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HOT TOPICS IN PAIN AND HEADACHE (N ROSEN, SECTION EDITOR)

A Comprehensive Review of Analgesia and Pain Modalities in Hip Fracture Pathogenesis

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Abstract

Purpose of Review Hip fracture is common in the elderly population, painful and costly. The present investigation was undertaken to review epidemiology, socio-economic and medical implications, relevant anatomy, and anesthetic and pain modalities of hip fracture.

Recent Findings A literature search of PubMed, Ovid Medline, and Cochrane databases was conducted in December 2018 to identify relevant published clinical trials, review articles, and meta-analyses studies related to anesthetic and pain modalities of hip fracture. The acute pain management in these situations is often challenging. Common issues associated with morbidity and mortality include patients' physiological decrease in function, medical comorbidities, and cognitive impairment, which all can confound and complicate pain assessment and treatment.

Summary Perioperative multidisciplinary and multimodal approaches require medical, surgical, and anesthesiology teams employing adequate preoperative optimization. Reduction in pain and disability utilizing opioid and non-opioid therapies, regional anesthesia, patient-tailored anesthetic approach, and delirium prevention strategies seems to ensure best outcomes.

Keywords Hip fracture · Anesthesia · Pain management · Regional nerve blocks

Introduction

Management of hip fracture in elderly patients with often underlying multiple medical comorbidities is a common and challenging medical and surgical intervention, considered urgent or emergent, with a great deal of associated morbidity and mortality. This article comprehensively reviews the epidemiology, socio-economic and medical implications, relevant anatomy as well as risks and benefits of anesthetic and analgesic modalities involved in order to provide insight on the best approach for safe care of hip fracture patient.

Methodology

For the present investigation, a literature search of the PubMed, Ovid Medline, and Cochrane databases was conducted in December 2018 to identify relevant published clinical trials, review articles, and meta-analyses studies. Articles were considered if they were published in English and involved adult patients. Abstracts were reviewed of retrieved citations to identify relevant articles.

Epidemiology

Hip fractures in the elderly patients over 65 years of age are serious injuries with considerable morbidity and mortality. The estimated annual incidence of hip fracture in the United States is 280,000 [1]. The incidence increases with age and is twice as high in women than in men. Osteoporosis is a major

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contributing factor in the elderly, with approximately 90% of hip fractures in this population resulting from a simple fall [2].

Hip fracture rates had declined steadily since 1995, concomitant with the introduction of bone mineral density screening with DXA, increased awareness of healthy calcium and vitamin D intake, and treatment for osteoporosis with bisphosphonate therapy [1]. However, since 2013, there has still been a higher-than-projected incidence of hip fractures, with multifactorial causes including low rates of DXA testing, safety concerns leading to decreased utilization of bisphosphonates, shifting demographics, and increasing life expectancy [1].

Economic Implications

Hip fractures result in substantial personal, societal, and economic costs and are associated with increased morbidity and mortality, especially in elderly patients [1, 3]. One-year mortality following hip fracture is approximately 30%, and mortality risk is increased for up to 10 years post-fracture [4••]. Of patients who survive, approximately half do not regain baseline level of function, are never able to ambulate independently, and about a quarter will require long-term care. Early surgical management is associated with a reduction of postoperative pneumonia, pressure ulcers, urinary tract infection, deep vein thrombosis, thrombotic embolism, and stroke [4••].

According to 2010 data, the estimated economic impact of hip fractures in the United States is $20 billion annually [5]. The direct medical costs incurred by Medicare average $40,000 per hip fracture, making it the 13th most expensive diagnosis [1, 5]. As the consequences of hip fractures can be profound, with decreased quality of life, increased healthcare expenses, and high mortality, this condition represents a major public health concern that warrants timely and effective management.

In a 2019 study of bundled care for hip fractures, 98,562 Medicare patients from 2009 to 2016 were studied in New York state and a machine learning algorithm was able to provide excellent accuracy and responsiveness in the prediction of length of stay and cost using preoperative variables, implying that non-modifiable patient-specific risk factors such as age, gender, ethnicity, race, type of admission, risk of mortality, and illness severity are involved in determining the cost of care [6].

Types of Hip Fractures

The term hip fracture generally refers to a fracture of the proximal femur [3]. Injuries are classified based on their anatomic location (Fig. 1). Femoral neck and intertrochanteric fractures occur with approximately equal frequency and comprise the vast majority, accounting for over 90% of hip fractures [2].

The hip is a ball-and-socket joint composed of the femoral head and acetabulum [7]. Femoral neck fractures are considered intra-capsular because they are located within the capsule of the hip joint in the region between the distal femoral head and proximal greater and lesser trochanters. The femoral neck is the site of disproportionate bone resorption in osteoporosis. Additionally, fractures in this area can disrupt blood supply to the femoral head, leading to nonunion and osteonecrosis of the femoral head [8].

Intertrochanteric fractures are extracapsular fractures that occur in the area between the greater and lesser trochanters. This type of injury does not interfere with blood supply to the proximal femur and thus is not associated with the healing complications seen in femoral neck fractures. The most common complications of intertrochanteric fractures are malunion and shortening. Subtrochanteric fractures are less common but have a higher rate of complications due to mechanical stress in the area.

