

# OSTEOPOROSIS IN SOUTH AFRICA

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## 1. INTRODUCTION

Recent developments in osteoporosis involve a reassessment of our conceptual understanding of its definition and approach to diagnosis, as well as technological advances in acute and long-term management. The latter includes the introduction of new anabolic agents like teriparatide and strontium ranelate to treat patients with severe fracturing osteoporosis, more evidence-based data from randomised controlled trials (RCTs) on the efficacy and safety of known bone-active agents, and new techniques like percutaneous kyphoplasty to manage acute vertebral fractures.

This report will not attempt to provide an extensive review of osteoporosis. Instead, it will define the osteoporosis problem from a South African perspective, and then largely concentrate on recent developments in the field.

## 2. EPIDEMIOLOGY

Osteoporosis is a common and costly disease, which affects one out of every four postmenopausal Caucasian women.<sup>1-3</sup> It is also serious and 20% of all hip fracture victims die within one year of the event. Even more disconcerting is the fact that less than 50% of patients are able to live an independent life following a hip fracture, most requiring institutionalisation. In South Africa, the acute care costs of a hip fracture amounts to about R50 000 per patient. In 1992, the annual cost of osteoporosis in the United States exceeded \$20 billion. Vertebral compression fractures are also associated with an increased morbidity and mortality. Moreover, the incidence of all osteoporosis fractures is clearly on the rise.<sup>4-6</sup>

In developed countries, spinal osteoporosis is about 4-6 times, and hip fractures 2-3 times more common in women than in men. In developing countries, including South Africa, the incidence of hip fractures in men approximates that of women. Although reasons for this remain poorly understood, it does underscore the clinical importance of osteoporosis in males.

Accurate epidemiologic data on fracture incidence in different ethnic populations in South Africa are not available. The bone mineral density (BMD), which is currently regarded as the diagnostic criterion for the disease (*vide infra*), appears to be comparable among white, Asian and mixed race/coloured populations in the country. Osteoporosis is therefore thought to occur with equal frequency among these groups, although no fracture data exist.

Osteoporosis is thought rarely to affect blacks, and Solomon<sup>7,8</sup> has reported hip fractures to be ten times less prevalent in these populations. However, these data are more than 30 years old, and do not take into account recent developments that include urbanisation, cannot be extrapolated to vertebral and other fractures, and need to be verified. Osteoporotic fractures are also much less prevalent in Afro-Americans in the USA, where the observation is readily explained, based on an approximate 15% higher BMD in this population compared to Caucasians. Recent studies by Daniels *et al.*,<sup>9</sup> Nelson *et al.*,<sup>10</sup> and Conradie *et al.*,<sup>11</sup> suggest that the BMD in black and white South Africans do not differ substantially – at least not to the extent where a tenfold difference in fracture prevalence can be readily explained. Clearly, more work on both BMD and fracture prevalence in different populations in this country is urgently required.<sup>12</sup>

## 3. DEFINITION OF OSTEOPOROSIS

### 3.1 Conventional definitions of osteoporosis

Osteoporosis was historically defined on a histological and radiological basis. In the mid-nineties, the World Health Organization (WHO) adopted a largely densitometric definition, regarding osteoporosis as a systemic skeletal disease characterised by a low bone mass and

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micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture.<sup>13</sup> Since bone mass is thought to account for up to 70% of the variance in bone strength *in vivo*, and is the only variable that can be accurately determined, its measurement (as BMD) currently embodies the practical basis for the diagnosis of osteoporosis.<sup>14</sup>

