: Apart from its benefit in osteoporosis, raloxifene is associated with a reduced risk of invasive breast cancer. There is an increased risk in deep venous thromboembolism (DVT) with raloxifene, which needs to be stopped (at least 3 days) before a planned surgery or a long period of remaining still (e.g. long flight or car trip). Raloxifene may also cause hot flashes and leg cramps.

Strontium ranelate:- Strontium ranelate was approved in some European countries for osteoporosis. It both inhibits bone resorption and stimulates bone formation. It absorption is reduced by food, milk and related products. Patients are therefore advised to take the 2-g sachet once daily at bed-time, at least two hours after eating. Strontium should be used with caution in patients at increased risk of DVT.

Hormonal Replacement therapy (HRT): - The use of oestrogen/hormonal replacement therapy is nowadays more limited after the Women’s Health Initiative showing its association with myocardial infarction, stroke, invasive breast cancer and thromboembolic events. American and Canadian guidelines recommended that oestrogen/hormone therapy can be used in menopausal women requiring treatment for osteoporosis together with vasomotor symptoms. If osteoporosis is the only target, non-oestrogen treatment should be considered first.

Teriparatide:- Teriparatide is a powerful bone-forming agent administered by daily subcutaneous injections. The usual duration of use is 18 months. It raised the risk of osteosarcoma in rats and is not advised in patients with elevated risks of osteosarcoma. Teriparatide can cause hypercalciuria and hypercalcaemia, both are generally mild and resolve spontaneously with/without stopping of calcium supplement.

RANK ligand (RANKL) inhibitor/human monoclonal antibody:- Denosumab may be available in Hong Kong shortly. It is given by subcutaneous injections every six months. Denosumab significantly reduced the incidence of new spine fractures, hip fractures and non-spine fractures over three years.

Additional Notes:- It is worth taking note that evidences of benefits for most anti-osteoporosis agents are shown in patients with satisfactory renal functions (with creatinine clearance of more than 30-40ml/min). Many elderly patients may have a renal function lower than this. Physicians should be aware of this when considering anti-osteoporosis agents. In addition, the issues of polypharmacy and drug interactions are very common in elderly. This also warrants special attention.

Conclusions

Osteoporosis is a disease of high relevance to elderly care. Its impact and management is closely related to other giants of geriatric medicine like falls, dementia (affecting the risk of falls and drug compliance), polypharmacy (additional concern on drug interactions) and immobility (worsening osteoporosis and imposing concern on drug choices). A good practice of osteoporosis medicine may serve as a marker of good geriatric care to our senior citizens.

References