Basics of Hip Joint Anatomy

The acetabulofemoral joint is the interface between the pelvis and the head of the femur, which allows for upright, weight-bearing movement in humans. Also known as the hip joint, this provides mobility and stabilization to the entire hip girdle. In the human embryo, this joint arises from the mesoderm

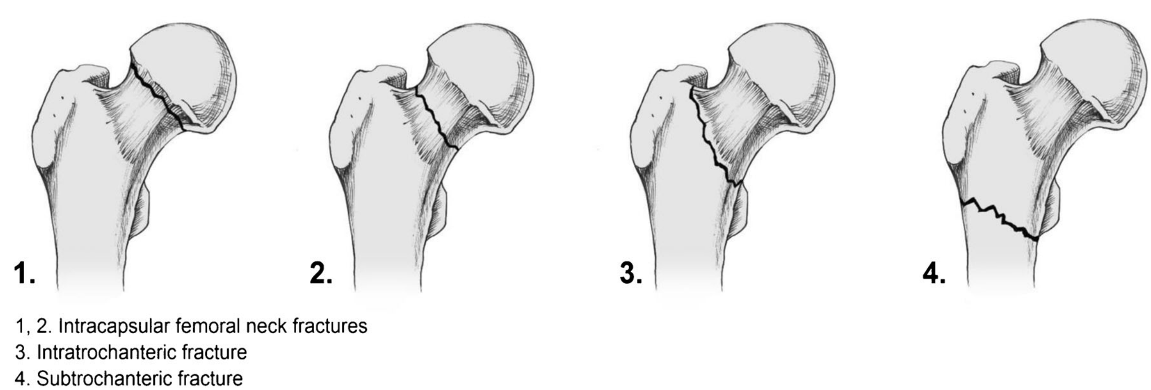

Fig. 1 Hip fracture classification

around 4 weeks' gestational age and completes development around 11 weeks [9]. Careful examination of this anatomy gives insight into the management of patients with hip fractures.

Musculoskeletal Anatomy

As stated above, the hip joint is known as a ball-and-socket type attachment, with the head of the femur rotating within the cup-like acetabulum of the pelvis. The spherical femoral head is secured within the joint by the acetabular labrum, a circular lip of fibrocartilaginous tissue [10]. Within the joint, both bony surfaces are covered by articular cartilage. Moving inferiorly, the head of the femur connects to the thinner neck and then the thicker shaft. The entire joint is encased by a dense, fibrous capsule that is continuous with periosteum. The capsule is attached at the base of the neck by circular fibers known as the zona orbicularis and superiorly by longitudinal fibers known as the zona reticularis.

The hip is stabilized by several ligaments in and around the joint (Figs. 2 and 3). Within the capsule, the ligamentum teres connects the acetabular notch and femoral head. This ligament is stretched when the hip becomes dislocated, thereby preventing further dislocation. Additionally, this ligament carries a branch of the obturator artery known as the foveal artery, which has a minor contribution to the hip's blood supply. Outside of the capsule, the large, bifurcating iliofemoral ligament spans from the anterior iliac crest to the intertrochanteric line. By preventing excessive extension, adduction, or rotation of the hip, the iliofemoral ligament provides stability while upright and flexibility while sitting [11]. Inferiorly, the pubofemoral ligament attaches the superior pubic rami to the intertrochanteric spine, thereby preventing excessive abduction and internal rotation. Posteriorly, the ischiofemoral ligament connects the ischium with the greater trochanter, providing posterior stability and maintaining joint contact (Fig. 3). Many smaller ligaments stretch from the hip through the femoral shaft, crisscrossing and reinforcing the entire hip joint [12].

The hip's large range of motion is commanded by several muscle groups. Posteriorly, the gluteus maximus, medius, and minimus allow for sitting, standing, and walking by providing hip extension [13]. Additionally, several hamstring muscles (semimembranosus, semitendinosus) and long head of biceps femoris also provide hip extension. Hip flexion is also pivotal to stability while stationary or moving, and is provided by the iliopsoas, originating from the lower back and pelvis with extension to the medial femur, and rectus femoris muscle in

