INTRODUCTION

Hemophilia is the most common hereditary bleeding disease caused by a mutation of factor VIII or IX, which are essential components of the coagulation cascade. Hemophilia is inherited as an X-linked recessive trait, mainly affecting males and homozygous females. About 30% of patients with hemophilia have no family history of the disease. Hemophilia presents with easy bruising and spontaneous hemorrhage in various regions of the body. Bleeding into joints is also a common manifestation of hemophilia; hemorrhages in the joints are known as hemarthrosis [1].

Joint bleeding causes inflammation of the synovial cartilage, followed by cartilage and subsequent bone destruction in the joints. Blood, cytokines, metalloproteinases, and hydroxyl free radicals cause this cartilage damage by inducing...
chondrocyte apoptosis [2]. Hemarthrosis is a disabling condition involving joint pain and restricted joint movement. The diarthrodial joints, such as the knee, elbow, and ankle, are most commonly involved owing to their relatively larger synovial content [3]. If not initially managed, hemarthrosis may lead to severe complications and require arthroplasty. In its earlier stages, treated plasma-derived or recombinant factors are used to manage the condition. If bleeding occurs frequently, patients should begin with prophylaxis. To prevent further bone damage, hypertrophied synovium can be removed using chemical or radioactive agents [4]. In severe cases, joint replacement surgery may become necessary. However, performing surgery on patients with hemophilia presents a challenge to anesthesiologists. Maintenance of hemodynamic conditions is crucial to prevent intraoperative and postoperative bleeding, as well as issues like tachycardia and hypotension. This review aimed to provide anesthesiologists with a comprehensive outline of important considerations when performing joint replacement surgeries on patients with hemophilia.

**PREOPERATIVE ASSESSMENT**

**Coagulation profile**

Coagulation profile examination plays a pivotal role in the preoperative assessment of patients with hemophilia. First, measuring baseline factor VIII or factor IX levels is essential to guide preoperative factor replacement therapy dosing and monitoring. This ensures that adequate factor levels are maintained during surgery to achieve hemostasis and minimize bleeding complications. Additionally, screening for the presence of inhibitors is crucial, especially in patients with severe hemophilia or those with histories of previous exposure to factor concentrates. The presence of inhibitors can neutralize the effects of exogenous clotting factors, leading to inadequate hemostasis during surgery [5]. Early identification of inhibitors allows for appropriate implementation of management strategies to mitigate the risk of bleeding complications. Emicizumab is an important drug for routine prophylaxis, previously reserved for patients with hemophilia A and factor VIII inhibitors who are not currently undergoing immune tolerance induction (ITI). While it has proven to be an effective prophylactic therapy in these patients [6], evidence now suggests that emicizumab has become a preferred first-line approach to protect against bleeds and represents an alternative to burdensome ITI in certain patient groups [7].

Comorbidities also significantly influence preoperative evaluation, as they may impact management strategies and introduce the potential for physiological imbalances or drug interactions [8,9]. Notably, drugs causing platelet inhibition, including aspirin, glycoprotein IIb/IIIa inhibitors, β-lactam antibiotics, selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and dietary components affecting platelet function such as fish oils containing vitamin B3 and omega-3 fatty acids, ethanol, ginger, aspartame, blueberries, cinnamon, tarragon, and willow, should be discontinued whenever feasible [10-14]. Fig. 1 illustrates a decision tree which outlines a systematic approach to assess platelet function-affecting factors in patients with hemophilia, guiding clinical management decisions to optimize perioperative outcomes and minimize bleeding risks.

Coagulation tests such as activated partial thromboplastin time (aPTT) and prothrombin time (PT) are routinely performed to assess overall coagulation function. These tests provide valuable information about patients’ coagulation statuses and help guide perioperative hemostatic management decisions [15]. Furthermore, considering the use of viscoelastic tests such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM) can offer real-time assessment of coagulation status during surgery [16,17]. These tests provide dynamic information about clot formation and strength, allowing for timely adjustments in transfusion therapy and other hemostatic interventions as needed. Lastly, multidisciplinary collaboration with hematologists and transfusion medicine specialists is essential [18]. Collaborating with experts in the field allows for the interpretation of coagulation test results and the development of optimal perioperative hemostatic management strategies.

