

# Recommendations for the acute and long-term medical management of low-trauma hip fractures

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## Abstract

Hip fractures are the most serious complication of osteoporosis and are associated with high morbidity and mortality. Generally, patients who sustain osteoporotic hip fractures are older adults who have a number of co-morbid diseases which predispose them to perioperative complications, disability and death. Furthermore, patients who survive a hip fracture are at higher risk of a subsequent fracture. The morbidity and mortality of hip fractures can be substantially reduced by a structured multidisciplinary approach to pre- and postoperative management. This review will focus on the epidemiology of hip fractures, predictors of mortality and the acute and long-term management of hip fractures.

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## Introduction

The association between hip fractures and an age-related reduction in bone mass and quality was first recognised over 160 years ago by Sir Astley Cooper.<sup>1</sup> It is estimated that one in two women and one in five men over the age of 50 years will sustain an osteoporotic fracture in their lifetime.<sup>2</sup> The wrist, spine and hip are common fracture sites.

The global prevalence of hip fractures is rising. Of the global 9 million osteoporotic fractures that occurred in 2000, 1.6 million were hip fractures.<sup>3</sup> It is estimated that this number will increase to 2.6 million in 2025 and to 6.3 million by the year 2050.<sup>4</sup> While part of this increase can be explained by the worldwide increase in life expectancy, longevity alone does not entirely explain the increase, and several other factors, such as a decline in physical activity and increasing frailty, have been implicated.

Fractures at the hip represent the most severe consequence of osteoporosis as they require admission and are associated with significant morbidity and mortality. In the first year following hip fractures, 20-24% of patients die, either owing to the fracture itself or to co-morbid disease. Fifty per cent are unable to walk without assistance and 33% are totally dependent or live in a nursing home. Mortality is significantly higher in men.

The combined annual cost of hip fractures was estimated to be €30 billion in the European Union and US\$20 billion in the USA in 2002.<sup>5</sup> Sixty-three per cent of the latter was for management of the hip fractures.<sup>6</sup> Drug therapy and hospital admissions further added to this expense.<sup>7</sup> Fifteen years ago, the acute cost of treating a hip fracture in South Africa was estimated to be R50 000.<sup>8</sup> Currently, it is approximately R150 000.

## Epidemiology of hip fractures

There are significant variations in hip fracture rates according to different geographic areas, and ethnic and gender groups.

### Geographic and ethnic variations

The highest hip fracture rates, at greater than 6 per 1 000 per year, are seen in the white Scandinavian and North American populations, followed by a rate of 4-6 per 1 000 per year in England, Scotland, New Zealand and Finland.<sup>9</sup> In Europe, the incident rate varies from the north, where it is highest, to lower rates in France and Switzerland. The lowest rates are in the Mediterranean countries.<sup>10</sup> Intermediate fracture rates have been reported in Turkey, Kuwait and Iran, and the Asian communities of Singapore, Hong Kong and Japan.<sup>10-13</sup> The lowest rates have been described in developing countries and in black populations in Africa.

There have been limited studies on osteoporotic fractures in Africa. In earlier studies, no minimal trauma fractures

were identified in rural Gambia,<sup>14</sup> and an age-related increase in hip fractures was not observed in Nigeria.<sup>15</sup> However, in a more recent study from Cameroon, hip fractures were identified in 40 subjects (27 women and 13 men) aged 50 years and above.<sup>16</sup> Compared to the USA, the substantially lower fracture rate was attributed to the significantly lower life expectancy. Similarly, the lower incidence of osteoporotic fractures in Morocco has also been ascribed to a lower life expectancy.<sup>17</sup> However, these studies do show that osteoporotic fractures occur in Africa.

In South Africa, studies have examined risk factors and the prevalence of osteoporosis in the different ethnic groups. Until recently, there has been only one study on the prevalence of hip fractures. This study<sup>18</sup> reported an extremely low prevalence of hip fractures in black South Africans, which could not be explained by differences in bone mass. Bone mineral density (BMD) has been reported to be the same or higher in blacks than whites<sup>19, 20</sup> and persons of mixed ancestry.<sup>21</sup> However, a recent study reported hip fractures in all ethnic groups in South Africa and supports clinical experience that hip fractures are more common than previously thought.<sup>22</sup>

While the incidence of hip fractures appears to be stabilising in the more developed countries, it is projected that the burden of osteoporotic hip fractures will shift to Latin American, Asia and Africa, where the population are rapidly ageing. It is predicted that in the year 2050, 70% of over 6-million predicted fractures will occur in these populations.

Within countries, ethnic differences have also been reported in the incidence of hip fractures. In the USA, the age-adjusted incidence rates of hip fractures were higher in whites than Asians, blacks and Hispanics.<sup>23</sup> Higher bone mass and shorter hip-axis lengths in black and Hispanic populations may explain these differences.<sup>24</sup> Similarly, differences in hip-axis length have also been suggested as a cause of the lower adjusted fracture rates in Indians than in Chinese and Malay subjects in Singapore.<sup>25</sup> Other contributing factors for ethnic differences include variations in bone size, levels of physical activity, diet, neuromuscular functioning and frequency of falls.