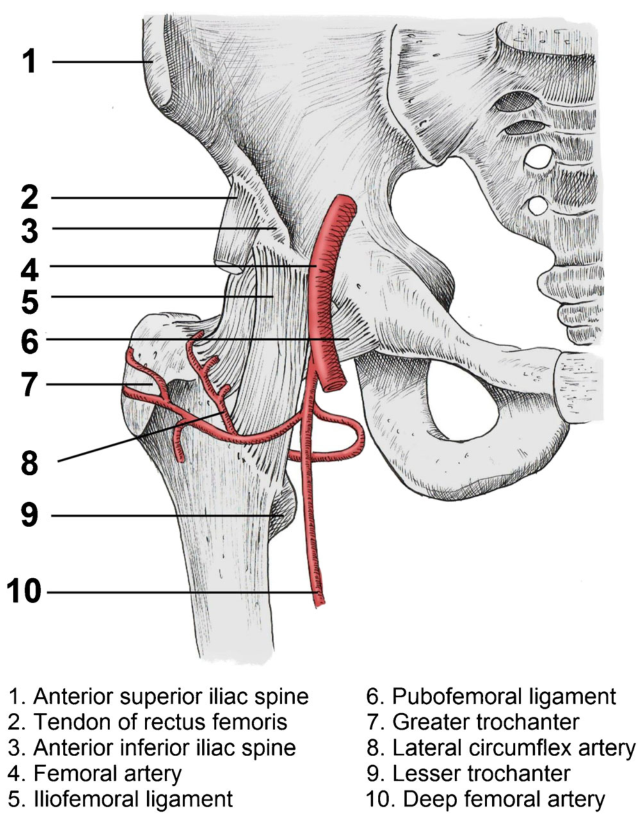

Fig. 2 Anterior hip anatomy

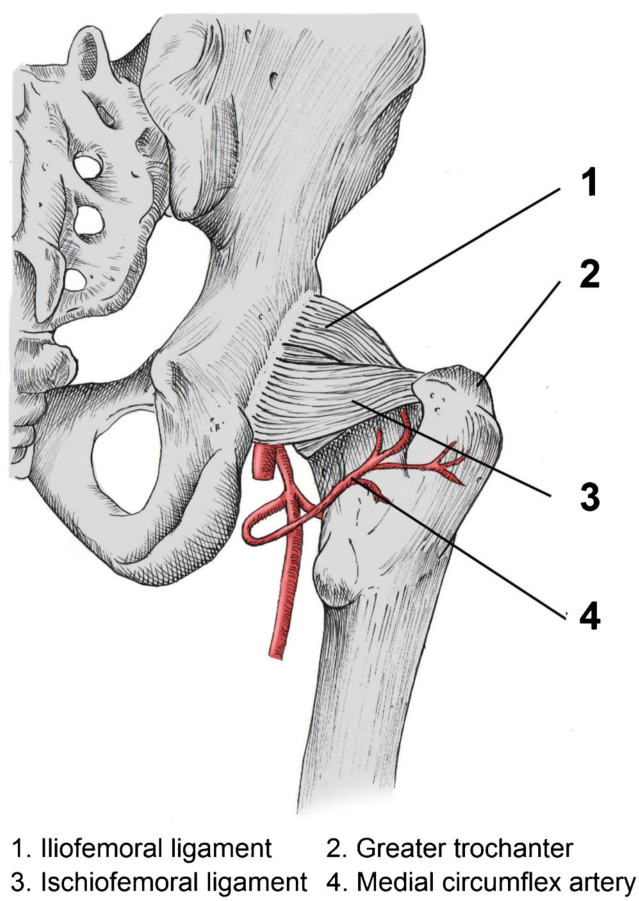

Fig. 3 Posterior hip anatomy

the thigh [14]. The tensor fasciae latae, adductors, pectineus, and gracilis also assist in hip flexion. Several medial muscle groups provide for adduction of the hip, including the adductor magnus, minimus, longus, and brevis, as well as the gluteal muscles, gracilis, pectineus, and semitendinosus muscles. Conversely, hip abduction is caused by the gluteal, piriformis, and tensor fascia latae muscles. External and internal rotational movements are provided by a combination of the gluteal, adductor, obturator, and iliopsoas muscles, with contributions from the tensor fascia latae, piriformis, sartorius, and pectineus muscles dependent on the leg position.

Neurovascular Anatomy

Perfusion to the hip joint is primarily supplied by two branches of the deep femoral artery, the medial and lateral circumflex arteries (Figs. 2 and 3). The medial circumflex artery provides the majority of the hip's blood supply, as the lateral circumflex must penetrate the iliofemoral ligament. The foveal artery, a branch of the obturator artery, has a minor vascular contribution, which becomes important to avoid avascular necrosis when perfusion through the circumflex arteries is interrupted through the neck fracture, typically [15]. Smaller vessels including branches of the gluteal arteries provide some additional blood supply.

The majority of sensory innervation at the hip is provided by the femoral nerve anteriorly and sciatic nerve posteriorly, as well as the obturator nerve and other smaller nerve branches (Fig. 4). Cutaneous innervation is supplied by the obturator and genitofemoral nerves anteromedially, and by the lateral femoral cutaneous nerve laterally [16].

Timing of Hip Fracture Perioperative Management in Reducing Morbidity and Mortality: Importance of Early Surgery

Timely diagnosis of hip fracture is essential for appropriate management. Early surgery is important, with decreased complication and mortality rates in patients receiving surgery within 48 h [7, 17••]. Delays in surgical treatment may result in avascular necrosis, fracture nonunion or malunion, or failure of fixation hardware.

In a 2008 meta-analysis of 257,367 patients, a delay in surgery for greater than 48 h after admission was associated with a 41% greater 30-day all-cause mortality and a 32% higher 1-year all-cause mortality [18]. It is currently recommended that patients undergo surgery as soon as possible once they have been optimized medically [19].

Early interventions are also critical in minimizing delirium, which has been associated with poorer outcomes including higher risk of dementia and death [20••]. Severe pain increases the risk of delirium in elderly hip fracture patients. Additional risk factors include patient factors as well as perioperative factors [21].

Results of meta-analyses by Yang et al. showed that elderly patients with preoperative cognitive impairment, advanced age, living in an institution, heart failure, total hip arthroplasty, multiple comorbidities, and morphine usage were more likely to sustain delirium after hip surgery. Females were less likely to develop delirium after hip surgery [22]. Minimization of opioid use with preoperative regional analgesia and multimodal pain control may reduce the incidence of delirium [5].

