

## REVIEW

# Postoperative management of hip fractures: interventions associated with improved outcomes

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The annual number of hip fractures worldwide is expected to exceed 6 million by 2050. Currently, nearly 50% of hip fracture patients will develop at least one short-term complication including infection, delirium, venous thromboembolism (VTE), pressure ulcers or cardiovascular events. More than half will experience an adverse long-term outcomes including worsened ambulation or functional status, additional fractures and excess mortality. This paper summarizes current evidence for postoperative interventions attempting to improve these outcomes, including pain management, anemia management, delirium prevention strategies, VTE prophylaxis, rehabilitation type, nutritional supplements, anabolic steroids and secondary fracture prevention. Models of care that have been tested in this population including interdisciplinary orthogeriatric services, clinical pathways and hospitalist care are summarized. In general, good quality evidence supports routine use of VTE prophylaxis, and moderate quality evidence supports multifactorial delirium prevention protocols, and a conservative transfusion strategy. Aggressive pain control with higher doses of opiates and/or regional blocks are associated with lower delirium rates. Low-moderate quality evidence supports the use of clinical pathways, and dedicated orthogeriatric consultative services or wards. After hospital discharge, good quality evidence supports the use of bisphosphonates for secondary fracture prevention and mortality reduction. Rehabilitation services are important, but evidence to guide quantity, type or venue is lacking. Additional research is needed to clarify the role of nutritional supplements, anabolic steroids, home care and psychosocial interventions.

*BoneKEy Reports* 1, Article number: 241 (2012) | doi:10.1038/bonekey.2012.241

## Introduction

Hip fractures remain one of the most dreaded complications of osteoporosis in older adults.<sup>1</sup> Although hip fracture rates appear to have declined or remained stable in recent years,<sup>2</sup> perhaps due to a combination of improved treatment for osteoporosis and the obesity epidemic, the aging of the baby boomer generation will result in a large number of patients experiencing this potentially devastating event over the next 10 years.

Adverse outcomes after hip fracture are generally divided into early complications occurring in the first 30–90 days, and long-term outcomes. Common and potentially preventable early complications include venous thromboembolism (VTE), delirium, pressure ulcers, cardiovascular events and infections such as urinary tract infections, surgical site infections and pneumonia. One or more such event occurs in up to 50% of hip fracture patients; high American Society of Anesthesiologists class and prior inability to ambulate were the strongest

predictors of one or more in-hospital complications in a single-site cohort.<sup>3</sup> Pain and anemia occur in nearly all patients after hip fracture repair, and their management may impact these outcomes.

Long-term outcomes commonly measured after hip fracture include functional disability, secondary fractures and mortality. Functional disability, especially gait impairment is alarmingly common after hip fracture. Fewer than half of hip fracture patients regain their prior level of ambulation at 1 year, and nearly 20% become immobile.<sup>4</sup> More than 50% of previously independent patients develop a new requirement for assistance with lower extremity functional tasks or instrumental activities of daily living.<sup>5</sup> These functional declines may be made worse if the patient experiences another osteoporotic fracture; one in five hip fracture patients will suffer another fracture in the 2 years after their hip fracture.<sup>6</sup>

Finally, the risk of mortality following hip fracture is substantial. In a meta-analysis of 75 studies including over 64 000 patients from multiple countries, the overall mortality at

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Received 21 September 2012; revised 16 November 2012; accepted 16 November 2012; published online 12 December 2012

1 month was 13.3%, 3–6 months 15.8, 1 year 24.5 and 2 years 34.5%.<sup>7</sup> Among nursing home residents with hip fracture, mortality is as high as 75% at 1.4 years.<sup>8</sup> Strong predictors of mortality include advanced age, male gender, nursing home residence, poor preoperative walking capacity, poor activities of daily living, higher American Society of Anesthesiologists grading, multiple comorbidities, dementia or cognitive impairment, diabetes, cancer and cardiac disease. Conflicting evidence has been observed for the association between race and mortality.<sup>7</sup> Although the increased mortality risk decreases after the first year, excess mortality of 20–22% persists at 10 years after the fracture.<sup>9</sup>

The purpose of this paper is to review recent evidence informing the postoperative care of the hip fracture patient, with a goal of reducing the substantial morbidity and mortality they face. Because of the broad nature of this topic, this paper presents a survey of relevant current studies informing clinical questions where there is currently controversy or suboptimal clinical practice, and is not a complete or systematic review of each topic. Topics where widely accepted guidelines exist (for example, antibiotic prophylaxis) or that are related to preoperative and intraoperative management (for example, timing of surgery, who to operate on, type of fixation, esophageal Doppler monitoring) are beyond the scope of this paper.