While the four diagnostic categories of the WHO classification<sup>13</sup> (Table 13.1), which defines osteoporosis as a BMD of at least 2.5 standard deviations (SD) below the average for a 30-year-old Caucasian female, have provided a practical basis for identifying those at risk of sustaining a fracture, we need to take cognisance of its limitations, namely i) a single BMD measurement lacks sensitivity and up to 50% of patients with a known osteoporotic fracture may have a normal BMD, ii) the WHO criteria are based on data obtained from white, postmenopausal women, employing dual energy x-ray absorptiometry (DEXA) of the axial skeleton (spine and hip), and cannot be extrapolated to other populations (blacks, males, young individuals) or other techniques for measuring BMD (e.g. QCT, ultrasound), iii) causes of a low BMD other than osteoporosis (e.g. primary hyperparathyroidism, osteomalacia) are not considered, iv) extra-skeletal risk factors for fracture (e.g. propensity to fall) are not addressed, and v) qualitative bone changes are not assessed.<sup>4</sup>

Table 13.1. WHO criteria for osteoporosis in women<sup>13</sup>

Normal	BMD or BMC within 1SD of the young adult reference mean
Low bone mass	BMD or BMC 1-2.5 SD below the mean of young healthy women
Osteoporosis	BMD or BMC >2.5 SD below the mean of young healthy women
Severe (established) osteoporosis	BMD or BMC >2.5 SD below the mean of young healthy women and the presence of one or more fragility fractures

### 3.2 New definitions of osteoporosis

Although still recognising the importance of BMD, the most recent National Institutes of Health consensus statement defines osteoporosis as, "a skeletal disorder characterised by compromised bone strength that results in an increased risk of fracture".<sup>1</sup> The concept of bone strength has evolved to integrate those traditional measures of bone quantity (e.g. BMD) with more recently examined components of bone quality, namely i) macro-architecture (bone size and geometry), ii) micro-architecture (cortical thinning, porosity; trabecular size, number, connectivity), iii) bone turnover, and iv) material properties of bone (e.g. mineralisation, micro-fracture, collagen cross-linking) (Table 13.2).<sup>6,15-18</sup>

Table 13.2. Determinants of osteoporotic fractures

• Bone quantity	
-BMD	
• Bone quality	
-Macro-architecture	• Bone geometry/size
-Micro-architecture	• Cortical: porosity, thinning
	• Trabecular: size, number, connectivity
-Bone turnover	
-Material properties	• Mineralisation, micro-fracture, collagen cross linking
• Propensity to falls	

## 4. BMD-INDEPENDENT DETERMINANTS OF BONE STRENGTH AND FRACTURE

Although bone quality is difficult to assess clinically, a number of BMD-independent risk factors for osteoporotic fracture are now recognised, and these can aid the physician in identifying those at risk (Table 13.3). Age is one of the best-known risk factors, independent of BMD, and various changes in bone quality have been proposed to explain this observation. Up to 80% of the variation in peak BMD is determined genetically. However, a genetic predisposition to fracture, independent of BMD, has recently been documented. Polymorphisms in a number of genes (e.g. those encoding the oestrogen receptor, collagen and growth factors) have been proposed to explain this observation. Ethnicity affords another example, and I have alluded to the fact that the small differences in the BMD of black and white populations in this country are unlikely to explain the several-fold difference in fracture prevalence between groups.

In large osteoporosis drug trials, involving the bisphosphonates (FIT, VERT), selective oestrogen receptor modulators (MORE) and calcitonin (PROOF), a history of vertebral fractures was shown to increase the risk of a subsequent fracture three- to five-fold. Moreover, these studies revealed no correlation between changes in BMD and the degree of fracture risk reduction following drug therapy. A low body mass and bone toxins (glucocorticoids, alcohol, and tobacco) are other examples of BMD-independent determinants of bone strength. A high bone turnover is known to cause trabecular perforation and decreased interconnectivity, which markedly increase the likelihood of fracture, independent of BMD. Recently, animal studies have suggested that a chronically suppressed bone turnover may also predispose to fracture, but data in patients are lacking. Finally, the importance of extra-skeletal factors should not be ignored – falls, especially falling sideways, are incriminated in more than 80% of femoral neck fractures.

Table 13.3. BMD-independent determinants of bone strength and fracture

• Age
• Genetic susceptibility
• Ethnicity
• History of previous fracture(s)
• Low body mass
• Bone turnover (high/?low)
• Propensity to falls
• Bone toxins (glucocorticoids; alcohol, tobacco).