Untreated severe pain can cause delirium but also delirium risk may be increased with opioid use. Thus, balancing adequate and timely analgesia with the avoidance of opioid

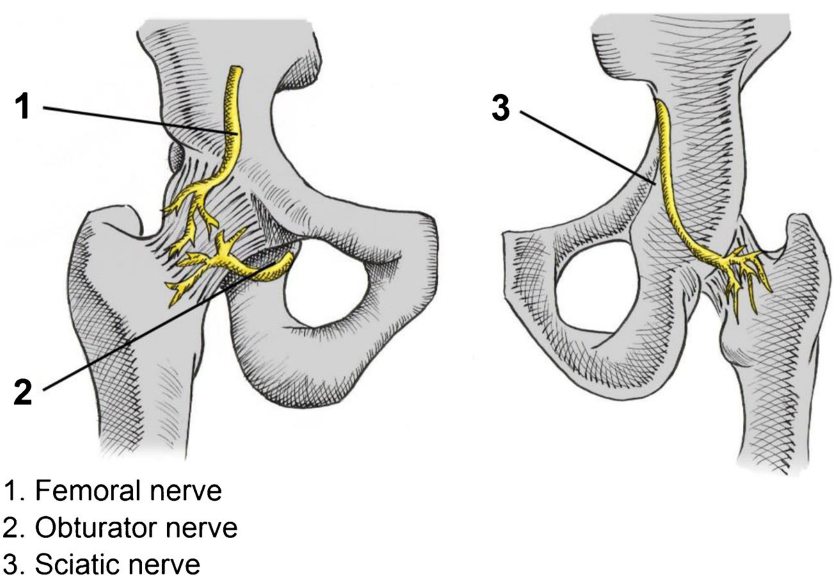

Fig. 4 Hip joint innervation

overmedication creates a clinical challenge in the treatment of elderly patients with hip fracture. A systematic review found moderate-quality evidence suggesting that the use of lower doses of opioids in treating severe acute pain in hip fracture may be paradoxically associated with higher delirium risk [23]. A 2003 prospective cohort study of 541 patients at New York hospitals found that cognitively intact patients with undertreated pain were nine times more likely to develop delirium compared to patients whose pain was adequately treated [24]. Withholding opioids in hip fracture is clinically inappropriate; instead, the lowest dose to achieve adequate pain control should be used.

Perioperative Analgesia, Multimodal Therapies, and Interdisciplinary Approach—Global Considerations

Effective pain management is critical since pain has been found to increase morbidity from hip fracture [25]. Even at rest, pain after hip fracture is relatively high [3]. Furthermore, studies have shown that pain is typically undertreated in elderly hip fracture patients [20••]. Severe pain significantly increases delirium in elderly patients and is associated with longer time to mobilization, increased hospital stay, and decreased functional outcomes. Hung et al. advocate the importance of optimal pain control following hip fracture to minimize complications of pain and immobility ranging from delirium to functional loss and death [26].

Practice guidelines from the American Academy of Orthopedic Surgeons (AAOS) recommend the use of regional and multimodal analgesia to reduce pain in the preoperative period [5].

Cognitive impairment poses a unique challenge in the management of pain in hip fracture patients due to patients' inability to reliably communicate their pain [27]. Multiple studies have shown that hip fracture pain is undertreated in elderly patients with dementia [27, 28]. In a prospective cohort study of 97 elderly hip fracture patients, patients with dementia received one third the amount of opioids compared to those who were cognitively intact [28]. This suggests that elderly patients with dementia are at especially high risk for undetected or undertreated pain after hip fracture, and that improved pain assessment and adequate analgesic modalities are needed in this vulnerable population.

Comprehensive pain management after hip fracture includes the use of pharmacologic and non-pharmacologic interventions. AAOS practice guidelines recommend multimodal analgesia initiated in the emergency room [5].

Systemic analgesia for hip fracture patients includes opioid and non-opioid therapies. Opioids must be administered cautiously in the elderly due to the risk of serious adverse effects [29]. A retrospective, observational study conducted by White et al. found that 36% of hip fracture patients have renal dysfunction on admission to hospital, which can increase the risk of morphine metabolic accumulation and subsequent sedation and respiratory depression [30].

A systemic review on acute pain management in hip fracture found insufficient evidence on the benefits and harms of most interventions, including spinal anesthesia, systemic analgesia, multimodal pain management, acupressure, relaxation therapy, transcutaneous electrical neurostimulation, and physical therapy regimens. There was moderate evidence to suggest that nerve blockades are effective for relieving acute pain and reducing delirium [31••]. Use of non-steroidal anti-inflammatory drugs is of limited value in elderly patients due to their side effect profile. Randomized controlled trials on the use of dexmedetomidine in elderly patients after hip fracture are limited, though some results suggest that dexmedetomidine, an alpha-2 adrenoreceptor antagonist, has sedative and analgesic effects that decrease anesthetic requirements and reduce pain scores and postoperative delirium after hip fracture surgery in the elderly [32]. More studies on the subject are warranted.

Pain management in hip fracture should be integrated into a multimodal, multidisciplinary model of care. Ideally, patients should be admitted to an integrated service, such as an orthogeriatric ward. This model of patient care can improve long-term clinical outcomes following hip fracture in the elderly [17••]. Moreover, standardized approaches to care may be implemented with a dedicated clinical protocol such as an enhanced recovery after surgery (ERAS) pathway [33••].

Regional Analgesia

The American Academy of Orthopedic Surgeons guidelines for management of hip fractures in the elderly finds "strong evidence supports regional analgesia to improve preoperative pain control in patients with hip fracture" [34]. The potential outcome benefits of nerve blocks include superior analgesia, decreased use of opioids in this elderly population, decrease in opioid-related side effects, and possible decreases in rates of postoperative delirium or cognitive dysfunction [35, 36••]. In addition, a 2018 retrospective review of 16,695 patients in 38 facilities in the USA found that in-hospital mortality, time to death, increased length of stay, and discharge to an institution rather than home were all negatively influenced by general anesthesia when compared to regional anesthesia [37••].