### Age and gender

The exponential rise in the prevalence of osteoporotic hip fractures with advancing age is explained by the age-related decrease in bone strength and the increase in frequency of falls in the elderly, especially women. Over their lifetime, bone density at the femoral neck is estimated to decrease by 58% in women and 39% in men, and by 53% and 35% at the proximal femur, in women and men respectively.<sup>26</sup>

The female to male ratio of osteoporotic hip fractures in countries with a high incidence rate of osteoporosis is 2:1, but approaches 1:1 with advancing age<sup>27</sup> and in countries with a low hip fracture incidence.<sup>17</sup> Hip fractures generally occur at a later age in men, but regional differences have been reported. In an Australian study, the burden of hip fractures was shown to occur at an earlier age in men, than in women.<sup>28</sup> In this study, the incidence of fractures peaked at 84 years in men. Forty-eight per cent experienced fractures before the age of 80 years, compared to 66% of women who had fractures before the age of 85 years.<sup>28</sup> Analysts predict that by the year 2040, with increasing life expectancy in men, there will be as many hip fractures in men as there are in women today.

### Other risk factors for hip fractures

Numerous large epidemiological studies have identified risk factors for hip fractures. In addition to age, gender and ethnicity, these include:

- Low BMD.
- Frequency of falls.
- Prior fractures.
- Low bodyweight.
- Excessive alcohol intake and smoking.
- Cognitive impairment.
- Vitamin D deficiency or insufficiency.
- Secondary causes of osteoporosis.

BMD is one of the most important determinants of fracture. Although geometry, micro-architectural integrity, length and cross-section of the proximal femur all contribute to bone strength, the relationship between BMD and fracture has been best established. For every one standard deviation decrease in BMD, there is a 2.4 to threefold increase in age-adjusted hip fractures.<sup>29</sup> The existence of a prevalent fracture is also a strong predictor of future hip fractures. The presence of a prior distal arm or vertebral fracture has been shown to increase the risk of hip fractures<sup>30, 31</sup> and a person with one hip fracture has a 60% increased risk of having a subsequent hip fracture.<sup>32</sup> Previous childhood fractures and a maternal history of hip fractures are also strongly associated with increased risk.<sup>33</sup>

Almost all hip fractures are preceded by a fall. Important risk factors for falls include advanced age, frailty, cognitive impairment, postural hypotension, visual, gait and balance disturbances, use of drugs such as sedatives and alcohol, and environmental hazards.<sup>34</sup>

The World Health Organization recognised that clinical risk factors increase risk fractures independently of BMD, and that the risk of fracture increases with the number of risk factors present. It developed a fracture risk assessment tool called FRAX®.<sup>35</sup> This tool integrates

the risk associated with clinical risk factors that were identified from meta-analyses of large epidemiological studies, as well as BMD at the femoral neck, to calculate the 10-year probability of fractures for men and women. The FRAX<sup>®</sup> score improves the prediction of future fractures. However, the derived intervention thresholds are dependent on epidemiological and health economic data, and are therefore country-specific. While a study is underway, there are no available incidence data on hip fractures in South Africa. Consequently, the FRAX<sup>®</sup> cannot be applied to South African populations at present.

### Morbidity and mortality post hip fractures

Osteoporotic hip fractures account for more disability-adjusted life years (DALYs) than most cancers, asthma and rheumatoid arthritis.<sup>3</sup> Up to 50% of patients have permanent disability post a hip fracture, and only 30% regain full function. One year post a hip fracture, 40% of patients are unable to walk independently, 60% require assistance with one essential daily living activity (such as dressing), and 80% require assistance with at least one instrumental daily living activity (such as shopping).<sup>36</sup>

Globally, there is a 10-20% mortality rate following hip fractures. Mortality and morbidity rates increase with increasing age, the presence of co-existing diseases and poor functional status prior to the fracture. Mortality is highest within the first six months, and relates to the fracture itself, whereas after six months, it is more likely to be due to pre-existing diseases and functional status.<sup>37</sup> In a prospective study in Britain, the mortality rate post hip fracture was 33% at 12 months, and 15% of patients died in hospital prior to discharge.<sup>38</sup>

### Predictors of mortality

A higher mortality rate has been reported in men than in women. In one study, 14% of men died in hospital in the immediate period following a hip fracture, compared to 6% of women.<sup>39</sup> Hospital stay is also longer for men and days spent in hospital by men for osteoporotic hip fractures exceed those for carcinoma of the prostate.<sup>27</sup>

Strong evidence of 12 predictors of mortality was reported following a recent large meta-analysis of 64 316 patients, where overall in-patient or one-month mortality was 13.3%, and 15.8%, 24.5% and 34.5% at 3-6 months, one year and two years, respectively.<sup>40</sup> The predictors were advanced age, male gender, nursing home or facility residence, poor preoperative walking capacity, poor daily living activities, poorer global physical status and fitness for surgery (as defined by a higher American Society of Anesthesiologists grading), poor mental state, multiple co-morbidities, dementia or cognitive impairment, diabetes, cancer and cardiac disease.<sup>41</sup> Other studies have also identified low

albumin levels on admission and a delay in surgery as predictors of a poor outcome.<sup>42</sup>

### Acute management of hip fractures

Patients who sustain hip fractures are usually of advanced age with multiple co-morbidities and are therefore at high risk of peri- and postoperative complications, which can be mitigated by appropriate pre- and postoperative management, ideally by a multidisciplinary team (Table I).