**Hemophilia severity**

In patients with hemophilia undergoing joint replacement surgery, assessing the severity of the condition is crucial for effective perioperative management. This assessment involves several key considerations. First, evaluating factor VIII levels in hemophilia A or factor IX levels in hemophilia B provides essential information about the severity of the coagulation disorder [2]. Based on these levels, anesthesiologists in consultation with hematologists can determine the need for factor replacement therapy to ensure adequate hemostasis during and after surgery [19]. This information also helps determine the best therapy and drug regimens for pa-
Fig. 1. Decision tree for evaluating perioperative drug considerations of patients with hemophilia.
patients, as they may vary based on individual patient characteristics [20]. Patient characteristics that impact factor replacement therapy have been outlined and explained in Table 1. Assessing the factor to be used is also imperative. Switching from standard half-life recombinant factor VIII to extended half-life rFVIII in persons with hemophilia A aged ≥ 12 years reduced annual bleeds and improved quality of life [21]. In patients for whom joint replacement surgery can be postponed, switching to newer drugs may allow for better surgical outcomes. Administration of bolus clotting factor infusion is recommended [22]. This infusion should be supplemented to maintain factor levels at > 80% during the operation. Subsequently, factor levels should be sustained at > 60% within 1–3 days post-surgery and at > 40% for 4–7 days post-surgery. Notably, none of the patients had complications associated with the medication and no reports of thrombosis or inhibitors.

Moreover, understanding the extent of joint damage, particularly in weight-bearing joints like the hips and knees, is paramount, as these are the most often replaced joints in patients with hemophilia and severe arthropathy [23]. Chronic hemophilic arthropathy can lead to severe joint destruction, impacting surgical outcomes and postoperative rehabilitation. Therefore, a comprehensive evaluation of joint integrity and function helps anticipate intraoperative challenges and plan appropriate interventions to optimize postoperative mobility and function [24]. Reviewing each patient’s history of previous bleeding episodes is also critical. Examining the pattern, frequency, and severity of joint bleeds provides interesting insights into the patient’s bleeding phenotype and guides perioperative management strategies [25], allowing healthcare providers to tailor hemostatic therapy and prophylactic measures to minimize the risk of intraoperative and postoperative bleeding complications.

Furthermore, determining the presence of inhibitors for factor replacement therapy is essential. Inhibitors can neutralize the effect of exogenous clotting factors, making hemostasis challenging to achieve [5]. Identifying patients with inhibitors requires specialized testing and necessitates a multidisciplinary approach involving hematologists and transfusion medicine specialists to develop personalized hemostatic management plans [3]. Lastly, collaborating with orthopedic specialists is imperative in assessing joint function and mobility. Orthopedic consultation helps determine the optimal surgical approach and most appropriate implant type for each patient [26]. This collaborative approach ensures that surgical decisions align individual needs and optimize long-term outcomes following joint replacement surgery in patients with hemophilia. It also directly impacts the decisions of anesthetic delivery, pain management systems, and postoperative monitoring.

### Evaluating joint status

Joint status evaluation is a crucial aspect of preoperative assessment in patients with hemophilia undergoing major surgery. Identifying the extent of joint damage and selecting appropriate surgical interventions is critical. Table 1 outlines the influence of patient characteristics on the choice of factor replacement therapy.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Influence on factor replacement therapy</th>
<th>What should be done</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia type</td>
<td>Determines the specific factor deficiency (A or B)</td>
<td>Plasma-derived factor concentrates (Hemophilia A or B)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recombinant factor concentrates (Hemophilia A or B)</td>
</tr>
<tr>
<td>Inhibitor presence</td>
<td>Neutralizes exogenous factor replacement therapy</td>
<td>Bypassing agents (e.g., recombinant factor VIIa, activated prothrombin complex concentrate), Factor VIII or Factor IX concentrates are contraindicated.</td>
</tr>
<tr>
<td>Severity of hemophilia</td>
<td>Determines the dosage and frequency of factor replacement therapy</td>
<td>High-dose factor concentrate or extended half-life products for severe hemophilia. Standard-dose factor concentrate for mild hemophilia should not be given</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>Age-appropriate dosing adjustments</td>
</tr>
<tr>
<td>Weight</td>
<td>Influences dosing calculations and treatment regimens</td>
<td>Weight-based dosing of factor concentrate</td>
</tr>
<tr>
<td>Joint status</td>
<td>Reflects the extent of joint damage and bleeding risk</td>
<td>Preoperative prophylaxis or higher factor levels for patients with severe arthropathy</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>May impact drug metabolism, clearance, or hemostatic function</td>
<td>Careful consideration of drug interactions and potential adverse effects</td>
</tr>
<tr>
<td>Previous bleeding history</td>
<td>Indicates bleeding phenotype and risk of perioperative bleeding</td>
<td>Intensified prophylactic regimen or higher factor levels for patients with frequent or severe bleeds</td>
</tr>
</tbody>
</table>

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**Table 1. Influence of Patient Characteristics on Choice of Factor Replacement Therapy**

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surgery, particularly joint replacement procedures. This evaluation involves a comprehensive examination of various factors to ensure optimal surgical outcomes and postoperative recovery [24]. Joint functionality assessment encompasses evaluating the range of motion, stability, and presence of deformities in the affected joints. In their study, Ferreira et al. [27] noted that while mild hemophilia was not associated with significant joint involvement, joint status worsened in patients with moderate and severe cases of hemophilia and with age. They further recommended using the World Federation of Hemophilia Physical Examination Scale and Functional Independence Score in Hemophilia to clinically assess structural joint damage and functional deficits in patients with hemophilia [28,29]. These techniques are inexpensive, simple, and quick for anesthesiologists to use in preoperative evaluations. Particularly in severe cases, in which joint status is significantly compromised, special attention is warranted to prevent excessive intraoperative bleeding and subsequent joint damage.