There is strong evidence that preoperative regional analgesia is more effective than systemic analgesia alone in improving pain associated with hip fracture [20••]. A large-scale systematic review found that epidural, fascia iliaca block, femoral nerve block, psoas compartment block, and combined nerve blocks all provided statistically superior analgesia compared to no block or standard care [31••]. A recent Cochrane review on peripheral nerve blocks in hip fracture patients found high-quality evidence that peripheral nerve blockade reduces pain on movement within 30 min of block placement, thus allowing patients to sit more comfortably and experience less pain with transfer to the operating room table and positioning for spinal anesthesia [3]. Patient satisfaction is higher in patients who received a peripheral nerve block compared to those who received intravenous opioids only. Other advantages of regional analgesia include rapid onset and localized analgesia while avoiding side effects associated with standard systemic therapies. There is also evidence suggesting that regional analgesia may reduce the rate of delirium in the elderly, as previously discussed [20••, 31••].

Timely pain control is an important component of optimal pain management. Ideally, regional analgesia should be administered in the emergency room. Regional blocks are typically performed by a trained anesthesiologist. However, single-shot peripheral nerve blocks have been successfully performed by emergency medicine physicians as well. Continuous peripheral nerve blocks have the additional advantage of providing analgesia in postoperative period, although catheter placement is technically more challenging to perform than single-shot blocks [3].

The following are the regional anesthesia options that could be employed in the perioperative setting.

Femoral Nerve and Fascia Iliaca Block

Femoral nerve block results in anesthesia of the anterior and medial thigh down to the knee, as well as a variable strip of skin on the medial leg and foot.

Fascia iliaca block results in similar distribution of effect as the femoral nerve block, however with less assurance as the distribution depends on the extent of local anesthetic spread [38]. It is a field block in which local anesthetic is deposited beneath the fascia iliaca with the potential to spread to the lateral femoral cutaneous, femoral, and obturator nerve [39].

Femoral nerve block can be an effective method for pain relief from trauma/fracture involving the proximal femur and hip and can provide superior analgesia when compared to parenteral morphine thereby reducing dose and adverse effects associated with intravenous opioids [40–43].

In addition to a single-shot nerve block, a catheter can be placed to provide continuous nerve block for postoperative pain control. A continuous infusion of local anesthetic with a perineural catheter can provide analgesia for several days perioperatively. Continuous femoral nerve catheters placed in the emergency department following radiologic confirmation of hip fracture are associated with lower pain scores pre- and postoperatively, decreased opioid related side effects, and increased comfort during patient positioning for spinal anesthetic prior to surgical intervention [44, 45].

Fascia iliaca block despite the variability in nerve blockade, when performed correctly, offers superior analgesia to parenteral opioids during patient movement, resulted in lower preoperative analgesia consumption and a longer time for first request, and reduced time to perform spinal anesthesia [46]. This block was also found to decrease preoperative pain as well as the incidence of delirium postoperatively in patients who were at intermediate risk for delirium when compared to those treated with intravenous or intramuscular analgesics [47].

While there are limited studies comparing femoral nerve block to fascia iliaca block in the setting of hip fracture, studies comparing these two modalities for hip arthroplasty show no difference in visual analog scale scores at 12–48 h and opioid consumption at 12–48 h postoperatively between two groups. In the setting of hip fracture, both modalities are viable options for perioperative pain control and should be chosen based on physician experience and preference [48, 49].

Lumbar Plexus Block

The lumbar plexus block (LPB) is another regional technique used for hip fractures. The plexus is formed by the union of anterior rami of L1–L4 with variable contribution from T12 and L5. It provides sensory relief along the distribution of the femoral, lateral femoral cutaneous, and obturator nerve. LPB along with light sedation has been successfully used for surgical anesthesia for patients undergoing surgical correction for hip fractures [50, 51]. Furthermore, patients who received LPB reported lower visual analog scale pain scores when compared to GA or fascia iliaca block in the immediate recovery period [52]. Despite this, there was no difference in morphine equivalent dosing between the two groups.

The drawbacks of LPB are primarily centered around the technical difficulty and greater degree of skill necessary to successfully perform the block. The lumbar paravertebral region is highly vascular and contains the ascending lumbar veins and arteries. Therefore, a thorough history regarding patient anticoagulation status is imperative since the site where LPB is performed is non-compressible. There is also a risk of unintentional neuraxial block or inadvertent intravascular injection. Given the risk associated with LPB, it is likely that novel techniques such as the ESPB or QL block will gain more use and may provide similar analgesia for total hip arthroplasty [53].

Quadratus Lumborum Block

The quadratus lumborum block is a regional anesthesia technique originally described by Blanco in 2007 to provide analgesia for abdominal surgery [54]. The anatomic target of the block is at the anterolateral aspect of the QL muscle in the space between the muscle fascia and the posterior endoabdominal fascia.

The block typically spreads to the L1–L3 nerve roots, as well as within the psoas major quadratus lumborum muscles and paravertebral space, if deeper injection is performed.

With years of research and clinical applications, it was reported that the quadratus lumborum block could also provide analgesia to the painful hip, and studies have described efficacy in the setting of femoral neck fracture and hip arthroplasty [55–59]. It has also been studied in comparison to femoral block in femoral neck fracture with results showing superior analgesia [60]. The QL block has been proposed as better covering the complex innervation of the hip.

