Update on medical management of acute hip fracture

ABSTRACT

Morbidity and mortality rates associated with acute hip fracture remain high. Over the past decade, the management of hip fracture has shifted to emphasize prompt surgical treatment, multimodal analgesia to reduce opioid use, and incorporation of enhanced recovery pathways. Preoperative evaluation focuses on acutely correctable problems, with the understanding that delaying surgery may worsen the outcome. Prophylaxis of venous thromboembolism, treatment of preoperative anemia and acute kidney injury, and cardiac stabilization are important measures to reduce morbidity. Multimodal analgesia incorporating regional anesthesia techniques may help prevent delirium and facilitate early participation in physical therapy to reduce complications.

KEY POINTS

Follow evidence-based guidelines to minimize unnecessary testing and delay of surgery.

To minimize delirium and facilitate postoperative ambulation, consider multimodal analgesia, including peripheral nerve blocks that help minimize the need for opioids, in enhanced recovery pathways.

The best outcomes are achieved with prompt surgical repair, which should ideally be completed within 24 hours of presentation but not later than 48 hours, except in rare cases when critical medical optimization is needed.

The use of antiplatelet agents, warfarin, and direct oral anticoagulants should not delay surgery unless the benefit of spinal over general anesthesia is overwhelming.

HIP FRACTURES ARE THE MOST COMMON reason for urgent surgery in the elderly and often lead to long-term institutional care. Despite advances in perioperative management, postoperative mortality rates remain high, up to 10% in the first 30 days and 8% to 36% in the first year after repair. Even 10 years after fracture repair, the mortality rate due to comorbid medical conditions remains higher than in age-matched controls.

IS NONSURGICAL MANAGEMENT AN OPTION?

Without repair, the risk of death is exceedingly high due to infectious, thrombotic, and cardiopulmonary complications related to immobility. Unless the perioperative risk of death is exceptionally high due to severe comorbid illness, repair is recommended. Without surgery, patients are left with significant pain, immobility, and a shortened leg. In those who are terminally ill, cannot walk, have severe dementia, or have serious comorbid conditions, nonoperative management can be considered if pain is adequately controlled and the patient is comfortable. However, a large cohort study reported that the in-hospital mortality rate may be as high as 17.2% in those treated conservatively.

TIMING OF HIP FRACTURE REPAIR

A landmark retrospective cohort study in 42,230 adults demonstrated that wait time (time from emergency department arrival until surgery) greater than 24 hours was associated with a higher risk-adjusted likelihood of death within 30 days (6.5% vs 5.8%). The composite outcome of other medical complications (myocardial infarction, deep vein thrombosis,
pulmonary embolism, and pneumonia) was also reduced in those undergoing surgery within 24 hours (12.2% vs 10.1%). While the differences are not large, these results underscore the importance of timely surgery. In rare cases in which medical optimization is needed, delaying surgery up to no more than 48 hours from fracture may be necessary.6,7

**RISK STRATIFICATION IN THE GERIATRIC PATIENT**

The preoperative assessment should focus on stabilizing medical conditions that can be corrected, such as dehydration, hypovolemia, anemia, hypoxia, electrolyte disturbances, and arrhythmias.8 It should aim at recognizing chronic conditions that could modify the postoperative course, such as cognitive disorders and chronic cardiac, respiratory, and renal failure.8

A targeted preoperative evaluation9 is included in Table 1. Some of the major issues of particular significance in the elderly are discussed below.

**Diabetes, hypoglycemia**

Avoidance of hypoglycemia in the elderly is essential, as it is associated with a longer length of hospital stay and higher risk of death, and elderly patients undergoing surgical interventions often have reduced oral intake.10 For patients with diabetes with blood glucose levels greater than 180 mg/dL, the recommended total daily dose of insulin is 0.1–0.15 U/kg/day, given mainly as basal insulin, with correctional insulin coverage for glucose levels > 180 mg/dL before meals and at bedtime.10

**Anemia**

The prevalence of preoperative anemia due to bleeding from the fracture ranges from 24% to 44%, and that of postoperative anemia is even higher at 51% to 87%.11

The FOCUS trial (Functional Outcomes
in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair) was a randomized controlled trial designed to address a transfusion goal for patients over age 50 with hip fracture who had a history of or risk factors for ischemic heart disease. A postoperative hemoglobin transfusion threshold of 8 g/dL in the absence of symptomatic anemia was considered acceptable in elderly patients with or at risk of ischemic heart disease.