### Timing of surgery

Timing of surgery refers to the time from the fracture to the time of surgical fixation. There is no consistent definition as to what constitutes early surgery, but most studies have used a period of between 24 and 72 hours. (The International Osteoporosis Foundation (IOF) recommends 24 hours). In a meta-analysis of 16 observational studies, earlier surgery was associated with a significantly lower mortality rate [relative risk (RR) 0.81, 95% confidence interval (CI): 0.68-0.96, p-value = 0.01]. Earlier surgery also significantly reduced in-hospital pneumonia (RR 0.59, 95% CI: 0.37-0.93, p-value = 0.02) and pressure sores (RR 0.48, 95% CI: 0.34-0.69, p-value < 0.001). By contrast, earlier surgery has not been shown to reduce the risk of deep venous thrombosis (DVT) or pulmonary embolism.<sup>42</sup>

It is recommended that patients who are admitted with a hip fracture and who are medically fit should undergo surgical fracture management within 24 hours of fracture in non-after hours operating time (generally accepted as 08h00 to 20h00, seven days a week).<sup>43</sup>

### Delaying surgery for medical stabilisation

More than 60% of older patients who are admitted with a hip fracture will have significant co-existent medical pathology.<sup>44</sup> Briefly delaying surgery, but still aiming for its occurrence within 72 hours post fracture, is recommended for the medically unstable patient to allow for maximal medical optimisation.

Classes of major abnormalities associated with poor postoperative outcomes include:<sup>45</sup>

- *Cardiovascular disease:* Cardiovascular disease encompasses systolic blood pressure < 90 mmHg, ventricular tachycardia or supraventricular tachycardia (a rate > 120/minute), a third-degree heart block or heart rate of < 45/minute, a new myocardial infarction on electrocardiogram (ECG), or chest pain with an abnormal ECG, pulmonary oedema or heart failure confirmed on a chest X-ray.
- *Respiratory conditions:* These are defined by a temperature < 35°C. (This emphasises the need for special low-reading thermometers in the trauma unit) or ≥ 38.5°C plus a clinical diagnosis of pneumonia or chest infiltrates on radiograph,

**Table I: Recommendations for acute orthogeriatric fracture management in South Africa****Emergency department or casualty**

- Emergency resuscitation should be carried out, if needed.
- A patient with a suspected hip fracture should receive an appropriate X-ray of the hip, pelvis and chest.
- Intravenous fluids can be started.
- Blood should be sent for analysis. (This includes a full blood count, international normalised ratio/partial thromboplastin time, type and screen, urea, creatinine and electrolytes, and corrected calcium).
- An electrocardiograph must be carried out.
- Pain should be assessed at regular intervals, according to a standard pain treatment regimen.
- A urinary catheter needs to be placed, with drainage to gravity.
- Once the fracture has been confirmed, an urgent referral or transferral to a definitive orthopaedic service must be carried out.
- An associate geriatric physician team should be notified.
- An initial orthopaedic assessment can be performed.

**Preoperative management**

- The patient can be admitted preferentially to a designated unit or ward.
- Old records should be obtained as soon as possible.
- A physician or geriatrician assessment must be carried out, anaesthetics notified of the surgical plan and theatre booked.
- Assessments or vital signs must be taken 4-6 hourly, including blood pressure, pulse, temperature, pain, pulse oximetry, orientation or confusion, as well as neurovascular checks. Intake and output should be monitored.
- Bed rest is important and should encompass two-hourly pressure care, including heel protectors, anti-embolic compression devices and use of pressure-relief mattresses and an overhead trapeze, if available.
- Foot and ankle exercises can be conducted every 1-2 hours, as well as incentive spirometry (sustained maximal inspiration with visual feedback on a spirometer) every hour when awake.
- An assessment should be made of cardiac and thrombotic risk and the need for a beta blocker and/or statin.
- Team collaboration is important regarding anticoagulant (aspirin, warfarin or clopidogrel) issues.
- Low-molecular-weight heparins should be commenced, unless contraindicated.
- The standardised pain regimen should continue.
- A normal diet is allowed until six hours before surgery. Water, lemonade and clear carbohydrate-enriched drinks may be considered until two hours before surgery, if permitted by the anaesthetics' team.
- An assessment should be carried out of nutritional status, and supplementation provided for patients with poor nutrition, or those who are at-risk of poor nutrition.
- A bowel regimen can be commenced.
- Deliriogenic medications, such as hypnotics, antihistamines, anticholinergics and benzodiazepines, should be avoided or withdrawn. Low-dose haloperidol prophylaxis should be considered for high-delirium-risk patients who have no contraindication to neuroleptics.
- Low-dose maintenance hypnotics can be contemplated in hypnotic-dependent patients.
- An antiemetic regimen should be started, if needed.
- Continuous oxygen therapy can be implemented at 2 l/minute, or higher flows to keep saturations > 93%.
- Brochures may be handed over and discussions commenced with the patient and his or her family on hip fracture care, including aspects of rehabilitation and discharge planning.
- Cefazolin 1 g can be given preoperatively to nonallergic patients in the operating room.

respiratory failure with oxygen saturation of < 90% on pulse oximetry, or oxygen partial pressure (pO<sub>2</sub>) < 60 mmHg or carbon dioxide partial pressure (pCO<sub>2</sub>) of > 55 mmHg).