Lumbar Erector Spinae Plane Block

The erector spinae plane block (ESPB) was first described in 2016 as a regional anesthesia technique for thoracic neuropathic pain or pain relief from rib fractures [61, 62]. It is a paraspinal fascial plane block where local anesthetic is injected between the erector spinae muscle and superficial tips of the thoracic transverse process.

Recently, its efficacy in hip surgeries has been explored. When the erector spinae muscles are blocked at a lumbar level, specifically the L4 transverse process, it can provide local anesthetic spread from L2 to S1 [63]. This spread provides long-lasting pain relief following hip surgery, significantly decreasing postoperative analgesic requirement [63, 64]. Continuous erector spinae blocks have been used with similar efficacy to provide opioid-free analgesia [65]. The ESPB use for analgesia is likely to expand given its safety and proven value. Since there is no direct contact with nerves during block performance, there is no risk for needle-related nerve injury. Secondly, given its superficial location, neuraxial spread is unlikely to occur.

Epidural Analgesia

Lumbar epidural analgesia provides complete sensory and motor block to the lower extremities via anesthetics delivered to the nerve roots. This avoids the pitfall of incomplete sensory block that may be encountered with peripheral nerve blocks discussed above. It can thus provide surgical anesthesia more reliably.

Risks with this technique include bleeding, infection, and nerve damage. A thorough history and active medication list should be obtained prior to epidural placement. Medications that interfere with coagulation cascade as well as last dose of an anticoagulant should be elicited from patient history. Patients with medical conditions that worsen with reduced afterload or preload (e.g., severe AS, mitral stenosis, hypertrophic cardiomyopathy) and patients who may experience worsening shortness of breath, such as those with restrictive lung disease or severe COPD, may require additional testing [66].

Epidural catheter is a reasonable option for analgesia in hip fracture management that may provide superior analgesia compared no block or standard care [31••]. Within the context of pain management and rehabilitation postoperatively, epidural catheters reduced parenteral opioid consumption, incidence of myocardial ischemia, and pain at rest or during knee/hip movement [67, 68]. Furthermore, patients who received epidural catheters reported superior analgesia during basic physical functions required in a multimodal rehabilitation setting allowing less restriction in exercises to regain independent ambulation without significant motor blockade compared to parenteral-only treatment options [67].

Intrathecal Analgesia

This technique differs from epidural in that the analgesia, often a local anesthetic combined with an opioid, is injected into the subdural space. It is often performed below the second lumbar vertebrae to avoid damage to the spinal cord.

Intrathecal analgesia is used less frequently as an alternative to epidural analgesia secondary to increased frequency of dose-related adverse effects including hypotension, urinary retention, and respiratory depression [69]. Injection of LA into the intrathecal space may produce significant motor blockade limiting postoperative mobility, an important factor in management of trauma patients. Despite these limitations, intrathecal analgesia has been used for postoperative pain management of hip fracture patients. Specifically, formulations that include a local anesthetic, typically bupivacaine, mixed with intrathecal morphine have consistently shown an increased pain-free period when compared with intrathecal strategies with local anesthetics alone [70]. Intrathecal morphine has also been used for patients undergoing total hip arthroplasty for osteoarthritis and is associated with less parenteral opioid consumption, lower visual analog scale scores on POD 0, and beneficial analgesic effect up to 1 week after surgery [71, 72]. Again, the benefits of improved pain control may be truncated by the risk of postoperative mobility secondary to motor blockade.

Anesthetic Considerations in Elderly Patients with Hip Fractures

The perioperative period surrounding patients with any kind of urgent and emergent surgery can provide challenges in management for the anesthesiologist. Hip fractures may require complex surgeries and a multitude of potential complications, both during and after the procedure. In the geriatric population, there is an added component of advanced age which lends a multitude of additional medical problems. In fact, the presence of three or more comorbidities puts these patients at a high risk of pulmonary and cardiac postoperative complications as well as overall mortality [73]. The management of elderly patients with hip fractures involves a multifaceted approach that should focus on all portions of perioperative care [74].

Preoperative Period

Timely medical optimization is crucial for patients undergoing hip fracture surgery, as this population often carries other medical comorbidities and chronic conditions. At the same time, potentially delaying this urgent surgery should be weighed against the true benefits of any medical intervention. As previously mentioned, the time to surgery in these cases is critical, and a shortened delay in surgical treatment can improve outcomes across the board [7, 17••, 18, 19]. To that end, preoperative evaluation, testing, and optimization should focus on acute, treatable derangements, such as abnormalities in electrolytes and blood glucose, arrhythmias, hypovolemia or anemia, and hypoxia [75]. In the interest of early surgery, preoperative cardiac optimization and clearance must be performed in an expedited period of time, leading to potentially an increased risk of cardiac events. Patients with unstable coronary symptoms, worsening or new heart failure, pulmonary hypertension, significant arrhythmia, or severe valvular disease may require further preoperative workup and intervention if needed. Aortic stenosis in particular is a relatively common valvular lesion seen in elderly patients with hip fractures, and echocardiography may be recommended if significant aortic stenosis is suspected as it may be missed on physical examination [76]. The information from the preoperative assessment can be crucially important in choosing and guiding the optimal and safe anesthetic care during surgery and postoperatively.

