Surgical management of osteonecrosis of the femoral head in patients with sickle cell disease

Atul F Kamath, Michael H McGraw, Craig L Israelite

Atul F Kamath, Michael H McGraw, Craig L Israelite, Department of Orthopedic Surgery, the Center for Hip Preservation, Penn Medicine, University of Pennsylvania, Philadelphia, PA 19107, United States

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Correspondence to: Atul F Kamath, MD, Department of Orthopedic Surgery, the Center for Hip Preservation, Penn Medicine, University of Pennsylvania, 800 Spruce Street, 8th Floor Preston, Philadelphia, PA 19107, United States. akamath@post.harvard.edu
Telephone: +1-215-6878169
Fax: +1-215-8292492

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Abstract
Sickle cell disease is a known risk factor for osteonecrosis of the hip. Necrosis within the femoral head may cause severe pain, functional limitations, and compromise quality of life in this patient population. Early stages of avascular necrosis of the hip may be managed surgically with core decompression with or without autologous bone grafting. Total hip arthroplasty is the mainstay of treatment of advanced stages of the disease in patients who have intractable pain and are medically fit to undergo the procedure. The management of hip pathology in sickle cell disease presents numerous medical and surgical challenges, and the careful perioperative management of patients is mandatory. Although there is an increased risk of medical and surgical complications in patients with sickle cell disease, total hip arthroplasty can provide substantial relief of pain and improvement of function in the appropriately selected patient.

Key words: Sickle cell disease; Total hip arthroplasty; Core decompression; Orthopedic; Osteonecrosis; Avascular necrosis; Hip

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Core tip: The management of hip pathology in sickle cell disease presents numerous medical and surgical challenges, and the careful perioperative management of patients is mandatory. Key aspects of medical optimization and surgical care are presented in this brief review.

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INTRODUCTION
Sickle-cell anemia results from a point mutation in the β-globin chain of hemoglobin, replacing the amino acid glutamate with the amino acid valine at the
sickling of red blood cells causes vascular congestion, venostasis, and thrombosis in the microvasculature of the bone. Resulting ischemia is compounded by an increase in intraosseus pressure secondary to medullary hyperplasia. This produces bone infarction and necrosis[4]. Patients with symptomatic ONFH typically report groin pain and pain with ambulation. Physical examination reveals painful restrictions in the hip range of motion. Multiple other joints may be affected, including the knees, feet, and back, so a comprehensive examination is important. The hips may be involved bilaterally (Figure 1), and it is not uncommon for necrosis to be asymptomatic, especially in early stages[4]. One study reported radiographic evidence of AVN in the contralateral, asymptomatic hip in 39% of patients with unilateral hip pain[7].

NON-SURGICAL MANAGEMENT

Red blood cell transfusion therapy is used to prevent the primary manifestations of SCD. Transfusion therapy may be warranted for the primary prevention of stroke, chronic pain crises, pulmonary hypertension, chronic renal failure, acute chest syndrome (ACS), and end-organ damage[8]. Hydroxyurea is a widely prescribed drug for management of SCD. It induces HbF synthesis, resulting in decreased sickling and improved red-cell survival. Hydroxyurea is also metabolized into the vasodilator nitric oxide with positive effects on vascular inflammation. Patients with SCD treated with hydroxyurea have significantly fewer acute painful episodes and episodes of ACS, decreased transfusion requirements, and enhanced survival[9,10]. Stem cell transplantation is a novel treatment modality and can be curative in individuals with SCD. Due to inherent risks of the procedure, stem cell transplantation is reserved for patients with significant complications, such as a history of stroke, and those who have a matched sibling stem cell donor[11,12]. There is more than a 90% survival rate after this procedure and approximately 85% survive free from SCD[12,13]. Many patients with SCD develop AVN of the hip, as well as other synovial joints (knee, foot, and back) despite the advances in medical management. Unfortunately, the natural history of symptomatic AVN of the femoral head secondary to SCD is progressive degenerative changes. Non-surgical management of AVN of the femoral head should be used initially and consists of pain management, activity modification, and ambulatory assistive devices. In addition to plain X-rays, magnetic resonance imaging may be used to assess the severity of femoral head involvement (Figure 2). Nonoperative treatments may provide maximal benefit in early stages of disease, prior to collapse of the femoral head articular surface[14].