## 5. DIAGNOSTIC CRITERIA VS. INTERVENTION THRESHOLDS

The diagnostic categories developed by the WHO for postmenopausal Caucasian women should not be regarded as intervention thresholds for all.<sup>5</sup> The need to treat should not depend on the establishment of a largely BMD-based diagnosis alone but, similar to other chronic diseases of lifestyle, should also be determined by: i) the patient profile (age, life expectancy and general health, ongoing clinical risk factors, propensity to fall, etc.); ii) the nature of the disease (presence of fragility fractures, abnormal bone turnover, severity and rate of bone loss, etc.); and iii) the cost-effectiveness and side-effects of available treatment.

The assessment of BMD-independent risk factors is particularly important in those cases where BMD values are not markedly decreased (i.e. not within the so-called osteoporosis range of  $\geq 2.5$  SD below peak BMD), yet the patient is clearly at risk. Certain forms of the disease, for example glucocorticoid-induced osteoporosis (GCOP), are known to fracture at higher BMD values than postmenopausal or senile osteoporosis. An intervention threshold of  $\geq 1.5$  SD below peak BMD has been recommended for GCOP, whereas the British Rheumatology Society recommends bone active drugs in all subjects over the age of 65 years who receive glucocorticoids for longer than three months, irrespective of the bone mass. A known fragility-fracture – probably the single strongest predictor of future fractures – constitutes another indication for treatment, regardless of the BMD.

In this regard, the principles of osteoporosis management do not differ fundamentally from those of most other chronic degenerative diseases. For example, although diagnostic cut-off values for an increased blood pressure or plasma cholesterol have been clearly established, intervention thresholds and the nature of therapy are determined by very similar co-morbid factors. Clearly, health-care workers, as well as medical-aid funders, need to take cognisance of this paradigm shift in our approach to the management of patients with osteoporosis.

## 6. NON-PHARMACOLOGICAL MEASURES TO IMPROVE BONE STRENGTH AND PREVENT FRACTURES

These include a balanced diet rich in dairy products, physical exercise (30-minute walk, 3 times per week), limiting alcohol intake (not more than 7-10 drinks per week), the avoidance of smoking and bone toxic drugs, and the prevention of falls.<sup>1-4</sup> Particularly in older patients, the comprehensive assessment of falls and appropriate preventive measures may be more important than pharmacological intervention to reduce the risk of fractures. Risk factors include:

- i) Muscle weakness (the term “sarcopenia” was coined to emphasise the importance of this risk factor) and disturbances in balance and gait should be assessed, and exercise programmes implemented.
- ii) Medication, particularly sedatives and major tranquillisers, is the single most important reversible risk factor for falls in the elderly. Antidepressants, antihypertensives, hypoglycaemic agents, and alcohol may also predispose.

- iii) Other important potentially reversible risk factors include postural and postprandial hypotension, visual impairment, vertigo and drop attacks.
- iv) Environmental safety should be ensured. Up to 40% of falls are accident or environment-related (slippery surfaces, poor lighting, high-heeled shoes, etc).
- v) Previous falls (especially sideways falls) should be assessed and use of external hip protectors considered.

## 7. DRUGS USED TO TREAT OSTEOPOROSIS

These are conventionally classified as antiresorptive agents and those which stimulate bone formation. Some drugs have complex actions on bone. A comprehensive review of these drugs is beyond the scope of this report, which will largely focus on recent developments in antiresorptive therapy and on the introduction of new anabolic agents to treat osteoporosis.

### 7.1 Antiresorptive drugs/supplements

#### *Calcium and vitamin D*

Calcium supplementation and prophylactic doses of vitamin D (400-800 IU per day) cause a modest (approximately 25%), but significant, improvement in BMD and reduction in risk of vertebral and non-vertebral fractures. These nutrients are, however, less effective in patients with advanced, fracturing disease. All patients at risk should receive additional calcium, either in their diet or as a supplement. Vitamin D supplementation is recommended, especially in the elderly, the institutionalised, and those with a negative calcium balance and secondary hyperparathyroidism who are at risk of sustaining a hip fracture. Evidence for the routine use of pharmacologic doses of vitamin D, as well as the use of vitamin D metabolites (e.g. calcitriol), is unconvincing. Their use in the management of osteoporosis is further limited by the risk of hypercalcaemia and hypercalciuria, and the need for regular monitoring.