An additional common factor in elderly patients is the use of multiple medications [77]. Because of the urgent nature of hip fracture surgery, a delay may not always be possible even if medications have been taken recently. In patients taking anticoagulants, an INR greater than 1.5 could be reversed with prothrombin complex concentrates, as its effects are more rapid than with FFP and vitamin K administration [78]. Other relevant medications should be continued in the perioperative period, specifically β-blockers, aspirin, and statins. Certain anticoagulants such as clopidogrel and apixaban may necessitate risk (bleeding) versus benefit (early surgery) analysis and may also contraindicate a regional anesthetic technique [79]. Furthermore, interruption of anticoagulation in patients with conditions such as atrial fibrillation may lead to a higher risk of stroke and mortality. In these patients, optimizing rate or rhythm control is essential to preventing thromboembolic events as well as hemodynamic instability in the perioperative period [80].

Intraoperative Period

In elderly patients undergoing surgery, there is generally a relative loss of functional reserve across all organ systems [81, 82]. The frailty of this patient population demands careful titration of anesthetics and very close hemodynamic monitoring. Intraoperatively, most anesthetic medications, including inhalational and intravenous agents, will show more profound and lasting effect, with slower clearance. Even with regional anesthesia, the duration of blockade is largely affected by the patient's age, and therefore dosages should be decreased and adjusted accordingly.

Elderly patients undergoing emergency surgery are also at a higher risk of exaggerated response to anesthetics and surgical stimulation and are especially vulnerable to complications from periods of hemodynamic instability. The need for invasive monitoring such as arterial and central lines should be assessed on a case-by-case basis to provide safe and effective surgical anesthesia. Additionally, extensive research has demonstrated that the length of surgery is directly correlated with the rate of perioperative complications in patients having hip fracture surgery [83, 84].

Intraoperatively, maintaining normothermia is especially important in reducing infection, blood loss, opioid requirements, coagulopathy, and cardiac complications, as elderly patients have much more limited physiologic temperature regulation [85]. The most effective way to achieve normothermia is with forced air blanket warming. More recently, protocols have advised goal-directed fluid therapy intraoperatively, which uses markers of volume status such as pulse pressure variation to guide fluid administration. Although many regimens exist, none have been specifically validated for patients undergoing hip fracture surgery. Additionally, elderly patients are at an increased risk of bleeding and having a transfusion requirement, and correction of perioperative anemia while avoiding volume overload is critical [86]. Prothrombotic agents such as tranexamic acid have been shown to decrease the risk of intraoperative blood loss and transfusion in these patients [87].

The choice of anesthetic technique in patients undergoing hip fracture surgery is dependent on a multitude of factors. Regional techniques have demonstrated better outcomes and fewer complications in most patients, although the need for general anesthesia does remain in certain cases [36••, 88]. The anesthetic options for hip fracture surgery including regional versus general are discussed further in the paper.

Postoperative Period

The risk of complications from hip surgery remains present even in the postoperative period, especially in elderly patients. One of the most common adverse events in this population is acute delirium, as discussed previously. Hip fracture surgery maintains one of the highest rates of postoperative delirium across all procedures [89]. Although there are a number of un-modifiable risk factors such as advanced age, type and urgency of surgery, existing cognitive impairment, delirium, and medical comorbidities, delirium may also be brought on by any number of other triggers. As previously mentioned, peripheral nerve blockade may assist with postoperative pain while decreasing the incidence of delirium. Postoperative cognitive dysfunction, distinct from acute delirium, is another common adverse effect seen in the elderly population after hip fracture surgery. Occurring in the days and weeks following surgery, postoperative cognitive dysfunction can be precipitated by a large number of factors but could be reversible [90].

Finally, elderly patients also suffer from an increased incidence of pulmonary complication, including desaturation and aspiration, given reduced airway reflexes and laryngeal muscle tone. More acute monitoring for these and other postoperative complications is undoubtedly important in this patient population. However, the need for an intensive care unit stay postoperatively and enhanced care should be determined on a case-by-case basis as to avoid complications due to delays in surgery and patient transfers [91].

Type of Anesthesia and Outcomes in Hip Fracture Surgery

1. Mortality

Hip fracture surgery, as previously mentioned, is associated with a high postoperative mortality, including 30 days, 1 year, and 10 years post-fracture, despite advances in surgical and anesthetic techniques [4••, 92]. The implication of the anesthetic technique on mortality has been studied for years with renewed interest recently.

Overall, evidence from randomized studies regarding the optimal technique is limited. Most of the published literature consists of retrospective and observational studies. Analyses of observational data may be limited because of the non-random selection of patients for one form of anesthesia or another. Difficulties met by the researchers who want to study the effect of anesthesia technique on mortality as a primary outcome are divided into several categories: studying the timing of outcome (in-hospital, 30 days vs. 1 year), patient comorbidities (sicker patients receiving neuraxial anesthesia), and differences in hospital practice and country's health care system. Furthermore, there are difficulties specific to anesthesia such as anesthesiologists' experience and variation in technique. To correct for the multitude of confounding factors, it has been estimated that such a trial would need more than 9000 patients allocated to either group [93]. Another confounding factor is the surgical technique as there are, with no doubt, huge differences in the surgical trauma between merely a screw fixation and a joint replacement.

Historically, general anesthesia had been used more frequently. This changed after a meta-analysis, published in 2000 and included 141 clinical trials, showed a reduction in postoperative mortality associated with neuraxial anesthesia [94]. The results of the meta-analysis lead to the publication of new recommendations by multiple national societies recommending for more widespread use of neuraxial anesthesia instead of general anesthesia in hip fracture surgery [95, 96].

However, upon further scrutiny, most of the studies included in that meta-analysis were small, dated, and included many trials published in the 1980s when the surgical technique and anesthesia medications were different and often did not distinguish between neuraxial and combined general and neuraxial anesthesia.