- *Haematological abnormalities:* These are classified as an international normalised ratio > 1.6 and haemoglobin < 7.5 g/dl.
- *Serum electrolytes and/or renal abnormalities:* This refers to sodium < 125 mmol/l or potassium < 2.5 mmol/l, urea > 18 mmol/l, creatinine > 225 µmol/l or serum glucose > 33 mmol/l. It is recommended that the aim should be a serum glucose level of 6-10 mmol/l during the perioperative period.

**Type of anaesthesia: regional (spinal or epidural) versus general**

There is no evidence to support a preference for regional over general anaesthesia.<sup>46</sup> On the contrary, the Scottish Hip Fracture Audit showed a very small, but statistically significant, lower absolute mortality

in patients who received general versus regional anaesthesia.<sup>44</sup>

**Managing cardiac risk: beta blockers, statins and anti-platelet agents**

Death from cardiovascular disease occurs 90 times more commonly than that from fatal pulmonary embolism within the first six months of hip fracture.<sup>47</sup>

**Cardioselective beta blockers**

Orthopaedic surgery is considered to be intermediate risk surgery, with a reported risk of cardiac death or nonfatal myocardial infarction of up to 5%.<sup>48</sup> The American College of Cardiology and the American Heart Association recommends that patients who are scheduled to undergo intermediate-risk surgery with more than one clinical risk factor should be treated with cardioselective beta blockers such as atenolol, bisoprolol and metoprolol, and that the dose should be titrated to achieve a heart rate between 60 and 80

**Table I: Recommendations for acute orthogeriatric fracture management in South Africa cont.****Postoperative management**

- The patient should be seen daily by the orthopaedic surgeon and a physician or geriatrician, with frequent communication between the teams.
- The patient can then be started on clear fluids and the diet advanced, according to tolerance. The diet should include additional supplementation for malnourished or at-risk patients. Dentures must be used properly, and patients properly positioned for and assisted with meals, if necessary.
- Oxygen therapy can be implemented through a nasal catheter when the patient is resting and during the first four nights postoperatively. The patient should turn, cough and breathe deeply every 1-2 hours, while awake.
- Transfusion may take place to keep the haemoglobin > 10 g/dl.
- Prophylactic antibiotics can be continued for 24 hours postoperatively (cefazolin 1 g eight-hourly).
- An assessment should be made of the patient's vital signs 4-6 hourly, including blood pressure, pulse, temperature, pain, pulse oximetry, orientation and confusion, as well as neurovascular checks. Intake and output must also be monitored.
- The standardised pain regimen can be continued.
- Anticoagulation should be continued or commenced with unfractionated or a low-molecular-weight heparin, and the dose adjusted according to renal function. The duration of the anticoagulation will need to be individualised and may be from 2-6 weeks.
- The bowel regimen must be continued, with the aim for a bowel movement by postoperative day two and every 48 hours thereafter.
- The catheter may be removed by 10h00 on day one postoperatively. If retention is suspected, this should be confirmed using either an immediate ultrasound bladder scan or single catheterisation to measure the residual volume. (There is retention if there is > 300 ml). If a second episode of retention occurs, then scheduled intermittent catheterisation should either be sustained 4-6 hourly, or continuous catheterisation for 1-2 days. It is important to screen for and treat urinary tract infections. A skin care programme can be implemented for patients with established incontinence.
- Intake and output must be recorded to assess fluid balance.
- Activity should comprise the patient walking from the bed to the chair twice a day by day one postoperatively. Further activity is dependent on the patient's weight-bearing status.
- Occupational and physiotherapy should be commenced on day one postoperatively. Pre-emptive analgesia is recommended before mobilisation takes place.
- Use of adaptive devices, such as glasses and hearing aids, should be ensured, as well as regular orientation.
- Calm reassurance, the family presence or a sitter should be used to assist with agitation.
- Appropriate postoperative surgical films can be ordered.
- Rehabilitation or social services consultation can take place for the purposes of discharge planning.
- An assessment of recurrent fall risk should be carried out and a fall prevention programme devised.
- Management, and additional investigation of the underlying cause, of established severe osteoporosis should be implemented. This must include vitamin D and calcium supplementation, as well as specific bone therapies. In-patient vitamin D repletion is recommended with three daily doses of 50 000 iu of calciferol, or a 150 000 iu loading dose of calciferol. Specific bone therapy should be commenced in stable patients within 48 hours of discharge. Detailed referral is necessary on discharge, including written instructions and follow-up arrangements.

**Standard pain treatment regimen**

- Paracetamol 1g, six-hourly orally or intravenously, should be given.
- Tramadol is an intermediate-efficacy atypical opioid. Dose adjustment is necessary in older persons. Dosage is 50-100 mg intravenously or orally, at 12-hourly intervals.
- Morphine 5-10 mg can be used 4-6 hourly subcutaneously or intramuscularly, or sustained-release given orally, initially at 10 mg twice daily. Intravenous morphine should only be utilised in high care or intensive care settings. A naloxone injection must be immediately available if morphine is utilised.
- Nonsteroidal anti-inflammatories should only be given to non-frail patients (generally those who are younger than 75 years old), without cardiovascular co-morbidity, and who are haemodynamically stable with normal renal function. If necessary, ibuprofen 200-400 mg eight-hourly can be considered. Regular monitoring of renal function and prophylactic anti-acid therapy with a proton-pump inhibitor is recommended. Intramuscular preparations should never be used.
- Dihydrocodeine is an intermediate-efficacy opioid. Doses of 30 mg should be given orally 4-6 hourly, or 50 mg intramuscularly or subcutaneously 4-6 hourly.