#### *Hormone therapy*

Hormone therapy (HT), employing oestrogen plus progestin (EPHT) or oestrogen alone (EHT), was previously regarded as the gold standard for the prevention and treatment of osteoporosis. Although initially based on data from observational studies, the large randomised controlled Women's Health Initiative (WHI) recently demonstrated a significant reduction in vertebral (35%), hip (33%) and total fractures (25%), with EPHT and EHT.<sup>19,20</sup> These benefits were, however, outweighed by an increase of 40% in strokes (EPHT and EHT), 50-100% in thromboembolism (EPHT and EHT), 26% in breast cancer (EPHT only) and 26% in cardiovascular events (EPHT only). Although the absolute number of patients adversely affected (as opposed to the relative risk) was small, total mortality unchanged, and prolonged exposure (> 5 years) required to result in most side effects, this study disproved a cardio-protective effect of EPHT as well as EHT, previously suggested by observational data. HT remains the only effective treatment for troublesome vasomotor and urogenital symptoms of the menopause. It may also alleviate emotional lability, but does not prevent Alzheimer's disease and may in fact increase the incidence of dementia in the elderly.

Hormone therapy remains a cost-effective method for preventing and treating osteoporosis. Unlike many antiresorptive drugs, HT appears to be highly effective in low-risk subjects, including those with only a modest decrease in BMD. Rapid, "catch-up" bone loss, however, occurs after HT is discontinued. Given the potential adverse extra-skeletal effects of HT following prolonged use, it is best reserved for the relative short-term (< 5 years) stabilisation of bone strength in patients younger than 60 years – ideally, in those who also have troublesome menopausal symptoms. Once stopped, consideration should be given to its replacement with an alternative agent.

The male menopause is presently receiving increasing attention. However, a discussion of the topic is beyond the scope of this report. Suffice it to say that in the symptomatic male a serum testosterone level below 8 nmol/l is generally regarded as an indication to treat. Serum levels beyond 15 nmol/l do not warrant intervention, whereas levels between 8 nmol/l and 15 nmol/l usually require further assessment (e.g. serum LH, FSH) before a decision on therapy can be made. However, very little evidence-based data on the efficacy or safety of testosterone treatment exist, and many physicians prefer to treat hypogonadal male osteoporotic patients with drugs like the bisphosphonates or teriparatide (*vide infra*).

#### *Selective oestrogen receptor modulators (SERMS)*

Raloxifene is a SERM, which has oestrogen agonist actions on the skeleton and lipid profile, yet acts as an oestrogen antagonist on the breast and endometrium. In the MORE study on 7 705 postmenopausal women, raloxifene decreased vertebral fractures by 49% after four years,

despite a very modest increase in BMD of only 3%. Although the risk of non-vertebral fractures was not altered, re-analysis of the MORE data demonstrated a significant 47% decrease in non-vertebral fractures in those patients with severe (SQ grade 3) vertebral fractures.<sup>21</sup> Raloxifene decreased the risk of vertebral fractures in osteoporotic and osteopenic patients. Raloxifene has been shown to decrease the risk of breast cancer by 62-84% and has no effect on the endometrium. Adverse events include an increase in thromboembolism, hot flushes, and leg cramps. Unlike EPHT, raloxifene does not increase the risk of cardiovascular disease, and may in fact be cardio-protective in patients at high risk of cardiovascular disease. While studies, such as the RUTH and CORE, continue to generate data on raloxifene, trials on other SERMS, including lasofoxifene and arzoxifene, are underway.