**Acute kidney injury**

Hong et al reported that patients who experienced acute kidney injury during hospitalization had significantly longer hospital stays and higher in-hospital and long-term mortality rates. A low preoperative albumin level, use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs), the need for blood transfusion, and coronary artery disease were found to be independent risk factors for acute kidney injury.

Aggressive hydration with isotonic fluids should be started early, and ACE inhibitors or ARBs should be held before surgery to prevent intraoperative hypotension and acute kidney injury. Doses of antihypertensive and rate-control drugs should be reduced to avoid hypotension. However, routine use of normal saline infusion per standing orders without evidence of dehydration or acute kidney injury should be avoided, as it can lead to peripheral fluid overload and decompensated heart failure.

**Cardiovascular risk**

The American College of Cardiology/American Heart Association and the Canadian Cardiovascular Society (CCS) guidelines caution about indiscriminate use of preoperative testing that, in many circumstances, does not serve to reduce the patient’s risk but may instead delay needed surgery. It is our policy to screen patients on admission for high-risk conditions and to use cardiology consultation or preoperative testing only when it would lead to a change in perioperative management, because delays are associated with increased mortality.

The impact of preoperative testing in terms of delaying surgery is substantial. In acute hip fractures, preoperative echocardiography and nuclear stress testing can delay surgery by up to 6 days, leading to further postoperative complications. In one study, echocardiography alone led to a delay of surgery of 32 to 48 hours without a demonstrable difference in complications or mortality.

In terms of preoperative cardiac screening, cardiac consultation delayed surgery by a mean of 9.9 hours due to an overestimation of cardiac risk. Preoperative subspecialty consultation was associated with delays to surgery of over 24 hours, and only 37% of the time did consultation lead to an identifiable change in treatment.

The main role of cardiology consultation should be to assist in the management of the patient who has a high-risk or unstable cardiac condition, to advise regarding risk-reduction strategies, and to assist with postoperative management.

A good exertional capacity is an excellent prognostic feature. However, if the patient has a poor or unknown functional capacity, objective data such as the physical examination and electrocardiogram should be used to assess for high-risk cardiac conditions.

We typically obtain an expedited preoperative transthoracic echocardiogram if the patient has any of the following conditions:

- Physical signs or symptoms of acute heart failure, including recently worsened dyspnea on exertion, orthopnea, and pulmonary or lower extremity edema
- Signs or symptoms suggestive of severe pulmonary hypertension
- A newly discovered murmur that raises concern for an obstructive process (e.g., left ventricular intracavitary obstruction, hypertrophic obstructive cardiomyopathy)
- Clinical signs or symptoms suggesting critical aortic stenosis, such as a systolic murmur or unexplained syncope, or severe mitral stenosis in a patient who has not had an echocardiogram in the past 12 months.
- The finding of critical aortic stenosis, hypertrophic obstructive cardiomyopathy, or severe pulmonary hypertension may affect the anesthetic plan, including the choice of general or regional anesthesia, placement of invasive monitors, and use of vasoactive medications.

We usually perform transthoracic echocardiography to estimate the degree of valve stenosis and left ventricular dysfunction. Even if severe aortic stenosis is detected in a patient who has no symptoms, hip repair surgery may be safely performed, and reduction of risk can be at-
ACUTE HIP FRACTURE

tempted on an individualized basis.
While preoperative balloon aortic valvuloplasty to reduce the degree of valve stenosis has been suggested as an approach to lower the perioperative risk, the delay in surgery and the complication rate of the valvuloplasty must be considered. We do not believe that transcatheter aortic valve replacement before emergency hip surgery is a practical option, given the delay to fracture repair. Transcatheter aortic valve replacement requires a comprehensive evaluation including coronary angiography and is rarely done as an emergency procedure.

Arrhythmias
Patients with rapid atrial fibrillation, atrial flutter, or supraventricular tachycardia can proceed to surgery after the ventricular rate is controlled. Patients with advanced atrioventricular block—eg, second-degree (Mobitz type II) atrioventricular block or third-degree atrioventricular block—may require temporary pacemaker placement before surgery. Placement of a permanent pacemaker may be indicated before discharge.