### Strategies to Manage Select Postoperative Issues

**Pain management.** Severe pain is experienced by nearly all hip fracture patients in the pre and postoperative periods, and contributes not only to poor quality of life, but is also associated with a higher risk of postoperative delirium. Both opiate medications and regional nerve blocks are commonly used after hip fracture. In a meta-analysis of randomized or quasi-randomized trials including over 800 hip fracture patients, pre or perioperative nerve blocks appear to improve pain control with few complications.<sup>10</sup> In a single center study, initiation of a standard pain control program using preoperative femoral nerve blocks, avoidance of general anesthesia and the resulting liberalization of preoperative oral intake was associated with a significantly lower rate of postoperative complications including pneumonia, urinary tract infection and delirium compared with preprogram rates.<sup>11</sup>

Patients with dementia are treated with a lower cumulative dose of opiates, and those with mild to moderate cognitive impairment report worse pain scores compared with patients without dementia.<sup>12</sup> Less aggressive pain management in patients with dementia is likely due in part to their clinicians' concern about precipitating postoperative delirium with opiates. However, a well-constructed prospective cohort study showed that prescription of <10 mg per day parenteral morphine equivalent and higher reported pain scores are both associated with a significantly higher risk of incident delirium after adjustment for baseline cognitive status,<sup>13</sup> suggesting that poorly treated pain is a greater risk than the adverse effects of opiate medications. Although objective data are limited, clinical experience suggests that undertreated pain also limits efforts at early mobilization, and therefore contributes to risk of pressure ulcers or other complications related to immobility.

Overall, evidence suggests that that aggressive pain control is an important goal in managing hip fracture patients. Frequent

pain assessment, especially in patients with dementia, and regular use of parenteral or oral opiates is generally required. Clinical tools to assess pain in nonverbal patients with dementia are available,<sup>14</sup> but have not been extensively validated across languages and cultures. Use of nerve blocks where available is strongly encouraged.

**Venous thromboembolism.** In a meta-analysis of prospective cohort studies in Asian patients after hip fracture surgery or total hip arthroplasty, the rates of all-site and proximal deep vein thrombosis (DVT) without prophylaxis were 26% and 10%, respectively.<sup>15</sup> Therefore, close attention to prevention of this potentially life-threatening complication is required. Regional anesthesia appears to reduce the risk of DVT compared with general anesthesia (relative risk 0.64, 95% confidence interval (CI) 0.48–0.86).<sup>16</sup>

Several classes of agents have been shown to be effective in preventing DVT among hip fracture patients, including low molecular weight and unfractionated heparins, warfarin and fondaparinux.<sup>17</sup> Intermittent pneumatic compression devices also have some supporting evidence, decreasing risk of DVT and PE compared with no prophylaxis by nearly 70% in meta-analysis (relative risk 0.31; 95% CI 0.19–0.51), although compliance is a significant problem.<sup>17</sup> Head to head trials of anticoagulation strategies are limited; a meta-analysis of trials comparing fondaparinux to enoxaparin reported significantly lower rates of any venous thromboembolic event with fondaparinux (13.7% vs 6.8%); however, the absolute risk reduction for proximal DVT or PE was quite small (1.3% vs 2.9%), and fondaparinux significantly increased the risk of major bleeding (2.7% vs 1.7%).<sup>18</sup> Newer oral agents such as apixiban, rivaroxaban and dabigatran are approved for DVT prophylaxis in patients undergoing elective hip and knee surgery, but their evidence in hip fracture is limited.

Extended duration of anticoagulation (28–35 vs 7–10 days) is associated with a slightly lower risk of symptomatic DVT (0.3% vs 2.3%), but at the cost of increased major bleeding events.<sup>19</sup>

Practice guidelines released in 2012 from the American College of Chest Physicians recommend a minimum of 10–14 days of prophylaxis with either low molecular weight heparin, fondaparinux, low-dose unfractionated heparin, adjusted dose warfarin, aspirin or an intermittent pneumatic compression device. The group's preference is for low molecular weight heparin initiated at least 12 h before or 12 h after surgery, extended to 35 days in most patients, and in combination with an intermittent pneumatic compression device.<sup>20</sup> The risk of bleeding must be weighed against the risk of DVT in individual patients. The overall mortality benefit of DVT prophylaxis is unclear.