Radiographic imaging, including X-rays or magnetic resonance imaging (MRI), plays a pivotal role in evaluating joint integrity, degree of arthropathy, and bone quality. Understanding imaging techniques is essential for anesthesiologists to critically interpret findings and guide appropriate decision making [30-38]. Furthermore, evaluating joint stability, including assessing ligamentous laxity and joint stability, helps determine the need for additional surgical procedures, such as ligament repair or reconstruction, in conjunction with joint replacement. Similarly, Jiménez-Yuste et al. [39] noted that postoperative rehabilitation itself carries an increased bleeding risk for which adequate hemostatic coverage must be scheduled.

**Bleeding history**

When reviewing the bleeding history of a patient with hemophilia, comprehensive documentation of various aspects is imperative to inform perioperative management decisions. Assessing the frequency, duration, and severity of previous joint bleeds provides valuable insights into the patient’s bleeding phenotype and helps estimate the risk of intraoperative and postoperative bleeding complications. Soucie et al. [15] noted that the mean number of joint bleeds per month over a 6 month period was higher in patients with hemophilia A than those in patients with hemophilia B. Understanding the pattern of previous bleeds allows healthcare providers to anticipate potential challenges during surgery and implement appropriate preventive measures. Spontaneous bleeding occurrences are rare in individuals with mild hemophilia [40,41]. Typically, hemophilia diagnosis is incidental or identified during routine preoperative laboratory assessments. In cases of moderate hemophilia, where factor activity levels range from 1% to 5% of normal, bleeding episodes commonly manifest following trauma, injury, dental procedures, or surgical interventions. However, patients with severe hemophilia are often candidates for joint replacement surgeries, in which spontaneous bleeding has a higher risk [42].

Identifying the specific joints affected by previous bleeding episodes is also important. By pinpointing the sites of previous bleeds, healthcare providers can anticipate intraoperative challenges and implement measures to minimize bleeding risk, such as optimizing hemostasis and using joint-sparing surgical approaches whenever feasible [43]. Furthermore, evaluating patient responses to previous hemostatic therapy, including factor replacement therapy and adjunctive medications, is crucial for guiding perioperative management decisions [44]. Understanding different patient responses to various treatment modalities helps tailor hemostatic regimens to optimize hemostasis during surgery and prevent postoperative bleeding complications. History of previous surgeries, particularly major surgeries and orthopedic surgeries, and evaluating old intraoperative notes wherever feasible are extremely important for anesthesiologists during preoperative planning to ensure appropriate hemostasis and risk mitigation [45].

Finally, patient education plays a vital role in perioperative management. Educating patients and caregivers about the importance of adherence to prophylactic hemostatic therapy and early recognition of signs of bleeding complications during the perioperative period is crucial for optimizing patient safety and outcomes [46]. Thornburg and Duncan [47] emphasize that regular education is a key strategy for enhancing adherence in hemophilia treatment, as belief in the necessity of treatment serves as a significant motivator for adherence. Empowering patients with knowledge and skills to recognize and respond to potential bleeding events enhances their abilities to actively participate in their care and contributes to improved perioperative outcomes. Pitance et al. [48] noted that when switching from a standard to an extended half-life FVIII, adherence increased, and age was the most significant factor impacting adherence. These characteristics should be considered as risk factors for non-adherence by anesthesiologists, and more attention should be giv-
en in educating these patients.

**Factor replacement**

Factor levels are closely monitored during and after surgery and are accordingly replaced [49]. Table 2 provides a detailed overview of the desired preoperative and postoperative levels of clotting factor concentrates (measured in international units per deciliter [IU/dL]) for patients with hemophilia undergoing major and minor surgeries. Table 2 also accounts for resource constraint settings wherein factors such as availability and affordability play a big role in the decision making process.

**Medication adjustment**

About half of patients undergoing surgery take regular medications. A complete medication history, including the drugs used, dosages, and regimens, should be obtained and reviewed by all clinicians involved in patient care. Over-the-counter drugs, herbal medications, and complementary medications should also be noted. Substance use information, including the use of alcohol, nicotine, and illicit drugs, must also be reported [50].