Medications
ACE inhibitors and ARBs may be withheld during the 24 hours before surgery to avoid perioperative hypotension if being prescribed for essential hypertension.20 For patients receiving an ACE inhibitor or ARB as treatment for chronic heart failure, we weigh the risks vs benefits of their discontinuation with the patient’s outpatient physician, if possible, and with the anesthesiology team.

Because there is a risk of bradycardia and hypotension, we do not initiate beta blockers for patients not already receiving them in the immediate preoperative period. For patients with chronic systolic heart failure taking beta blockers before surgery, we continue these agents unless there is evidence of decompen-sated heart failure.

Troponin
Troponin T and troponin I are measured to evaluate the diagnosis of an acute cardiac injury. A troponin level is often drawn on admission to evaluate for a possible ischemic cause of syncope. Troponin is frequently elevated in patients with renal insufficiency in the absence of acute myocardial injury. It may be elevated due to chronic congestive heart failure and should be considered a marker of poorer prognosis. Troponin elevation with a significant increase is concerning for type 1 or type 2 myocardial infarction. If preoperative troponin is elevated and the elevation attributed to myocardial injury or the etiology is unclear, cardiology consultation should be considered.

Most perioperative myocardial infarctions are not accompanied by classic chest pain or ST-segment elevation. In this situation, we treat patients using the same guideline-directed approach as for non-ST-elevation myocardial infarction in the nonoperative setting.

Isolated perioperative troponin elevation, without other features of myocardial infarction, is deemed myocardial injury after noncardiac surgery. In general, the risk of death within 30 days is higher in patients in whom this happens.21 Currently, the clinical significance of isolated troponin elevation in a patient who has sustained a hip fracture is unknown. If the patient is hemodynamically stable, we typically proceed to hip repair surgery with enhanced surveillance in the postoperative period. After surgery, we decide whether an assessment of myocardial perfusion is warranted for risk assessment.

Risk assessment
Repair of an acute hip fracture is urgent surgery, and hip fracture is considered an intermediate-risk surgery, with a 1% to 5% risk of major adverse cardiac events.14 Elderly patients with hip fractures are frail, and many have a poor or unknown functional status and risk factors for cardiac disease. Urgent surgery increases the risk of a perioperative cardiovascular event.

As preoperative pharmacologic stress testing leads to delays without a clear benefit in acute hip fractures, we follow the CCS guidelines,15 which do not include pharmacologic stress testing preoperatively for perioperative cardiovascular risk estimation. Instead, they recommend risk stratification using the Revised Cardiac Risk Index. The CCS also uses preoperative N-terminal pro-brain natriuretic peptide or B-type natriuretic peptide (BNP) measurement to aid in risk stratification and recommends postoperative troponin measurement to detect myocardial infarction.

Aspirin should be continued, as its effect on perioperative bleeding is minimal.
In our practice, we consider the elderly patient with hip fracture to be at increased risk; we do not order preoperative BNP testing but proceed as if the BNP were elevated and follow serial troponin levels postoperatively in the patients at highest risk.

Shared decision-making, involving the patient and the family, is critical in a patient with a high-risk cardiac condition to explain the elevated risk of morbidity and death. We offer surgery for high-risk patients, involving cardiac anesthesiology in the management, and admission to the intensive care unit postoperatively if needed.

**PERIOPERATIVE INTERVENTIONS THAT MAY AFFECT OUTCOMES**

**Anesthesia type**

Studies comparing anesthesia techniques for hip fracture repair have had conflicting results. One large database study found that regional anesthesia reduced the incidence of pulmonary complications and conferred lower odds of mortality than general anesthesia. However, the same researcher in a subsequent retrospective database study reported no difference in mortality based on anesthesia technique.

Current practices vary by institution, and the decision is typically made after the patient, surgeon, anesthesiologist, and consultants discuss the risks and benefits of each technique as they relate the specific patient.

**Pain control**

An opioid-sparing strategy is recommended for optimal perioperative pain control. Neuraxial blockade and peripheral nerve blocks provide the best combination of pain control with the least amount of sedation.
Acetaminophen, in scheduled intravenous or oral doses, is associated with shorter hospital stay, lower pain levels, less opioid use, fewer missed physical therapy sessions, and higher rate of discharge to home.25

Nonsteroidal anti-inflammatory drugs provide effective analgesia but can be problematic in elderly patients with stage 3 chronic kidney disease (glomerular filtration rate < 60 mL/min) or higher, given the risk of perioperative acute kidney injury.26 In a cohort of geriatric trauma patients over a 6-year period, these drugs were associated with decreased opioid requirements without an overall increase in bleeding.27 We generally avoid nonsteroidal anti-inflammatory drugs in patients with preexisting renal dysfunction.