### *Bisphosphonates*

The amino-bisphosphonates (alendronate, risedronate, pamidronate, zoledronate) are analogues of pyrophosphate, which decrease bone resorption by reducing osteoclast recruitment and function, and inducing osteoclast apoptosis, resulting in a 5% to 8% increase in spinal BMD and a 3% to 6% increase in femoral BMD. The antiresorptive effects of the bisphosphonates are ascribed, at least in part, to their ability to inhibit rate-limiting enzymes (e.g. FPP-synthase) in the mevalonate pathway. Large RCTs employing alendronate and risedronate have documented a significant 40% to 60% reduction in risk of both vertebral and non-vertebral (including hip) fractures. Bisphosphonates are also effective in the treatment of glucocorticoid-induced and male osteoporosis.<sup>22-25</sup>

Fracture reduction is a function of increased BMD and reduced bone turnover. The latter effect presumably explains the reduced fracture risk demonstrated within six months of starting risedronate therapy. Unlike HT, bisphosphonates persist in the skeleton for months to years, which results in a prolonged action. Large differences exist among the bisphosphonates in their ability to suppress FPP-synthase activity, their binding affinity to bone tissue, and their accumulation in the skeleton. These factors ultimately determine the degree of suppression of bone turnover. The first ten-year's experience of alendronate treatment for osteoporosis was recently published.<sup>22</sup> Although the increase in BMD was most pronounced during the first few years of therapy, the reduction in fracture risk appeared to persist. Over-suppression of bone turnover after prolonged administration has raised concerns in animal experiments that employ large doses of bisphosphonates, but this is not supported by current clinical data, although further studies are required.

Bisphosphonates are poorly absorbed from the gut and may cause upper gastro-intestinal side effects. Daily dose regimens have largely been replaced by once-weekly schedules, and much research is currently focussing on the development of regimens, which range from monthly to even once-a-year administration.

### *Calcitonin*

This naturally occurring hormone has a rapid, but short-lived antiresorptive effect. Injectable and nasal spray preparations are available in this country. Fracture efficacy data are largely limited to the PROOF study,<sup>26</sup> employing 1 255 osteoporotic women, which showed a negligible increase in BMD, yet a 36% reduction in new vertebral fractures with a dose of 200 IU calcitonin daily – no significant decrease in fracture risk was, however, observed with 100 IU or 400 IU per day. Calcitonin has a central, opiate-mediated analgesic effect, which is recommended for the management of painful acute vertebral fractures. Until more evidence-based data on fracture efficacy become available, its long-term use should be reserved for those patients who cannot tolerate other antiresorptive agents.

## 7.2 Anabolic agents

While the mainstay of current therapies for osteoporosis is the antiresorptive agents discussed above, these drugs reduce but do not eliminate fracture risk, and do not restore lost bone structure. Anabolic agents have the potential to increase BMD, restore micro-architecture, and restore fracture risk to a greater extent than the antiresorptives. Fluoride was the first anabolic agent to be used in the treatment of osteoporosis. Although a marked increase in BMD followed the administration of fluoride, this never related to a significant decrease in fracture risk. Growth hormone, IGF, and more recently the lipid lowering statins have been proposed, but bothersome side effects and inability to target these agents to the skeleton have limited their use. Anabolic steroids and calcitriol may have modest anabolic effects on bone, but their utility is also limited by adverse effects. More recently, strontium ranelate and parathyroid hormone (PTH) have emerged as promising osteo-anabolic agents.

### *Teriparatide (PTH1-34)*

Intermittent, low-dose PTH administration causes rapid stimulation of bone formation resulting in a marked increase in bone mass, size and strength, as well as improvement in trabecular micro-architecture and cortical geometry. Following a few smaller studies, the results of a large randomised placebo-controlled trial involving 1 637 women with postmenopausal osteoporosis were recently published.<sup>27</sup> Compared with placebo, daily subcutaneous injection of HPTH (1-34), for as little as 21 months, increased lumbar BMD by 9% to 13% and femoral BMD by 3% to 6%, and reduced the risk of spinal and non-vertebral fractures by 65% and 40%, respectively. Favourable results of PTH on BMD and biomarkers of bone turnover have also been reported in male and glucocorticoid-induced osteoporosis.<sup>28-31</sup>