beats per minute. Clinical risk factors include ischaemic heart disease, a history of congestive cardiac failure, a history of cerebrovascular disease, diabetes mellitus with insulin therapy and renal impairment. Extended release beta blockers should be avoided in these patients as they may increase the risk of sustained significant perioperative hypotension. Therapy should be continued for at least seven days postoperatively, unless the patient develops significant hypotension or bradycardia.<sup>49</sup>

**Perioperative statins**

Patients with established coronary artery or other vascular disease should be considered for statin use, if not already on statin therapy. A meta-analysis to determine the influence of statin treatment on adverse postoperative outcomes (including patients undergoing noncardiovascular surgery) showed a significant reduction in mortality and in acute coronary syndromes in patients taking statins.<sup>50</sup> Patients who are already taking statins should continue this therapy during the perioperative period. However, presently

there is not sufficient evidence to support the routine use of statin therapy for all patients undergoing hip-fracture repair surgery.<sup>50</sup>

#### Anti-platelet agents

- *Aspirin*: Patients taking aspirin for cardiovascular risk reduction should continue therapy throughout the perioperative period as this benefit outweighs the risk of bleeding.<sup>51</sup> Used alone, aspirin does not appear to increase the risk of spinal haematoma during regional anaesthesia.<sup>52</sup> A meta-analysis of 10 orthopaedic trauma trials found that aspirin significantly reduced the rate of DVT and pulmonary embolism, compared with placebo. However, this reduction was significantly less when compared with other agents, such as warfarin and a low-molecular-weight heparin.<sup>53</sup>
- *Clopidogrel*: The use of clopidogrel, either alone or in combination with aspirin, is associated with increased perioperative blood loss. This risk is further enhanced with a shorter time between the last dose and surgery and longer operative times.<sup>54</sup> Patients taking clopidogrel require careful individualised assessment of perioperative bleeding risk versus the risk of vascular events. Options include delaying surgery for five days post clopidogrel cessation when the bleeding risk will be lower. However, the risks of thrombosis and immobility complications will be higher. Alternatively, surgery may be performed 48 hours after cessation of clopidogrel, when although antiplatelet activity persists, active metabolites will have been cleared, allowing for platelet transfusion in the event of severe bleeding.<sup>55</sup>
- *Warfarin*: Rapid correction of warfarin anticoagulation is possible with the use of fresh frozen plasma and vitamin K infusion. Ongoing perioperative anticoagulation, with either unfractionated or a low-molecular-weight heparin, is recommended for high-risk patients, e.g. patients with metal prosthetic heart valves.

#### Prevention of deep vein thrombosis and pulmonary thromboembolic disease

The prevalence of DVT in patients with hip fractures is as high as 40-60%. The risk occurs from the time of fracture. Mechanical pumping devices may protect against DVT. Handoll et al reported a significantly lower prevalence of DVT in patients when mechanical pumping devices were used, than when they were not (7% vs. 22%, RR 0.31, 95% CI: 0.19-0.51). Problems with skin abrasion and compliance have been reported.<sup>56</sup>

Prophylaxis, with an unfractionated heparin or a low-molecular-weight heparin, has been shown to reduce the incidence of lower-limb DVT (26% vs. 42%, RR 0.60, 95% CI: 0.50-0.71). There was no mortality difference between treatment and placebo. There is insufficient evidence to establish if low-molecular-weight heparins

are superior to unfractionated heparins in the acute hip-fracture setting.<sup>57</sup> Excessive bleeding, or the need for transfusion, is significantly increased (6% vs. 3.8%) with the use of subcutaneous heparin prophylaxis.<sup>58</sup> Prospective large-scale observational cohort studies from France and Norway show that the use of heparin prophylaxis reduces the incidence of DVT to 1.3-2.7%, and that of pulmonary embolism to 0.25-1.7%.<sup>47,59</sup>

#### Nutrition

All patients should undergo an assessment of nutritional status on admission, using validated bedside nutritional tools, such as the Mini-Nutritional Assessment<sup>®</sup>,<sup>60</sup> or an assessment by a dietitian. Measures to alleviate poor food intake during hospital admission aim to prevent malnutrition which may hinder recovery. One systematic review has found that oral protein and energy feeds reduced unfavourable outcomes after surgery for a hip fracture.<sup>61</sup>

#### Perioperative antibiotics

Perioperative antibiotics, either single- or multiple-dose regimens (Table I), reduce the incidence of deep wound, superficial wound, urinary tract and respiratory tract infections. Adverse effects, such as an allergy, rash or gastrointestinal complaints, are rare (< 2%).<sup>62</sup>

#### Delirium

Delirium is an acute brain failure syndrome or confusional state. It is associated with acute hip fractures, as both a potential contributor to sustaining the fracture, as well as a complication of the physiological stress of the fracture, its surgical repair and the associated hospital care and environment. Delirium occurs in 35-65% of patients with hip fractures and is associated with adverse outcomes, high morbidity and mortality, longer length of hospital stay, greater functional decline and a high rate of institutionalisation after discharge.<sup>63-65</sup> Risk factors for delirium in patients with hip fractures include visual impairment, severe illness, pre-existing cognitive impairment, use of anticholinergic drugs, dehydration, perioperative blood pressure falls and infection.<sup>64</sup> Proactive geriatric or physician consultation to facilitate multicomponent nonpharmacological interventions, i.e. multidisciplinary interventions which integrate supportive, environmental, nursing and other components of care, have been shown to reduce both delirium incidence (by over one third), and severity (severe delirium was reduced by over a half) in older in-patients.<sup>66, 67</sup> Specific pharmacological therapy with low-dose (1.5 mg daily) haloperidol prophylaxis in high-risk, older patients undergoing hip surgery was shown to significantly reduce the severity and duration (by 6.4 days, 95% CI: 4-8 days), but not the incidence of postoperative delirium. No haloperidol-related side-effects were noted in this double-blind, placebo-controlled randomised trial with 430 participants.<sup>68</sup>