**Delirium prevention.** Delirium occurs in a quarter of patients without baseline dementia, and over half of dementia patients who experience a hip fracture.<sup>21</sup> Although usually considered a transient problem, delirium persists for >4 weeks in 20% of patients.<sup>22</sup> Risk factors for the development of delirium include male sex, older age, more comorbidities, low body mass index, longer duration of surgery and delay of operative repair. Importantly, delirium is associated with lower functional recovery 1 year after fracture,<sup>4</sup> and higher mortality rates.<sup>22</sup> Therefore, delirium prevention efforts become extremely important after hip fracture.

Regional compared with general anesthesia appears to decrease the risk of postoperative delirium by half (95% CI, 0.26–0.95), and should be encouraged where feasible.<sup>16</sup> Several trials of multifactorial interventions have also shown promising results. Proactive geriatrics consultation, with attention to fluid and electrolyte normalization, oxygenation, pain control, ensuring urinary and fecal elimination, psychoactive medication review and early mobilization, significantly reduced the incidence of postoperative delirium (relative risk 0.64 95% CI 0.37, 0.98); six patients would need to receive this service to prevent one case of delirium.<sup>23,24</sup> In a Belgian trial, randomization to consultation from an interdisciplinary orthogeriatrics team including a geriatrician, social worker, occupational and physical therapist reduced the risk of delirium from 53 to 37% compared with usual orthopedic care.<sup>25</sup> Thus, it appears that careful attention to medical and geriatric issues with an interdisciplinary team is an effective strategy in preventing delirium in this population.

Several medications have also been tested in hip fracture patients. Perioperative prophylaxis with low-dose haloperidol does not appear to reduce the incidence of delirium, but may reduce its severity and reduce length of stay.<sup>24</sup> However, the potential harms of antipsychotics in older adults are significant, and include an increased risk of cardiovascular events and death; therefore, antipsychotic use is generally limited to those patients with severe agitation in clinical practice. In a phase 2 study, donepezil prophylaxis did not reduce the incidence or severity of delirium after hip fracture and was associated with gastrointestinal side effects.<sup>26</sup> Thus, there are no currently accepted pharmacotherapies that safely prevent delirium in hip fracture patients.

**Anemia.** Anemia, typically defined as a hemoglobin level  $<10\text{ g dl}^{-1}$  ( $100\text{ g l}^{-1}$ ), is present in approximately half of hip fracture patients at hospital admission, and  $>90\%$  postoperatively.<sup>27</sup> Observational studies suggest that anemia is associated with poor functional outcomes and mortality after hip fracture,<sup>28</sup> therefore, several studies have explored whether interventions to improve anemia result in better outcomes.

Individual, nonrandomized, parallel control group studies of perioperative iron with or without erythropoietin suggest potential benefits including decreased length of stay and lower infection rate.<sup>29,30</sup> However, a meta-analysis of six randomized controlled trials found that while oral or intravenous iron was effective in raising the hemoglobin by a weighted average of  $2.8\text{ g dl}^{-1}$  at 6 weeks after hip fracture, there was no significant difference in clinical outcomes including transfusion rate, length of stay, postoperative complications or infections. A nonsignificantly higher 1-month mortality was observed in the iron treatment group.<sup>31</sup> Tranexemic acid, an inhibitor of fibrinolysis, has been shown in randomized trials to reduce the need for transfusion after hip fracture, but increased the incidence of vascular events from 6 to 16%;<sup>32</sup> additional trials of this agent are ongoing. Finally, a randomized trial of a liberal vs restrictive transfusion strategy after hip fracture (routine transfusion for hemoglobin  $<10\text{ g dl}^{-1}$ , vs transfusion for symptomatic anemia only) showed no between group differences in 60-day mortality, ambulatory ability, cardiovascular events, symptoms or function.<sup>33</sup> Given the potential for adverse events with transfusion, a conservative strategy of transfusing only when

symptomatic, or in high-risk patients with hemoglobin  $<8\text{ g dl}^{-1}$  is recommended.