SURGICAL OPTIONS

Core decompression

The use of core decompression for the treatment of ONFH is controversial because well-controlled prospective trials are lacking. This procedure is reserved for the early stages of AVN (Figure 3). A prospective case-
control study showed that core decompression was most efficacious in the early stages of ONFH\(^{15}\). Radiographic and clinical outcomes in this study were best in Steinberg Classification (Table 1) stages I and II. Another study reported symptomatic improvement in eleven of thirteen patients who underwent core decompression in pre-collapse stages\(^{16}\). Core decompression combined with autologous bone grafting may provide superior clinical outcomes than core decompression alone: a significant difference in Harris Hip Scores and visual analog scores, at a year post-operatively, were seen in patients who underwent core decompression with bone grafting when compared with core decompression alone\(^{17}\). Traditionally, there has been debate regarding whether core decompression should be performed in asymptomatic patients. Hsu et al\(^{18}\) examined thirty-one patients with ONFH who underwent simultaneous bilateral core decompression and grafting. Ten patients with asymptomatic hips at the time of surgical decompression went on to require total hip arthroplasty (THA); thirteen patients required THA in the symptomatic side. The authors found that the proportion of hips ultimately requiring THA were similar between the two groups. When compared to AVN secondary to other etiologies, ONFH secondary to SCD has a poor clinical and radiographic response after core decompression. It has been posited that these inferior results after core decompression are because the decompression may decrease intraosseous pressure but not successfully relieve vascular congestion to prevent future vaso-occlusive events. Furthermore, there are diffuse changes in the femoral head in SCD patients, which may make complete decompression difficult\(^{19}\). In a study by Hernigou et al\(^{7}\), more than 40% of the femoral head in SCD was involved, regardless of the stage of ONFH.

Table 1  University of Pennsylvania System for staging avascular necrosis\(^{14}\)

| Stage | Criteria |
|-------|----------|
| 0     | Normal or non-diagnostic radiograph, bone scan, MRI |
| I     | Normal radiographs, abnormal bone scan and/or MRI  
A: Mild (< 15% of femoral head affected)  
B: Moderate (15%-30%)  
C: Severe (> 30%) |
| II    | Cystic and sclerotic changes in femoral head  
A: Mild (< 15% of femoral head affected)  
B: Moderate (15%-30%)  
C: Severe (> 30%) |
| III   | Subchondral collapse (crescent sign) without flattening  
A: Mild (< 15% of articular surface)  
B: Moderate (15%-30%)  
C: Severe (> 30%) |
| IV    | Flattening of femoral head  
A: Mild (< 15% of surface and < 2 mm depression)  
B: Moderate (15%-30% of surface and 2-4 mm depression)  
C: Severe (> 30% of surface and 4 mm depression) |
| V     | Joint narrowing or acetabular changes  
A: Mild\(^{1}\)  
B: Moderate\(^{1}\)  
C: Severe\(^{1}\) |
| VI    | Advanced degenerative changes |

\(^{1}\)Average of femoral head involvement; as determined in stage IV and estimated acetabular involvement. MRI: Magnetic resonance imaging.
Multiple studies have reported a rate of aseptic loosening of 10%-38% in cementless THA components reported an 8% incidence of aseptic loosening in cementless THA. One study reported a 33% aseptic loosening rate in primary THA with cemented cups. A more recent retrospective study reported better results with cemented components. There are some advantages that cemented fixation may provide, including additional hemostasis, decreased risk of femoral perforation and avoidance of biologic fixation in avascular/necrotic bone. Furthermore, the use of cementless components relies on bony ingrowth for fixation in bone that may be largely necrotic. Hip dislocation has also been reported in patients with sickle cell hemoglobinopathy. The rate of hip dislocation has been reported in as many as 26% of hips in one study, and may be due to underlying abnormal anatomy seen in patients with SCD.

**Alternative surgical options**

Other surgical options for the management of AVN in this population include femoral osteotomy, hemiarthroplasty, arthrodesis, and resection arthroplasty. These are...
largely historical techniques when compared to core decompression or THA. By redirecting weight-bearing forces, osteotomy can alleviate pressure in discrete areas of the femoral head, but it does not address the underlying pathology and progression of diffuse hip disease. Long-term failure is related to the amount of femoral head involvement[32]. Likewise, hemiarthroplasty only addresses changes in the proximal femur, and the quality of the bone in the SCD acetabulum is often poor. Reciprocal acetabular changes or subsequent migration of the prosthesis into the pelvis have been reported[27,28,33]. Due to the frequency of bilateral hip involvement in ONFH due to SCD, arthrodesis is rarely indicated and leads to significant shortening of the limb after debridement of non-viable bone required for successful fusion. Primary resection arthroplasty is rarely performed because THA provides greater potential benefits, but acceptable results have been reported when used as a salvage procedure after failed primary THA[22].

**COMPLICATIONS**

Medical and surgical complications are increased in patients with SCD undergoing THA. These complications can be described according to procedural-related complications and those complications specifically related to SCD.