Medications that are known to cause medical morbidity if discontinued abruptly must be continued in the perioperative period. Oral drugs should be avoided owing to impairment of gastrointestinal absorption with restrictions in oral intake. Instead, intravenous, transdermal, or transmucosal medicines can be used. Medications thought to increase the risk of anesthetic or surgical complications and that are not essential for the short-term should be discontinued during the perioperative period [51].

**Cardiovascular drugs:**

Beta-blockers, alpha-2-agonists, calcium channel blockers, and digoxin are a few cardiovascular drugs that may be continued during the perioperative period. Angiotensin convertase enzyme inhibitors are avoided by anesthesiologists owing to the risk of perioperative hypotension [52].

**Pulmonary drugs:**

Beta agonists, anticholinergics, and glucocorticoids may be continued during the perioperative period. Leukotrienes should be avoided owing to the risk of arrhythmias [53].

**Endocrine drugs:**

Oral contraceptive pills and selective estrogen receptor modulators should be discontinued before surgery owing to their risk of venous thromboembolism, which may increase perioperative complications in patients with hemophilia [54].

**Non-steroidal anti-inflammatory agents:**

Non-steroidal anti-inflammatory agents should be discontinued ≥ 72 h prior to surgery, and ibuprofen should be discontinued 24 h before surgery owing to their inhibitory effects on platelet aggregation [55].

The use of most other medications depends on clinician judgment.

### INTRAOPERATIVE EVALUATION

**Antibiotic consideration**

Antibiotic choice depends on the susceptibility of colonizing microorganisms. Often, the prophylactic antibiotics used in patients with and without hemophilia are the same, with cephalosporins being the most commonly used antibiotic of choice and cefazolin and cefuroxime being the most commonly used cephalosporins. Clindamycin or vancomycin are used in cases of patients allergic to cephalosporins [56].

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Duration (d)</th>
<th>Desired levels (no significant resource constraint)-IU/dL</th>
<th>Desired levels (with significant resource constraint)-IU/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major preoperative</td>
<td>-</td>
<td>80–100</td>
<td>60–80</td>
</tr>
<tr>
<td>Major postoperative</td>
<td>1–3</td>
<td>60–80</td>
<td>40–60</td>
</tr>
<tr>
<td></td>
<td>4–6</td>
<td>40–60</td>
<td>20–30</td>
</tr>
<tr>
<td></td>
<td>7–14</td>
<td>30–40</td>
<td>10–20</td>
</tr>
<tr>
<td>Minor preoperative</td>
<td>-</td>
<td>50–80</td>
<td>40–80</td>
</tr>
<tr>
<td>Minor postoperative</td>
<td>1–5*</td>
<td>30–80</td>
<td>20–50</td>
</tr>
</tbody>
</table>

Surgical procedures may be classified as major or minor. A major surgical procedure is defined as one that requires hemostatic support for > 5 consecutive days. *Depends on the type of procedure.
Anesthetic considerations

Various anesthetic combinations have been utilized in arthroplasty, encompassing general anesthesia, neuraxial anesthesia (epidural/spinal), peripheral nerve block (PNB), and periarticular injections. General anesthesia is the most commonly employed method. However, it is associated with a higher incidence of postoperative nausea, vomiting, and other complications, which are not observed with neuraxial anesthesia [56]. Compared with general anesthesia, neuraxial anesthesia has shown a lower risk of complications, except for urinary retention [57].

Neuraxial anesthesia, in particular, provides targeted analgesia to the surgical site while sparing systemic opioid use, thereby reducing the risk of opioid-related side effects. However, Peterson et al. [58] noted significant gaps in our knowledge regarding risk factors for neuraxial anesthesia in patients with hemorrhagic disorders and tendencies. No evidence has established thresholds or a consensus on laboratory values in patients with hemorrhagic disorders who may be at true risk for complications. A recent study by Peterson et al. [58] also suggested that although neuraxial anesthesia may be used, general anesthesia should be favored in prolonged surgeries.

Another study illustrated a case of successful ultrasound-guided spinal anesthesia in a patient with severe hemophilia, which depended on extensive planning and evaluation [59]. However, they ultimately recommended neuraxial anesthesia over general anesthesia only for cases in which general anesthesia may be contraindicated. However, they agree that hemophilia is not an absolute contraindication for neuraxial anesthesia. It can be considered in appropriate cases following informed discussions between the patient and care team, taking into account risks, benefits, patient preference, and comfort level of the anesthesiologist [60].

Regional anesthesia has been shown to decrease pain, nausea, and vomiting; reduce the time to discharge; and lower cardiovascular and pulmonary complications [61]. A study revealed that during the first 72 h after surgery, PNB in combination with intravenous patient controlled analgesia (PCA) resulted in less pain, lower opioid consumption, and a decreased risk of nausea and vomiting, compared with PCA alone. However, this method did not demonstrate a significant advantage in pain relief, compared with neuraxial anesthesia [61]. PNBs used in knee arthroplasty include femoral nerve block (FNB) or adductor canal block (ACB).