### Strategies to Improve Long-Term Outcomes

**Rehabilitation.** Rehabilitation is a cornerstone in efforts to reduce rates of ambulatory and functional impairment, but limited evidence is available to inform on the optimal venue for such therapy. In a recent meta-analysis of five randomized studies, a significant and moderate impact of home physical therapy (PT) compared with no PT on quality of life, gait and physical performance measures was observed, but no significant differences were seen between home and inpatient or outpatient PT.<sup>34</sup> A meta-analysis of inpatient interdisciplinary geriatric rehabilitation interventions in Europe and Canada showed a substantial improvement in functional outcomes compared with usual care at discharge (2.3, 95% CI 1.6–3.3) that was sustained at 3–12 months (1.8, 1.2–2.6).<sup>35</sup> The evidence comparing different types of physical therapy interventions is similarly conflicting and limited; in general more intensive and longer programs appear to be associated with improved mobility outcomes, but have higher dropout rates among in older adults. A Cochrane review concluded that there is insufficient evidence to recommend any one form or exercise (treadmill, weight-bearing, resistance training and so on) over another.<sup>36</sup>

Psychosocial interventions have also been examined after hip fracture. A systematic review of inpatient intensive occupational therapy, cognitive behavioral therapy and re-orientation therapy suggested no consistent benefit. Outpatient group education similarly had minimal effect.<sup>37</sup> Specialist nurse care in the community may improve transitional care measures, but does not have consistent impact on other outcomes at 12 months.<sup>37</sup>

Although evidence supporting a specific type or venue of rehabilitation after hip fracture is lacking, a sensible approach in my opinion is to provide the most intensive regimen tolerated by the patient, addressing both physical and instrumental tasks with an interdisciplinary team. Inpatient, outpatient or home PT can be selected based on the patient's goals and social situation.

**Anabolic steroids and nutritional supplements.** Anabolic steroids and nutritional supplements have been purported as potentially reducing post-hip fracture muscle and bone mass loss, and their resulting disability. Small studies of anabolic steroids such as nandrolone in patients with hip fracture suggest a positive effect on bone and muscle mass,<sup>38,39</sup> but long-term safety and efficacy have not been established, and long-term impact on disability needs to be quantified.

Postoperative oral or nasogastric protein and micronutrient supplements have not been found to improve mortality or disability, but show a trend toward reduction in a composite outcome of mortality or medical complications after hip fracture (relative risk 0.76, 95% CI 0.55 to 1.04).<sup>40</sup> Additional studies are needed before these agents can be recommended.

**Fall prevention.** The ambulatory dysfunction resulting from hip fracture further increases the fall risk of this frail population. Persistent delirium, use of psychoactive pain medications, and frequent changes in care location are additional risk factors for

falls. Therefore, careful attention to fall prevention is an important part of post hip fracture care. Multifactorial risk factor reduction has been shown to reduce;<sup>41</sup> in addition to gait and balance assessment clinicians should consider optimizing vision and hearing, reducing psychoactive medications, assessing environmental safety and correcting orthostatic hypotension. Home occupational therapy visits can be helpful to assess home safety and equipment needs, but are only covered for homebound patients already receiving home health services in the United States assuring vitamin D sufficiency is important for reducing both falls and secondary fractures.

**Secondary fracture prevention.** Guidelines for preventing additional osteoporotic fractures have been reviewed previously, but a few comments specific for hip fracture patients are noted here. First, bisphosphonates should be strongly considered as first-line therapy for the hip fracture population as good evidence supports not only a 35% reduction in secondary fractures after hip fracture regardless of bone density but also a 20–28% reduction in mortality.<sup>42</sup> Although clinical trial evidence remains best for the intravenous bisphosphonate zoledronic acid, subsequent meta-analyses and population-based studies suggest that the mortality benefit probably extends to oral bisphosphonate formulations as well, and either intravenous or p.o. can be considered based on the patient's situation. As vitamin D deficiency is extremely common in hip fracture patients, routine high-dose supplementation or verification of sufficient serum 25(OH)D levels should be completed before initiation of bisphosphonates to avoid hypocalcemia.

Ongoing calcium and vitamin D supplements have been used as concomitant therapy in nearly all osteoporosis clinical trials, including HORIZON-recurrent fracture trial in hip fracture patients, and therefore should be offered to all hip fracture patients treated with an osteoporosis pharmacotherapy. However, they are probably not sufficient by themselves; the RECORD trial, randomizing > 5 000 patients with recent clinical fracture to vitamin D alone, calcium plus vitamin D or placebo showed no difference in secondary fracture rates or mortality.<sup>43</sup>

### Models of Care That Improve Outcomes in Hip Fracture Patients

Because of the multifactorial nature of morbidity and mortality after hip fracture, several models of interdisciplinary care delivery have been developed to optimize the delivery of the strategies discussed above. Evidence that these models of care result in improved outcomes is presented below.