Gabapentinoids have not been shown to help with pain and may not have a favorable risk-benefit ratio in the elderly.28 Muscle relaxants, anticholinergics, and benzodiazepines may increase the risk of delirium when used for perioperative pain.

Table 2 lists the preferred pain control regimens used at our institution.

Nerve blocks
Peripheral nerve blocks provide better analgesia than opioids alone. Common targets include the femoral nerve and fascia iliaca. Benefits are lower risk of pneumonia, shorter time to ambulation, less postoperative cognitive dysfunction, lower analgesia cost, and less opioid use. To date, studies have been small, and there are not enough data to determine if other outcomes such as delirium are affected.24 Effective control of postoperative pain using multimodal analgesia prevents delirium, encourages early participation in physical therapy, and reduces length of stay, hospital-acquired complications, and subsequent institutionalization.29

Delirium
The incidence of delirium after surgery ranges from 10% to 65%,29 and increases total cost by 50% as a result of longer length of stay, more nursing care, and more testing.30 Risk factors include multiple medical comorbidities, prolonged hospitalization, decreased mobility, and need for discharge into a facility.29 A Cochrane review of comprehensive geriatric assessments did not find an improvement in the incidence of delirium with nonpharmacologic interventions, but did find high-quality evidence for reduction in discharges to institutional facilities and moderate-quality evidence for mortality reduction.31

Simple nonpharmacologic interventions to prevent delirium include an adequate sleep protocol, use of eyeglasses or hearing aids, minimizing urinary catheters, early mobility and daily physical activity, maintaining hydration, and avoidance of constipation. Prophylactic antipsychotics are not recommended.31

■ PREOPERATIVE ANTICOAGULATION MANAGEMENT

Hip fracture repair carries an intermediate risk of bleeding, for which transfusion is often required. Anticoagulation management is discussed below.32

Antiplatelet agents
Patients receiving aspirin as primary prevention of cardiovascular disease. Aspirin may be discontinued even though the effect on bleeding is negligible.32

Patients receiving antiplatelet drugs as secondary prevention. Aspirin should be continued, as the effect on perioperative bleeding is minimal. Clopidogrel, used by itself, should also be continued, as there is no significant increase in bleeding, mortality, need for blood transfusion, length of surgery, or length of stay.32

In a prospective study of 1,225 patients receiving clopidogrel, delaying hip fracture repair led to a higher mortality rate: 29% for those who had surgery delayed vs only 4% for those who had immediate repair.33

Patients on dual antiplatelet therapy: aspirin plus clopidogrel, ticagrelor, or prasugrel. It is essential to know why the patient is receiving dual antiplatelet therapy. Typical reasons include an acute coronary syndrome during the previous 12 months, and a coronary stent implant.

Recommendations on dual antiplatelet therapy
• After a recent acute coronary syndrome event: ideally, dual antiplatelet therapy should be continued for 12 months after an event. If no stents are placed, the P2Y12 inhibitor (eg, clopidogrel) may be stopped earlier.32

Enhanced recovery protocols have been used in Europe for 20 years over a wide range of surgeries.
• After recent coronary stenting, with or without a recent acute coronary syndrome event: minimum of uninterrupted dual antiplatelet therapy for 1 month after bare-metal stent placement, or 3 to 6 months of uninterrupted dual antiplatelet therapy for a drug-eluting stent.32

There are few studies of dual antiplatelet therapy in acute hip fracture repair. In a study of 122 patients on dual antiplatelet therapy at the time of hip fracture repair, there was a similar risk of transfusion, independent of time to operation.34 Dual antiplatelet therapy was associated with a higher probability of major complications in early surgery. Delays to surgery for those on dual antiplatelet therapy led to higher mortality rate at 30 days.34 It is unclear if the higher complication rate from early surgery was from blood loss or from the medical complications resulting from the fracture.