Studies published after this landmark meta-analysis showed conflicting results, or in better terms, inadequately designed research, on the effect of the anesthesia technique on mortality in patients with hip fracture. The meta-analysis from 2017 analyzing data aggregated from 413,999 patients showed no difference in mortality [92]. The systematic review published in 2018 showed similar results but highlighted the need for agreement on outcome definitions and for a minimum core outcome set to be measured and reported in hip fracture studies [97]. In contrast, the two other recent studies from 2018 showed a lower mortality rate with neuraxial anesthesia [37••, 98].

2. Morbidity

Multiple studies analyzed the effect of the anesthesia technique on length of hospital stay, blood loss and transfusion, myocardial infarction, cardiac arrest, pneumonia, respiratory failure, unplanned intubation, deep vein thrombosis, and delirium.

There are few studies that focused on each of the aforementioned complications as a primary outcome. Most of the data have been pooled from small studies that address mortality with morbidity investigated as a secondary outcome.

Theoretically, neuraxial techniques (spinal and epidural) have the benefit of avoiding the need for airway management and having lesser effects on cerebral function. This could be beneficial in a patient with difficult airway or compromised cognitive function. However, no neuraxial technique provides a 100% success rate or is completely free of complications. Neuraxial anesthesia complications include hematoma, nerve injury, and local anesthetic–associated complications, such as cardiac arrest, seizures, and death.

When deciding whether to perform a neuraxial technique in lieu of securing the airway preoperatively, these complications should be considered because they may trigger the need for immediate and urgent control of the airway and conversion to general anesthesia due to sudden loss of respiratory function (total spinal), the development of local anesthesia–related complications (e.g., cardiac arrest, seizures), or failed neuraxial block.

In addition, as more patients are placed on anticoagulation and antiplatelet therapy, anesthesiologists have to choose between an early procedure under general anesthesia with an increased bleeding risk versus a delayed procedure under neuraxial anesthesia with an increased risk of pneumonia and deep vein thrombosis.

Pneumonia

The overall quality of the evidence on the effect of the anesthesia technique on the incidence of pneumonia after hip fracture surgery is low [99–104]. The studies showed overall no difference in the risk of pneumonia between general anesthesia and neuraxial anesthesia. The number of participants in these studies is small. It is estimated that 5106 patients would be required to show a difference of 25% [105]. Additional caveats in the evidence stems from the fact that most studies do not provide details on the depth of sedation and the steps taken to decrease the risk of pneumonia in the regional anesthesia arm.

A study from May 2018 reviewed 382,236 patients undergoing primary hip or knee arthroplasty in 2006–2010. When patients who received general anesthesia were compared to patients who received neuraxial or a combination of neuraxial and general, they were found to have higher rates of pulmonary compromise, infections, and acute renal failure. They also had a longer hospital length of stay [106]. Study using a large prospectively collected database of 16,555 knee arthroplasty patients showed that neuraxial anesthesia was associated with lower incidence of pneumonia and composite systemic infection relative to general anesthesia within 30 days postoperatively. The data suggested a 49% reduction in pneumonia risk and 23% reduction of any systemic infectious complication rates [107].

Myocardial Infarction

Traditionally, it is thought that the sympathectomy provided during neuraxial anesthesia is protective against myocardial ischemia. In addition, the use of isobaric bupivacaine decreased the incidence of hypotension associated with neuraxial anesthesia. On the other hand, the cardiac anesthesia literature described the protective effects of inhalational drugs on the heart during general anesthesia [108].

Four studies [88, 109–111] evaluated the effect of type of anesthesia on the risk of myocardial infarction. No difference on the risk of myocardial infarction was found. The studies are small; thus, the quality of the evidence is very low.

Postoperative Confusion and Delirium

Postoperative confusion and delirium are common in the perioperative period especially in the elderly. These cognitive deficits are reported in more than 50% of older patients after the repair of hip fractures and they are associated with increased mortality [113, 114, 115, 116]. Factors that may increase the risk of postoperative confusion and delirium include dehydration, hyponatremia, other electrolyte abnormalities, and medications such as benzodiazepines, ketamine, and high-dose opioids.

Several studies with delirium as a primary outcome showed conflicting results. Systematic review of 104 studies by Patel from 2018 showed overall that there was no evidence to suggest that anesthesia types influence postoperative delirium and recommended more adequately powered and methodologically rigorous studies [112].

Other systematic reviews suggested reduced incidence of postoperative delirium in patients having regional anesthesia [20••, 31••, 105, 113]. Some of the limitations mentioned were data from the use of outdated anesthetic medications, inclusion of only randomized controlled trials, and studying delirium as a secondary outcome.

Conclusion

Hip fracture in elderly patients represents a complex medical and surgical urgency with high morbidity and mortality. The acute pain management in these situations is often very challenging, with patients' physiological decrease in function, medical comorbidities, and cognitive impairment commonly confounding and complicating pain assessment and treatment. Multidisciplinary and multimodal approaches across the entire perioperative spectrum involving medical, surgical, and anesthesiology teams employing adequate preoperative optimization, decrease in pain and disability utilizing opioid and non-opioid therapies, regional anesthesia, patient-tailored anesthetic approach, and delirium prevention strategies seem to provide the best outcomes.

Compliance with Ethical Standards

Conflict of Interest A.D., F.F., J.D., S.S., A.B., M.K., and K.G. declare no conflict of interest. A.D.K. discloses that he is on the Speakers Bureau for Depomed, Inc. and Merck.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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