**Clinical pathways and audits.** The use of clinical pathways, or standard protocols to promote consistent care, is becoming widespread. Meta-analysis of nine clinical trials using clinical pathways promoting the use of regional anesthesia, antibiotic prophylaxis, pain control, pressure ulcer prevention, routine early removal of urinary catheters, DVT prophylaxis and nutritional supplementation showed no improvement in hospital mortality or pneumonia, but reduced the risk of preventable complications including DVT, pressure ulcers, urinary tract infection and surgical site infections.<sup>44</sup> Several European countries have instituted prospective hip fracture registries, which have called attention to adverse outcomes in the

population and been associated with improved outcomes over time.<sup>45</sup> Similarly, audits of hospital performance have been associated with improvements in some perioperative complications over time, but controlled trials of this practice are lacking.<sup>46</sup>

**Hospitalist care.** In reports from single centers, hospitalist care appears to shorten length of stay for hip fracture patients by about 0.8 days, without adversely impacting 30-day mortality or re-admission rates, but impact on functional outcomes is not known.<sup>47</sup> The impact of hospitalist care may be especially pronounced in those with significant medical comorbidities, or who require complex discharge plans.<sup>48</sup>

**Geriatrics consultation and wards.** As noted previously, interdisciplinary geriatrics consultation services have also been tested, and appear to reduce the incidence of delirium.<sup>23,25</sup> Co-management of hip fracture patients by orthopedists and geriatricians also appears to reduce in-hospital complications and length of stay.<sup>49</sup> In one Spanish study, lower in-hospital and 30-day mortality was observed with geriatrics co-management.<sup>50</sup> Care in specialized orthogeriatric wards where multidisciplinary staff have additional geriatric assessment training have also been shown in some centers to result in fewer in-hospital complications and improve functional outcomes at 4 and 12 months.<sup>51</sup> However, results are mixed with other studies showing no change in outcomes.<sup>52</sup>

These services have in common an interdisciplinary assessment of functional status, cognition and social supports in addition to monitoring for common physiologic issues (pain, elimination, electrolyte imbalance and so on). Interventions typically include early mobilization, reduction in psychoactive medication use, optimizing sensory input with hearing or vision aids, frequent orientation with clocks and reminders, and maintaining wake and sleep cycles with noise reduction or nonpharmacological strategies. The effectiveness of this interdisciplinary approach underscores the importance of addressing multiple risk factors for adverse outcomes in an individual patient.

### Conclusion

Hip fracture patients are among the most frail, high-risk patients that bone clinicians will encounter. Although morbidity and mortality rates are high, outcomes can be improved with systematic, interdisciplinary care addressing multiple domains as described above. Good evidence supports aggressive perioperative pain management and VTE prevention. Several studies suggest that multifactorial interventions can reduce perioperative delirium and its attendant complications; therefore, consultation with geriatrics or care on an orthogeriatrics ward should be considered for at-risk patients. Physical therapy is an important part of hip fracture care, but no strong evidence is available to inform where this should be delivered, the optimal type of exercise or duration. Multifactorial fall prevention programs appear to reduce falls in older adults in general, although data specific to the hip fracture population are lacking. Secondary fracture prevention, in particular bisphosphonate therapy, reduces subsequent fracture rates and mortality and should be considered in all hip fracture patients.

Because of the complexity of care after hip fracture, models of care including clinical pathways, geriatrics consultation or specialized wards may facilitate high quality, interdisciplinary care and therefore improve outcomes. Educating and engaging patients and families, and planning for comprehensive preventive care after discharge is essential.

### Conflict of Interest

Dr Colón-Emeric is a co-owner of Biscardia, Inc. and coinventor of US Provisional Patent Application: ‘Bisphosphonates and Mortality Reduction’ and a second US Provisional Patent relating to bisphosphonates and cardiovascular disease, ‘Bisphosphonate Compositions and Methods for Treating Heart Failure’. Dr Colón-Emeric is an advisory board member of Amgen and a consultant for Novartis on osteoporosis-related topics.

### Acknowledgements

I appreciate the helpful editorial suggestions from Kenneth Lyles and Megan Pearson.

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