The guidelines of the American Society of Regional Anesthesia and Pain Medicine suggest waiting 5 to 7 days before performing spinal anesthesia in patients taking clopidogrel or ticagrelor, and 7 to 10 days for patients taking prasugrel. Thus, it is impractical to delay surgery in order to perform spinal anesthesia, especially given the equivocal evidence thus far.35 We follow the guidelines outlined above on continuation of dual antiplatelet therapy through the perioperative period.32 For indications other than coronary stents or recent acute coronary syndrome, we typically continue aspirin alone in the perioperative period.

**Warfarin**

For a patient taking warfarin, we typically withhold 1 dose and consider giving vitamin K 2.5 to 5 mg if the international normalized ratio (INR) is greater than 1.8 before surgery;

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**TABLE 3**

Surgical repair of acute hip fracture: Indications for bridging therapy

<table>
<thead>
<tr>
<th>Mechanical valves</th>
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<tbody>
<tr>
<td>Mechanical mitral valve</td>
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<tr>
<td>Mechanical aortic valve in a patient with atrial fibrillation</td>
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<tr>
<td>Mechanical tricuspid valve</td>
</tr>
<tr>
<td>Mechanical aortic valve in a patient in sinus rhythm if it is anticipated that warfarin will not be promptly resumed after surgery</td>
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</tbody>
</table>

<table>
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<tr>
<th>Atrial fibrillation</th>
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<tbody>
<tr>
<td>CHA2DS2–VASc score 7–9 without additional bleeding risks: major bleeding event or intracerebral hemorrhage &lt; 3 months ago; international normalized ratio above the therapeutic range; prior bleeding event from previous bridging</td>
</tr>
<tr>
<td>Any history of stroke or transient ischemic attack (ischemic or cardioembolic)</td>
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<table>
<thead>
<tr>
<th>Venous thromboembolism (VTE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE event within 3 months</td>
</tr>
<tr>
<td>Severe thrombophilia with history of VTE or recurrent VTE (protein C or S deficiency, antithrombin deficiency, antiphospholipid antibodies, homozygous factor V Leiden, or multiple abnormalities); consider bridging for VTE in other thrombophilias (homozygous factor V Leiden, heterozygous factor II mutation)</td>
</tr>
<tr>
<td>History of VTE during discontinuation of anticoagulation</td>
</tr>
</tbody>
</table>

*CHADS2–VASc = 1 point each for congestive heart failure, hypertension, age 65–74, diabetes mellitus, vascular disease (coronary artery disease, peripheral arterial disease, aortic aneurysm), female sex; 2 points for age ≥ 75 and for prior stroke or transient ischemic attack (total possible points 9).
the goal ratio is 1.5 for surgery, and within normal range if neuraxial anesthesia is planned. In a retrospective study of patients on warfarin, delaying surgery by more than 48 hours to allow INR normalization increased the risk of mortality 1.5 times over those sent to surgery within 48 hours.36

For the patient at very high thrombotic risk (Table 3),37,38 heparin is used as an anticoagulation bridge. Timing of bridging should involve multidisciplinary conversation with orthopedics and cardiology.37,38

Direct-acting oral anticoagulants
Surgery must be delayed for 24 hours. For patients with acute renal failure, there should be a discussion between orthopedics, cardiology, and anesthesiology regarding delaying the procedure for 48 hours or using a reversal agent. Patients receiving these drugs have experienced longer delays to surgery than those receiving warfarin (6.9 hours vs 39.4 hours).39

■ PREVENTING VENOUS THROMBOEMBOLISM
According to the 2012 American College of Chest Physicians guidelines for prevention of venous thromboembolism in orthopedic surgery patients, the following medications have been approved for prophylaxis after hip fracture surgery: enoxaparin, fondaparinux, aspirin, and vitamin K antagonists. Table 4 presents dosing recommendations.

Enoxaparin is first-line, as it is highly effective and poses a low risk of bleeding.37 We use it as our preferred agent.

Data are lacking on the use of direct-acting oral anticoagulants in patients with acute hip fracture, and they are not yet approved for this by the US Food and Drug Administration. Most studies involving these agents included only patients undergoing elective total hip and knee replacement.39

Prophylaxis should be continued for 35 days, because the risk of venous thromboembolism is high (4.3%) in the first 5 weeks after hip fracture without prophylaxis.37,40

An intermittent pneumatic compression device should be used for 18 hours per day in addition to pharmacologic prophylaxis.37 If surgery is delayed, enoxaparin should be initiated at the time of presentation and continued up until 12 hours before surgery. Venous thromboembolism prophylaxis should be resumed 12 hours postoperatively, except for warfarin, which should be started the night of surgery.