Side effects of teriparatide have been limited to occasional nausea, headaches, and leg cramps. Mild hypercalcaemia occurs in up to 10% of patients receiving 20 µg PTH daily and serum uric acid levels may increase by 20%, but renal stones and clinical gout are not thought to be more prevalent. Of some concern is the tumourigenic potential of PTH. Long-term studies with high-dose PTH, administered to 6-week-old Fisher 344 rats, have demonstrated a dose-related increased risk of osteogenic sarcoma.<sup>32</sup> This effect is consistent with life-long exposure, in a growing rodent, to high-dose PTH and is unlikely to have relevance to human bone physiology. Shorter or lower dose exposure to PTH has not resulted in the development of osteosarcomas or other bone tumours. All primate studies have failed to show a similar association and osteogenic sarcomas do not occur with increased frequency in patients with primary hyperparathyroidism or from any of the clinical trials performed in over 2500 patients treated with PTH (1-34) for up to three years. It is, therefore, reasonable to conclude that PTH is safe in human subjects, although on-going safety data need to be collated.

Teriparatide has recently become available in South Africa. Given its high cost, the manufacturer and local funders approached the National Osteoporosis Foundation (NOFSA) to provide guidelines on its use, resulting in the publication of a position paper.<sup>33</sup> While many potential indications for its use may exist (e.g. very low prevalent BMD, high fracture risk), NOFSA recommends that teriparatide should be reserved for patients with severe, established osteoporosis. This involves either:

- (1) a low BMD and two or more prevalent fractures, or
- (2) failed antiresorptive therapy, after adhering to adequate antiresorptive therapy for at least 12 months, with the patient experiencing either i) an incident fragility fracture, or ii) an unacceptable rate of bone loss (e.g. a decrease in vertebral BMD of ≥ 5% per annum) as documented in two or more consecutive follow-up BMD measurements.

A number of contra-indications have been suggested, as well as the recommendation that 20 µg teriparatide per day be used for no longer than 18 months. All patients should be subjected to a full clinical and laboratory work-up to confirm a diagnosis of osteoporosis and to rule out other causes of a low BMD (primary hyperparathyroidism, osteomalacia). This should also rule out causes of secondary osteoporosis, which may require treatment in own right, evaluate the severity of the disease, and assess compliance and adherence to prior antiresorptive therapy for osteoporosis. Given recent reports that concurrent use of PTH and potent antiresorptive drugs like alendronate may ameliorate the anabolic effects of PTH,<sup>29,30</sup> concomitant treatment with teriparatide plus antiresorptive agents is not recommended. Careful clinical and laboratory follow-up of all subjects are required and following completion of the 18-month course of teriparatide therapy, treatment with a potent antiresorptive agent, like a bisphosphonate, is recommended to preserve bone mass gained.

### *Strontium ranelate*

Strontium ranelate has been shown to increase osteoblast proliferation and collagen synthesis, and to decrease osteoclast replication and activity *in vitro*. Bone histology has confirmed the dual action of this drug, increasing bone formation and decreasing resorption. Animal studies show an increase in BMD, bone size and strength following strontium ranelate administration. Two large RCTs have recently been published.<sup>34-36</sup> The SOTI trial employed 1 649 women, average age 69 years, with either osteoporosis or osteopenia.<sup>35</sup> After three years, strontium ranelate significantly increased biomarkers of bone formation and decreased parameters of resorption, resulting in an increase in lumbar BMD of 14%, and a 41% to 52% reduction of new spinal fractures. Quantitative bone histology revealed no evidence of a mineralisation defect. The TROPOS trial studied 5091 elderly (76-yr) women with an average femoral neck T-score of -3.1, for three years.<sup>36</sup> Femoral BMD increased by 8% and the incidence of hip fractures was reduced by 36%. Both the SOTI and TROPOS trials demonstrated excellent adherence to therapy

(83%) and no significant adverse effects. Strontium blood levels can be readily measured to monitor therapy. This drug, clearly holding much promise, will probably be launched in South Africa during 2006.