### Pressure sores

Measures to prevent the development of pressure sores should commence from the time of fracture. High-specification foam mattresses and pressure-relieving mattresses on operating tables prevent pressure sores (RR 0.29, 95% CI: 0.19-0.43).<sup>62</sup> Earlier surgery also reduces pressure sores.<sup>42</sup>

### Urinary retention

Older patients with hip fractures have a high risk of urinary retention (80% pre- and 50% post-surgery). Risk factors for urinary retention include advanced age, spinal anaesthesia, delirium, immobility, a previous history of bladder problems, prostatic hyperplasia, urethral strictures, pain, large amount of intravenous fluids, surgery of a long duration, longstanding diabetes (> 15 years), and use of anticholinergic medications and analgesics, and constipation. General evidence supports the removal of urinary catheters within 24 hours postoperatively with a programme to detect and then prevent retention. Should retention develop, short-duration urethral catheterisation or scheduled intermittent catheterisation is recommended. This programme reduces the 25% rate of urinary tract infection that is associated with hip fracture.<sup>69</sup>

### Pain control

Uncontrolled pain is a major impediment to postoperative functional recovery and is associated with longer hospital admission, more complications (such as delirium), a delay in ambulation, impaired functional recovery and greater suffering. Multi-component intervention, including pain assessment, protocols for standing analgesia and pre-emptive analgesia before physiotherapy, has been shown to improve postoperative pain, reduce chronic pain and improve function. The multi-component intervention also results in a small but significant reduction in hospital stay duration.<sup>70</sup>

Recommended analgesic agents for the management of hip-fracture-associated pain include opioids, weaker opioids, paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs). Prescribers need to be cognisant of the higher risk of adverse drug events in frail older persons.

Specific care regarding use of NSAIDs is required to avoid normotensive ischaemic renal failure. NSAIDs should be avoided in high-risk patients who have one or more of the following risk factors: older age (> 75 years), chronic renal disease, atherosclerosis, chronic hypertension, sepsis, perioperative hypotension, dehydration, excessive bleeding, heart failure, cardiac arrhythmias and concomitant use of angiotensin-receptor blockers or angiotensin-converting enzyme inhibitors.<sup>71</sup> There is also concern from animal and retrospective studies

that NSAIDs may delay fracture healing. However, this is controversial and one randomised controlled trial has shown no delay in fracture healing in patients who were given an NSAID.<sup>72</sup>

Use of femoral nerve blocks is advocated in some hip-fracture programmes.<sup>73</sup> Experience with this technique in the South African setting is limited.

### Pharmacological therapy for osteoporosis in patients with post hip fractures

It is well established that a prior fracture increases the risk of subsequent fractures.<sup>74, 75</sup> Importantly, the interval between fractures, even after a hip fracture, for those who survive, generally warrants intervention and treatment in order to reduce the risk of subsequent fracture.<sup>76,77</sup> Despite this, osteoporosis is seldom diagnosed, investigated or treated in patients after a hip fracture.<sup>78, 79</sup> The figure is as low as 10% in most studies.

Historically, the diagnosis of osteoporosis and even the therapeutic threshold, has been based on BMD criteria with a T-score of  $\leq -2.5$  considered to be diagnostic of osteoporosis. However, approximately 50% of patients who present with a hip fracture do not satisfy this criterion. This can partly be explained by the fact that 98% of hip fractures occur following a fall. Therefore, the risk of fracture is determined by bone strength, the risk of falling and other factors. Prevention of subsequent fractures, in particular at the hip and nonvertebral sites, is best achieved by interventions which focus on strengthening bone, as well as those that aim to reduce the risk of falls.

Elderly patients with a prevalent fracture should receive treatment for osteoporosis regardless of the BMD. Therefore, all patients who survive a hip fracture should receive treatment to reduce future fracture risk. Unfortunately, this is rarely the case in the elderly who are the most frail and who are at the greatest risk.

### Protein supplementation

Intervention studies, where protein intake was normalised by nasogastric feeding, parenteral nutrition or even oral dietary supplements, have reported an improved outcome after hip fracture. A daily oral protein supplement of 0.8 g/kg bodyweight has been shown to improve rehabilitation outcomes and reduce the risk of complications such as bed sores, anaemia, and respiratory and renal infections.<sup>80,81</sup> This simple intervention reduced the total length of stay in hospital and rehabilitation units by 25% in patients who received protein supplementation compared to controls.

### Calcium and vitamin D

Calcium and vitamin D are essential for bone throughout life. Deficiencies are common in the elderly, and

especially in the institutionalised and frail elderly, and in patients presenting with hip fractures.<sup>82,83</sup> Adequate calcium and vitamin D intake, in the elderly in particular, will prevent secondary hyperparathyroidism, maintain bone mass and architecture, improve muscle strength and reduce fracture risk. Therefore, vitamin D and calcium supplementation is a simple and inexpensive method of improving bone strength and reducing the risk of falling.