Aspirin is also an option.37 However, a meta-analysis of 8 randomized controlled trials comparing aspirin and anticoagulants in patients undergoing major lower extremity orthopedic surgery found a nonsignificant trend toward fewer episodes of deep vein thrombosis with anticoagulants after hip fracture repair, although the risk of bleeding was lower with aspirin.41

■ ENHANCED RECOVERY PATHWAYS
Enhanced recovery protocols have been used in Europe for about 20 years over a wide range of surgeries. Many of the recommendations in this review are aligned with such protocols, which have been shown to benefit the geriatric population.42

Principles of enhanced recovery pathways include avoiding a preoperative catabolic fasting state and resultant hypoglycemia.42 Clear carbohydrate drinks up to 2 hours before surgery can reduce delirium and acute kidney injury and minimize thirst and anxiety. Reduction of opioid use and the use of regional anesthesia whenever possible are other principles.

Intraoperatively, the goal is euvoemia without fluid overload. Postoperatively, the emphasis is on early removal of drains and tubes, continued use of peripheral nerve blocks, and multimodal analgesia to minimize need for opioids, as well as on early mobilization and ambulation and adequate nutrition. Oral nutritional supplementation is recommended in patients with hip fracture who are malnourished or at risk of undernutrition, as these factors increase the risks of fracture nonunion and death.26

A large multicenter study43 of an enhanced recovery pathway in 5,002 patients with acute hip fractures found significantly higher rates of discharge to home with early ambulation and decreased opioid use.

■ COMANAGEMENT
Comprehensive interdisciplinary care in a geriatric ward has been shown to significantly
improve mobility, activities of daily living, and quality of life compared with routine care in an orthopedic ward. The length of stay and complications were significantly reduced in the comprehensive geriatric care group, and significantly more patients in this group were discharged directly home.

We recommend consideration of geriatric medicine consultation if there is no geriatric ward or unit for acute care for elderly patients available, to improve outcomes in this population such as discharge to home and reduction in mortality.

### TAKE-HOME MESSAGES

In the elderly, acute hip fracture poses significant risks of illness and death. An expedited medical evaluation to ensure operative repair within 24 to 48 hours of admission is recommended for improved outcomes, and the patient's use of anticoagulants before admission should not delay surgery. Guidelines regarding consultation and cardiac testing should be followed, as routine testing is unlikely to produce a measurable impact on outcomes.

Multimodal analgesia, regional anesthesia, enhanced recovery pathways, and delirium precautions are paramount to producing the best outcomes.

Risk factors contributing to acute hip fracture such as chronic osteoporosis and frailty are often not addressed during the inpatient stay. On discharge, patients should be referred for pharmacologic treatment of osteoporosis, advised on calcium and vitamin D supplementation, and referred for physical therapy to prevent future fractures.

### DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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**TABLE 4**

**Prophylaxis of venous thromboembolism in elderly hip fracture patients**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing and route of administration</th>
<th>FDA-approved for VTE prophylaxis?</th>
</tr>
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<tbody>
<tr>
<td>Low-molecular-weight heparin</td>
<td>Enoxaparin 40 mg subcutaneously daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>2.5 mg subcutaneously daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Warfarin</td>
<td>3–5 mg by mouth daily for goal international normalized ratio 2–3</td>
<td>Yes</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>5,000 U every 8 hours, every 12 hours for patients weighing &lt; 50 kg Use if creatinine clearance rate is &lt; 230 mL/min</td>
<td>Yes</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Unclear, dosing ranges from 81 mg orally twice a day for creatinine clearance rate &lt; 30 mL/min, to 325 mg orally twice a day</td>
<td>No</td>
</tr>
<tr>
<td>Apixaban</td>
<td>2.5 mg orally twice a day</td>
<td>No</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>150 mg orally daily</td>
<td>No</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>10 mg orally daily</td>
<td>No</td>
</tr>
</tbody>
</table>

FDA = US Food and Drug Administration; VTE = venous thromboembolism

Based on information in reference 37.
REFERENCES


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