Studies have indicated that ACBs are equivalent to FNBs in terms of pain control, quadriceps strength, and incidence of nausea and vomiting [62]. However, a meta-analysis by Li et al. [63] demonstrated that ACBs improved Visual Analogue Scale pain scores at rest, 8 h, and 24 h postoperatively, compared with FNB, resulting in better ambulation and faster recovery after surgery. ACB, being a more selective sensory block, is preferred over FNB for total knee arthroplasty [63].

Periarticular anesthesia has been shown to lower pain scores, opioid consumption, and postoperative nausea and vomiting, while also increasing range of motion at 24 h postoperatively. Ketorolac is a key component of periarticular infiltration mixtures [64]. In another recent study, a mixture of ropivacaine, epinephrine, ketorolac, and morphine injection was compared with FNB and sciatic nerve block with 0.5% ropivacaine. No significant difference in pain scores was observed between the groups. Therefore, periarticular infiltration or FNB can be used depending on available resources [65,66].

Orthopedic considerations

The orthopedic considerations of patients with hemophilia are similar to those of patients without hemophilia. However, a few points must be kept in mind:

Preoperative examination of all the joints is essential in patients with hemophilia, as the involvement of multiple joints alters the surgical plan.

Intra-articular tranexamic acid is shown to reduce blood loss [67].

A tourniquet is used during the procedure to control hemostasis. The tourniquet is deflated prior to implantation of the components to ensure a full view of the joints; it is reinflated after the components have been cemented together [68].

The surgical approach varies among different joints. Cementless total hip arthroplasty can also be performed using a Mallory-Head acetabular shell (Biomet Inc.) and a Bi-Metric™ femoral stem. The 33 kGy Ɣ-irradiated conventional high molecular weight polyethylene is coupled with a 28 mm cobalt chromium alloy. For a knee replacement surgery, Duracon and Scorpio NRG have been used with a 30 kGy Ɣ-irradiated conventional ultrahigh molecular-weight polyethylene with cobalt chrome femoral components [66]. A mixture of cement and antibiotics are used in the procedure. Following implantation, the joint is irrigated, and a drain is kept in place for 1–2 days. Nonabsorbable sutures are used.
for the joint capsule, and staples are used for the skin [69].

Ankle arthropathy is managed using various methods. Arthroscopic ankle debridement can provide temporary relief, but surgical procedures are not very common in hemophilic arthropathy of the ankle. This is because effective conservative therapies such as radiosynovectomy and patellar tendon-bearing orthosis are available. If conservative alternatives prove unsuccessful, several surgical options may be considered. Tibiotalar fusion is the most commonly used technique for advanced hemophilic arthropathy. Arthroscopic ankle debridement is indicated in young patients with hemophilia and may alleviate pain intensity for many years. However, if articular destruction is limited, ankle radiosynovectomy or arthroscopic ankle debridement may be alternatively advised. Total ankle replacement should be considered only for patients experiencing intense pain that is unresponsive to less invasive surgical alternatives [70].

**Hemostatic considerations**

Surgery in patients with hemophilia must be performed at or in consultation with a comprehensive hemophilia treatment center. Surgery must be scheduled during the early hours of the day and week to ensure the availability of blood bank support throughout the procedure. Maintaining adequate hemostasis is essential in these patients. The definition of adequate hemostasis for surgical procedures is outlined in the table below. Adequate quantities of clotting factor concentrates (CFC) or bypassing agents must be available to adequate hemostasis, and 1-desamino-8-d-arginine vasopressin (DDAVP) is a commonly used hemostatic agent. However, patients using DDAVP may experience side effects such as water retention, hyponatremia, and tachyphylaxis. Therefore, DDAVP and factor VIII concentrate are administered together to mitigate these drawbacks. DDAVP may also be used with antifibrinolytic agents when CFCs are not available, and the most commonly used antifibrinolytic agent is tranexamic acid. The World Federation of Hemophilia recommends against the use of prothrombin complex concentrate (PCC) owing to the risk of accumulation of clotting factors II, VII, and X, which can increase thrombotic complications [49]. Table 3 outlines the key considerations regarding hemostatic levels during surgical procedures, as outlined by the aforementioned World Federation of Hemophilia.

As intraoperative bleeding is highly undesirable, surgeons take various preventative steps. Some of these measures include normovolemic hemodilution, hypotensive anesthesia, tourniquets, intramedullary femoral plugs, and computer-assisted surgeries. Preoperative arterial embolization also helps control intraoperative bleeding and is typically performed two weeks before the surgery [71].