**Immediate**

An immediate post-operative complication of THA is blood loss requiring transfusion and resulting transfusion reactions. Blood loss during THA in this population is often greater than blood loss seen in patients without the disease. The procedure in patients with SCD may be technically more difficult due to acetabular protrusion, or with difficulties preparing the femoral canal. These challenges may cause an increase in operative time and blood loss. There are also reports in the literature demonstrating that blood loss increases when patients have many preoperative transfusions, alloantibodies, or red blood cell exchange[10,34]. Vichinsky et al[21], in a series of 52 patients, reported excessive intra-operative blood loss in the majority of patients who underwent primary THA. The aggressive replacement of blood products is warranted and may decrease cardiopulmonary and neurological complications. It is currently recommended to keep the post-operative hemoglobin in patients with SCD > 10 mg/dL. Likewise, any signs and symptoms of anemia such as tachycardia, syncope, angina, ACS, and hypoxia should be addressed with transfusion[33]. Multiple transfusions throughout the lifetime of these patients lead to alloimmunization. Alloimmunization is seen in more than 20% of patients[27]. This accounts for the increased frequency of major transfusion reactions in this population. Hernigou reported an incidence of major transfusion reactions of 12% in his series of primary THA in patients with SCD[30]. Other studies have reported an incidence as high as 4%-25%[24,27].

Other immediate postoperative complications include SCD related events such as vaso-occlusive crises and ACS (17% incidence)[34]. Episodes of vaso-occlusive crisis can present as pain anywhere in the body. Sickle cell crises can be managed with administration of parenteral fluids and analgesics[10,36]. Optimal analgesia is generally achieved with opiates given at pre-determined time intervals or by patient-controlled analgesia. Non-steroidal anti-inflammatories, such as ketorolac or ibuprofen, are also effective but are typically avoided in the immediate post-operative setting secondary to the increased risk of hematoma formation. Other infectious etiologies (e.g., postoperative pneumonia) should be ruled out with appropriate testing.

Acute chest syndrome is a form of acute lung injury in sickle cell patients and presents a major cause of morbidity and mortality[36]. The diagnosis of ACS is clinical and involves the presence of a new pulmonary infiltrate on chest X-ray, along with respiratory tract symptoms, hypoxemia, and/or fever. Intubation and mechanical support may be necessary if the symptoms progress. Acute chest syndrome is associated with a high mortality; therefore, an aggressive treatment strategy should be initiated early. This treatment includes aggressive oxygenation, analgesics, antibiotics as needed, and/or simple or exchange transfusions[37]. Incentive spirometry should also be encouraged throughout the peri-operative period.

**Short term**

Patients with SCD are predisposed to infection. Studies have reported postoperative wound infections in 16%-25% of THAs[23,30]. A first generation cephalosporin should be used for antibiotic prophylaxis in these patients. No empiric coverage of Salmonella is generally necessary. However, authors have recommended the frequent use of intraoperative bone cultures to rule out infection before implanting the prosthesis[29]. Patients with SCD also have increased development of wound complications including increased wound drainage and hematoma formation, and complication rates have been reported in the literature[37].

**Late**

Late peri-prosthetic infection is a particular concern for patients with SCD because recurrent bacteremia is commonly seen and may result in hematogenous seeding of the prosthesis[30]. The risk of late infection has been reported and may ultimately require resection arthroplasty for treatment. Hernigou et al[30] reported that late infection, at a rate of 3%, was the main complication in his series. Late infection was the reason for resection arthroplasty in 100% of patients in another study[22]. Small series have reported rates of non-infectious (aseptic) prosthetic loosening of 10%-38%[27]. The reliance on bony ingrowth for fixation in necrotic
bone with cementless components may be the cause of this phenomenon. A recent study using cemented components reported a lower incidence of aseptic loosening (8%) and posited that a properly placed cemented component may decrease the risk of aseptic loosening[26]. Hip dislocation is also a late complication, and has been reported in patients with sickle cell hemoglobinopathy. The rate of dislocation has been reported in as many as 26% of hips, and may be due to changes in the bony anatomy seen in patients with SCD[26].

CONCLUSION

Avascular necrosis of the femoral head due to SCD can be quite debilitating. The surgical management of hip pathology in patients with SCD can be challenging, as there is an increase in medical and surgical complications in this patient population. To ensure a successful outcome, it is imperative that the surgeon consider all perioperative management strategies, including a multi-disciplinary approach to care with medical, anesthesia, and hematology colleagues. In early stages of ONFH, core decompression with or without bone grafting is a viable option to attempt to prevent progression of the disease. In patients with intractable pain and advanced disease, primary THA is the most reliable option for pain relief and functional improvement. The evaluation of the hemodynamic and oxygenation status of the patient minimizes sickle cell related complications in those undergoing operative interventions. Modern day cementless THA components have demonstrated encouraging outcomes in SCD patients. Total hip arthroplasty in the appropriately selected patient with SCD can provide improved hip function and enhanced quality of life.

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