In a meta-analysis of double-blind studies of vitamin D supplementation with or without calcium, high-dose vitamin D (800 IU per day) reduced the risk of falls by 19%, and by 23% when vitamin D levels of > 60 nmol/l were achieved.<sup>84</sup> Calcium and vitamin D supplementation has also been shown to reduce the risk of falls and fractures in elderly women (with a mean age of 81 years) with a recent hip fracture.<sup>85</sup> The relative risk of fracture was also reduced by 43% and 32% at hip and nonvertebral sites, respectively, in ambulatory institutionalised women (mean age 84 years) with severe calcium and vitamin D deficiency, after 18 months treatment with calcium 1 200 mg/day and vitamin D 800 IU/day, in a randomised, placebo-controlled study. The hip and nonvertebral fracture risk was reduced by 29% and 24%, respectively, after 36 months.<sup>86, 87</sup>

Supplementation of calcium and vitamin D in community living persons has shown smaller reductions in fracture risk. However, the baseline deficiencies of calcium and vitamin D in these subjects were less severe.<sup>88,89</sup> Three other community-based studies have shown no reduction in fracture risk in this population.<sup>90-92</sup> These conflicting results are likely to be the consequence of targeting low-risk populations of younger women who did not have baseline deficiencies of calcium and vitamin D.

Based on the available evidence, calcium and vitamin D should be supplemented in patients with known deficiency or those who are at high risk of insufficiency, using the correct dose and regimen. Patients who are in hospital after a hip fracture represent an extremely high-risk group and routine supplementation of calcium and vitamin D would be appropriate.

The recently published National Osteoporosis Foundation of South Africa (NOFSA) guidelines suggest a dose of vitamin D 800-1000 IU/day and calcium 1 000-1 200mg/day (a dose which is considered to be safe).<sup>8</sup> Meta-analyses indicate that a dose of 800 IU vitamin D is required for optimal benefit in terms of preventing falls and reducing fracture risk.<sup>93</sup> In addition, it is important to combine vitamin D with calcium in order to maximise outcomes post hip fracture, especially in elderly patients.<sup>94</sup> Compliance with calcium and vitamin D is essential to maintain benefit. Compliance is a challenge in this population. Clinicians should focus the same degree of energy that they would to maximise

compliance with any other chronic medication.

### Anti-osteoporosis medication

Several therapies, currently available in South Africa, have been proved in well-designed, placebo-controlled studies to increase bone strength and reduce fracture risk in postmenopausal women. Limited fracture data are available on men with osteoporosis, although BMD responses in men to the bisphosphonates, teriparatide and strontium ranelate have been similar to those observed in women. Studies on zoledronate and strontium ranelate to determine fracture reduction in men are currently underway. There has been only one trial on fracture reduction in patients who have recently suffered a hip fracture. Most other randomised controlled trials have included a small percentage of elderly patients only; the population that is most at risk of sustaining a hip fracture. It is also least likely for anti-osteoporosis medication to be initiated in the elderly. Data from the USA National Health and Nutrition Examination Survey (NHANES) showed that only 12% of women > 85 years who had a history of fracture received medication for osteoporosis.<sup>95</sup>

### Bisphosphonates

The efficacy of bisphosphonates (alendronate, risedronate and zoledronate) in preventing bone loss and reducing fracture risk is well established from large, randomised, placebo-controlled studies. However, limited data are available on elderly patients and patients who have experienced a hip fracture and those with osteopenia, as opposed to that on patients with osteoporosis following BMD measurement. However, limited data are available on elderly patients, patients with hip fractures, and those who have been diagnosed with osteopenia rather than osteoporosis on BMD measurement.

In a post hoc analysis of the Fracture Intervention Trial (FIT), there was a 38% reduction in vertebral fracture risk in women > 75 years who were treated with alendronate for three years.<sup>96</sup> There are no data for patients > 80 years.

Risedronate had no significant effect in preventing hip fractures in a subgroup of women aged > 80 years and recruited according to clinical risk factors only without a BMD diagnosis of osteoporosis, in the Hip Intervention Program Study Group.<sup>97</sup> In a pooled analysis from three clinical studies, risedronate reduced the risk of vertebral fracture by 44% after three years in women > 80 years, but had no effect on nonvertebral fractures.<sup>98</sup>

In a retrospective analysis of 20 664 patients with hip fracture, little benefit of antiresorptive agents in the prevention of hip fractures was seen in patients > 80 years, compared to those < 80 years (hazard ratio of 0.92 vs. 0.53).<sup>99</sup> These findings need to be interpreted with caution, as there was no suggestion of blunting



of treatment efficacy with age in the randomised controlled trials of bisphosphonates. However, the overall numbers of patients > 80 years were extremely low.