<table>
<thead>
<tr>
<th>Assessment category</th>
<th>Details</th>
</tr>
</thead>
</table>
| Excellent           | Intraoperative and postoperative blood loss similar (up to 10%) to that in patients without hemophilia  
  • No extra (unplanned) doses of FVIII/FIX/bypassing agents needed and  
  • Required blood component transfusions similar to those in patients without hemophilia |
| Good                | Intraoperative and/or postoperative blood loss slightly increased beyond the expectation (10–25%) for patients without hemophilia, but the difference is judged by the involved surgeon/anesthesiologist to be clinically insignificant  
  • No extra (unplanned) doses of FVIII/FIX/bypassing agents needed and  
  • Required blood component transfusions similar to those in patients without hemophilia |
| Fair                | Intraoperative and/or postoperative blood loss increased beyond the expectation (25–50%) for patients without hemophilia, and additional treatment is needed  
  • Extra (unplanned) dose of FVIII/FIX/bypassing agents needed or  
  • Increased blood component (within 2-fold) of the anticipated transfusion requirement |
| Poor/none           | Significant intraoperative and/or postoperative blood loss substantially increased beyond the expectation (> 50%) for patients without hemophilia, requiring intervention, and unexplained by a surgical/medical issue other than hemophilia  
  • Unexpected hypotension or unexpected transfer to ICU owing to bleeding or  
  • Substantially increased blood component (> 2-fold) of the anticipated transfusion requirement |

FVIII: factor VIII, FIX: factor IX, ICU: intensive care unit.
POSTOPERATIVE ASSESSMENT

Postoperative pain management

Pain management is a critical aspect of perioperative care in patients undergoing joint replacement surgery, particularly in those with hemophilia. Effective pain control not only improves patient comfort and satisfaction but also facilitates early mobilization and rehabilitation, ultimately contributing to better surgical outcomes [72]. In the context of hemophilia, special considerations must be taken into account owing to the increased risk of bleeding complications associated with certain analgesic modalities. Multimodal analgesia, which involves the use of multiple analgesic agents with different mechanisms of action, is commonly employed to manage postoperative pain while minimizing opioid use [73]. This approach allows for synergistic pain relief while reducing the individual doses of each medication, thereby mitigating the risk of opioid-related adverse effects such as respiratory depression, sedation, and ileus [74]. Moreover, multimodal analgesia has been shown to improve pain control and patient satisfaction following joint replacement surgery [75]. In selecting analgesic modalities for patients with hemophilia, the severity of hemophilia and the patient’s bleeding risk must be carefully considered [76]. While opioids remain an essential component of the analgesic regimen, their use should be titrated cautiously to avoid excessive sedation and respiratory depression [77]. Nonsteroidal anti-inflammatory drugs (NSAIDs), notably aspirin, are recognized for their ability to decrease blood clotting, thus elevating the risk of bleeding in individuals with bleeding disorders such as hemophilia. Consequently, their use should be limited, and alternative medications with proven safety in individuals with hemophilia should be explored. Specifically in cases of hemophilic arthropathy, managing pain becomes challenging owing to the impracticality of NSAID use. Cyclooxygenase-2 (COX-2) selective NSAIDs, offering comparable analgesic efficacy to traditional NSAIDs but with reduced upper gastrointestinal bleeding risk, emerge as a promising option for hemophilic arthropathy treatment. Nonetheless, COX-2 inhibitors come with an elevated risk of cardiovascular disease [78]. Regional anesthesia techniques, such as epidural analgesia and PNBs, offer effective pain relief with minimal systemic opioid requirements and are therefore favored in patients with hemophilia [62].

Postoperative hemostasis

Continued postoperative hemostatic therapy is crucial for patients with hemophilia undergoing joint replacement surgery to prevent bleeding complications and optimize surgical outcomes. The decision to continue hemostatic therapy is based on patients’ hemophilia severity, extent of surgical bleeding risk, and individualized assessment by a multidisciplinary care team. In their study, Kleiboer et al. [79] stated that total hip arthroplasty involved a higher risk of bleeding than total knee arthroplasty among patients with hemophilia. As the hip joint typically has a richer and more intricate blood supply than the knee joint, increased vascularity and complexity in the hip region may result in higher bleeding tendencies during surgical procedures such as arthroplasty. Studies have also demonstrated that 30% of patients with hemophilia experienced major bleeding following hip or knee arthroplasty, with bleeding risk being influenced by inhibitor status, body mass index, and use of antifibrinolytics [79]. However, no patients suffered bleeding into critical sites or fatal bleeding. Postoperative bleeding into the surgical joint space was observed in a few cases, predominantly after total knee arthroplasty, requiring one patient to return to the operating room for resolution. Half of the patients with active inhibitors experienced major bleeding, highlighting inhibitors as a significant risk factor. Patients who did not receive thromboprophylaxis, specifically low molecular weight heparin, experienced more severe bleeding than those who received thromboprophylaxis. The study concluded that factors independently associated with increased odds of major bleeding included undergoing total hip arthroplasty, having an active inhibitor at the time of surgery, being overweight or obese, and not using antifibrinolytic medication perioperatively.