## 8. ACUTE MANAGEMENT OF SYMPTOMATIC VERTEBRAL FRACTURES

Traditional management of the acute painful vertebral fracture consists of analgesia, bed rest with physical support (such as a corset) and gradual mobilisation. There is, however, no consensus as to the best treatment.<sup>37</sup> Strong analgesics, such as the opiates, should be used for short periods only. Non-steroidal anti-inflammatory drugs have been shown in some studies to suppress bone formation and fracture healing. Tricyclic antidepressants (to lower pain threshold and perception) and some muscle relaxants may predispose to falls. Calcitonin has central analgesic properties and two recent studies have reported the use of intravenous bisphosphonates in patients following acute vertebral fracture. Results, although encouraging, require further study.

Prolonged physical immobilisation and the use of a corset are generally discouraged since these are thought to promote bone loss and muscle wasting. The use of specialised corsets, which cause abdominal compression and an improvement in posture, however, may provide a viable option. Employing such a new spinal orthosis, a recent RCT documented a significant 40% decrease in pain, an 11% decrease in the angle of kyphosis and, surprisingly, a 73% increase in back extensor strength and a 58% increase in abdominal flexor strength.<sup>38</sup> Transcutaneous electrical nerve stimulation (TENS), intercostal nerve blocks, acupuncture, and implanted devices employing the "gate theory" of chronic pain control offer acceptable alternatives.

### Vertebral kyphoplasty

Conventional therapy of vertebral fractures allows the bone to heal in its fractured or deformed state. This may result in chronic pain, impaired mobility, pulmonary dysfunction, a decrease in overall quality of life and early mortality. Balloon kyphoplasty involves the percutaneous placement of an orthopaedic balloon inside the fractured vertebral body. The balloon is inflated, elevating the vertebral endplates and creating a cavity. After the balloon is removed, the cavity is filled with bone cement, usually polymethylmethacrylate, thereby stabilising the fracture that facilitates immediate mobility.<sup>39-41</sup>

Although more than 50 000 patients have apparently been treated worldwide, and the technique is also available in South Africa, published experience is limited and a recent review could only document two uncontrolled prospective studies and a number of case reports.<sup>37</sup> Significant pain relief and improved mobility was apparent within one to two days in up to 80% of patients. Complications appear to be uncommon, and were more prevalent when the bone cement was directly injected into a vertebral body without first creating a balloon cavity, but include leakage of cement into the paravertebral tissue, compression of the spinal nerve roots and pulmonary embolism.

Only patients with severe pain and loss of mobility who have not responded to conventional therapy should be considered. Timing of the procedure remains controversial; while some advocate kyphoplasty within the first two weeks following a fracture others suggest conservative treatment for at least six weeks. The latter certainly seems more rational. Other causes of pain must be excluded and only recent fractures are amenable to kyphoplasty. Total compressed vertebrae cannot be reduced, and it has been suggested that the affected vertebra should retain at least one third of its original height for the procedure to be successful. CT, MRI or isotope bone scans are employed to select those most likely to benefit from vertebroplasty.

Balloon kyphoplasty appears to be a safe and effective treatment to stabilise acute vertebral fractures, reduce pain, restore the bony anatomy and effect early mobilisation. However, no evidence-based data on the long-term effects of this procedure are available, in particular the incidence of new vertebral fracture near the cemented vertebra. Further RCTs are required before this technique can be recommended for the routine treatment of the acute vertebral fracture syndrome.

In conclusion, it is clear that a broadened conceptual understanding of the definition of osteoporosis has resulted in a more rational approach to its diagnosis and management. More evidence-based data on the efficacy and safety of known antiresorptive drugs employed in the prevention and treatment of patients with osteoporosis is reassuring. The availability of potent, safe osteo-anabolic agents offers much promise, even for those with advanced disease, particularly in South Africa.

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