Evidence which supports the treatment efficacy of bisphosphonates in older patients post hip fractures is provided from the Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly Recurrent Fracture Trial (HORIZON-RFT). A once-yearly infusion of zoledronate 5 mg significantly reduced the risk of both vertebral and nonvertebral fractures in patients with a mean age of 74.5 years with a recent hip fracture. The reduction in recurrent hip fractures was not significant, but the study was not powered to show this effect. In addition, zoledronate reduced the risk of death by 28%. This highlights the impact of osteoporotic fractures on mortality in this very frail and high risk population.<sup>100</sup>

In general, there is no apparent difference in the anti-fracture efficacy of the three bisphosphonates (alendronate, risedronate or zoledronate) that are registered for patients in this country. Therefore, no particular bisphosphonate is recommended. Until further safety and efficacy data become available, the use of generic bisphosphonates is not recommended.<sup>8</sup> There are also no convincing data to suggest that antiresorptives, such as the bisphosphonates, impair fracture healing.

### Teriparatide

Teriparatide is an anabolic bone agent that is administered by daily subcutaneous injection to patients with severe osteoporosis. Because of cost constraints, its use is limited to patients with severe osteoporosis as defined by a very low BMD, significant bone loss on treatment, and the presence of more than two vertebral fractures. A hip fracture is regarded as one of the most severe end-points of osteoporosis. A potent anabolic agent is an attractive option. Limited data on this agent are available. Teriparatide was shown to significantly reduce the risk of vertebral fractures by 65% in women > 75 years in a subgroup analysis. This effect is similar to that observed in women < 75 years. No significant effect on nonvertebral fractures was recorded after a median treatment duration of 19 months.<sup>101</sup> There are no available data on patients > 80 years and those post hip fractures.

There is mounting evidence that teriparatide significantly improves the healing of nonvertebral fractures (the long bones and pelvis). However, following a fracture, its routine administration cannot be recommended yet.

### Strontium ranelate

Pre-planned pooling of patients > 80 years from two major randomised controlled trials on strontium ranelate

[The Spinal Osteoporosis Therapeutic Intervention (SOTI) and The Treatment Of Peripheral Osteoporosis (TROPOS)] showed an increase in BMD, as well as a reduced risk for vertebral and nonvertebral fractures after 1.3 and 5 years. Vertebral fractures were reduced by 59% at one year, 32% at three years and 31% at five years; all highly significant. Significant reductions in nonvertebral fractures (which included hip fractures) by 41% at one year, 31% at three years and 26% at five years, were also noted. After three years, there was a nonsignificant 32% reduction in the risk of hip fracture in patients > 80 years. A statistically significant reduction in hip fracture of 43% was noted in a subset of women aged > 74 years (a mean age of 79.2 years), and who were at high risk of fracture based on BMD (T-score < -2.5). This effect continued for up to five years.<sup>102-104</sup>

No studies have been carried out on strontium ranelate in patients who have suffered a previous hip fracture. However, strontium ranelate is the only agent with documented efficacy against vertebral and nonvertebral fractures in women > 80 years. Fracture risk reduction has been documented within one year and sustained over five years, even in the very elderly. The safety profile of strontium ranelate in people > 80 years is favourable and similar to that observed in younger patients.

### Choice of agent

Given the lack of comparative data, it is difficult to make specific, evidence-based recommendations pertaining to choice of an anti-osteoporotic agent for patients post hip fracture. NOFSA recommends a bisphosphonate or strontium ranelate as the first choice for postmenopausal osteoporosis. Based on the only available evidence (HORIZON-RFT), it would be prudent and convenient to offer all patients who have survived a hip fracture an infusion of zoledronic acid 5 mg, in conjunction with adequate calcium and vitamin D. This can be repeated after one year, and again, after two years. Alternatively, an oral bisphosphonate or strontium ranelate could be considered. This would depend on several patient criteria, such as age. Strontium ranelate has been shown to be effective in patients > 80 years.<sup>8</sup> However, strontium ranelate should be avoided in patients with prior DVT, or in those who are at high risk of DVT.

### Benefits of dedicated orthogeriatric fracture unit/hip fracture programmes

The acute orthogeriatric unit is a model which provides joint care by geriatricians and orthopaedic surgeons and includes immediate geriatric assessment, coordinated daily clinical care, combined ward rounds, joint planning of the surgical schedule, initial mobilisation and discharge date and destination (discharge planning). Protocol-driven geriatric-

focused care is inherent in this model. It has been replicated in multiple (generally developed) countries, using the expertise of geriatricians. Most published studies confirm the benefits of this approach, which include reduced length of hospital stay, costs and time to surgery; lower readmission rates and in-patient complication rates such as pneumonia, urinary tract infections and confusion or delirium; functional improvement (short-term OR 2.33, 95% CI: 1.62-3.34), reduced mortality (long-term RR 0.77, 95% CI: 0.61-0.96, numbers needed to treat: 21), and reduced risk of nursing home admission (RR 0.72, 95% CI: 0.56-0.91, numbers needed to treat: 14).<sup>71,105-111</sup> Patients with mild or moderate cognitive impairment may show the most benefit.<sup>109</sup> It is likely that patients in a country such as South Africa would derive significant benefit from this approach. Given the shortage of geriatricians in this country, a physician who has an interest or experience in the field should be part of the multidisciplinary team.

## Summary and conclusion

Hip fractures generally occur in older patients who often have multiple co-morbidities, and who are at high risk of adverse outcomes and of incurring high medical costs. Increased morbidity and mortality can be reduced by a structured acute management plan and appropriate control of the risk factors. Ideally, a team-based approach should be employed. Patients with hip fractures should be assessed to exclude a secondary cause of osteoporosis and considered for specific osteoporosis therapy to prevent the next fracture.

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