Patients with severe hemophilia or those undergoing extensive surgical procedures may require prolonged hemostatic therapy to maintain adequate factor levels and prevent postoperative bleeding [80]. Conversely, patients with mild or moderate hemophilia undergoing less invasive procedures may have lower bleeding risks and may not require continued hemostatic therapy beyond the immediate postoperative period. Pathak et al. [81] recommended that consideration should be given to knee compression and an initial period of immobilization lasting 5–7 days to mitigate the risk of postoperative hemarthrosis. Additionally, in low-risk patients, surgeons may opt to refrain from venous thromboembolism chemoprophylaxis. Table 4 discusses potential
drugs that can be used for hemostasis in hemophiliacs.

**Joint mobilization and rehabilitation**

In the postoperative phase of joint replacement surgery for patients with hemophilia, early mobilization and rehabilitation play crucial roles in promoting optimal outcomes. Implementing early mobilization protocols is essential to prevent joint stiffness and muscle atrophy, which can occur after prolonged immobilization [82]. By encouraging patients to start moving their joints soon after surgery, joint mobility can be maintained or improved, reducing the risk of complications such as contractures [83]. Moreover, tailored rehabilitation strategies are necessary to address both the requirements of joint replacement surgery and the unique considerations associated with hemophilia. Stephensen [84] reports a case of beneficial physiotherapy after total knee replacement in which 6 weeks of preoperative and 6 weeks of postoperative physiotherapy enabled rapid mobilization and recovery of function while minimizing the risk of bleeding. Lobet et al. [85] assert that advancements in postoperative management following total knee arthroplasty contribute to its status as the preferred treatment for end-stage hemophilic arthropathy. However, the utilization of rehabilitation services remains one of the least explored aspects of knee arthroplasty in this population. Most studies advocate for the initiation of postoperative rehabilitation early during the hospitalization period. Rodriguez-Merchant [86] initiated intensive rehabilitation on the third postoperative day, with sessions conducted twice daily throughout the hospital stay. Upon discharge, the rehabilitation regimen continued for 6–8 weeks, five days per week. De Kleijn et al. [44] published guidelines in 2011 for multiple joint procedures in individuals with hemophilia. Mortazavi et al. [87] implemented rehabilitation immediately following surgery, with patients initiating walking and knee range of motion exercises on the same day. The effectiveness of Continuous Passive Motion machines following total knee arthroplasty in patients with hemophilia remains uncertain. Rehabilitation programs should focus on strengthening muscles around the replaced joint, improving range of motion, and enhancing overall functional capacity. However, clinicians must proceed with caution and consider the potential risk of bleeding complications associated with vigorous

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**Table 4. Pharmacological Management of Hemophilia**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Indication</th>
<th>Contraindication</th>
<th>Potential drug interactions</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII concentrate</td>
<td>Treatment of hemophilia A</td>
<td>Hypersensitivity to factor VIII</td>
<td>Antifibrinolytic agents may increase risk of thrombosis</td>
<td>Hypersensitivity reactions (e.g., rash, itching, anaphylaxis)</td>
</tr>
<tr>
<td>Factor IX concentrate</td>
<td>Treatment of hemophilia B</td>
<td>Hypersensitivity to factor IX</td>
<td>Anticoagulants may increase risk of bleeding</td>
<td>Hyponatremia; Fluid retention; Hyponatremia; Flushing</td>
</tr>
<tr>
<td>Desmopressin</td>
<td>Release of von Willebrand factor from endothelial cells; Used in hemophilia A patients with mild to moderate deficiency</td>
<td>Hyponatemia; Cardiovascular disease; Thrombosis</td>
<td>NSAIDs may decrease effectiveness of desmopressin</td>
<td></td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>Adjunctive therapy for bleeding control during surgery</td>
<td>Hypersensitivity to tranexamic acid; Subarachnoid hemorrhage</td>
<td>Antifibrinolytic agents may increase risk of thrombosis</td>
<td>Nausea; Vomiting; Diarrhea; Headache</td>
</tr>
<tr>
<td>Recombinant factor VIIIa</td>
<td>Treatment of bleeding episodes in hemophilia A or B patients with inhibitors</td>
<td>Thromboembolic events; Arterial thrombosis; Myocardial infarction</td>
<td>Anticoagulants may increase risk of bleeding</td>
<td>Thrombosis; Hypotension; Headache</td>
</tr>
<tr>
<td>Antifibrinolytic agents</td>
<td>Adjunctive therapy for bleeding control during surgery</td>
<td>Hypersensitivity to antifibrinolytic agents</td>
<td>Desmopressin may increase risk of hyponatremia</td>
<td>Gastrointestinal upset; Muscle cramps</td>
</tr>
<tr>
<td>Aminocaproic acid</td>
<td>Adjunctive therapy for bleeding control during surgery</td>
<td>Hypersensitivity to aminocaproic acid</td>
<td>Anticoagulants may increase risk of bleeding</td>
<td>Hyponatemia; Nausea; Diarrhea</td>
</tr>
<tr>
<td>Prothrombin complex concentrate</td>
<td>Treatment of bleeding episodes in patients with factor II, VII, IX, or X deficiency</td>
<td>Hypersensitivity to prothrombin complex concentrate</td>
<td>Anticoagulants may increase risk of bleeding</td>
<td>Thromboembolic events; Hypotension; Allergic reactions</td>
</tr>
</tbody>
</table>
physical activity [88]. Therefore, rehabilitation protocols should be customized based on individual patient characteristics, including hemophilia severity, bleeding history, and joint status.

Complications

Periprosthetic joint infection is one of the most severe complications of arthroplasty and is prevented through various approaches. Owing to its antimicrobial properties, silver coated prosthetics are a promising solution; however, their toxic effects on eukaryotic cells must also be considered [89]. Hydrofiber dressing has been shown to reduce risk of infection and is also economical [90]. Prevention of periprosthetic joint infection is crucial for good surgical prognosis, and the microorganisms causing the infection must be known to choose the correct antibiotic. Cefazolin and cefuroxime are the most commonly used antibiotics. Although antibiotic-infused cement and dressing powder are used, further research is currently being conducted to assess their effectiveness [91].

Recurrent hemarthrosis is an additional rare complication of arthroplasty. One study presented the case of a woman with hemophilia who developed recurrent hemorrhaxis 9 days after arthroplasty [92]. This condition did not resolve, and a pseudoaneurysm of the left superior geniculate artery additionally developed. Popliteal artery aneurysms have also been reported in postoperative cases of hemophilic arthroplasty. These patients present with increased pain and restricted movement in the knee joint during the first/second postoperative weeks. Owing to the increased frequency of this complication, preoperative angiography is recommended [93].

Postoperative endoprosthetic instability is also a complication of arthroplasty and can be prevented by using osteodensitometry, which facilitates the monitoring of bone mineral density around the prosthesis [94]. In a study presenting a case of intraoperative femoral fracture effectively treated with cerclage cables, a patient achieved bone union at 3 months postoperatively [95]. Hematoma formation is also a common complication associated with a high rate of unsatisfactory results when accompanied by positive cultures of microorganisms; these may include Propionibacterium acnes, Staphylococcus epidermidis, and Peptostreptococcus [96].

FUTURE DIRECTIONS

Despite significant advancements in the management of hemophilic arthropathy and joint replacement surgery, knowledge gaps persist, urging a focus on comprehensive studies to enhance understanding and optimize clinical outcomes. Long-term outcomes of surgical procedures such as tibial talar fusion and total ankle replacement require investigation through longitudinal studies assessing pain relief, joint function, and implant durability. Optimization of hemostatic strategies, including comparative studies on different agents and dosing regimens, is essential to minimize bleeding complications. Research on postoperative pain management should evaluate various analgesic modalities and techniques while considering individual patient needs. Preventing and managing complications such as periprosthetic joint infection demands prospective studies to inform evidence-based practice. Emphasizing patient-centered outcomes and incorporating patient-reported measures into research protocols ensures that interventions align with patient preferences. Lastly, assessment of health economics and resource utilization implications is crucial for healthcare policy and resource allocation decisions, promoting equitable access to surgical care for individuals with hemophilia.

CONCLUSION

In conclusion, managing hemophilia in patients undergoing joint replacement surgery requires a comprehensive approach integrating preoperative evaluation, meticulous intraoperative care, and tailored postoperative management. Preoperative assessment of joint integrity, bleeding history, and inhibitor presence guides surgical planning and hemostatic therapy selection, optimizing outcomes. Intraoperatively, attention to factor replacement, antibiotic prophylaxis, anesthetic techniques, and orthopedic strategies minimizes bleeding risk and enhances surgical success. Postoperatively, effective pain management, continued hemostatic therapy, and individualized rehabilitation programs are vital for facilitating recovery and preventing complications. A collaborative approach involving hematologists, orthopedic surgeons, anesthesiologists, and rehabilitation specialists ensures comprehensive care tailored to the unique needs of patients with hemophilia undergoing joint replacement surgery, ultimately optimizing outcomes and improving quality of life.
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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

22. Whitton TP, Healy WJ. Clinical use and interpretation of throm-
boelastography. ATS Sch 2023; 4: 96-7.


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Transfus 2018; 16: 535-44.