CURRENT CONCEPTS REVIEW

Total Hip Arthroplasty in Patients with Hemophilia: What Do We know?

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Abstract

Total hip arthroplasty (THA) is the mainstay therapy for terminally hemophilic arthropathy patients. Hemophilic patients have distinguishing characteristics, including the increased likelihood of bleeding, younger age, restricted pre-operative joint motion, disrupted anatomy, and more post-operative side effects. The present study aimed to assess the THA sequels in hemophilic patients from various perspectives, including indications, challenges, factor replacement post-operative outcomes, and other complications.

Level of evidence: V

Keywords: Hemophilia, Hemophilic arthropathy, Total hip arthroplasty

Introduction

Hemophilia is a hemorrhagic disorder caused by clotting factors deficiency or dysfunction, either factors VIII or IX, characterized by a defect in clot formation and spontaneous bleeding into the joints.[1,2] Repeated intra-articular hemorrhaging in this crucial morbidity caused severe problems in patients' daily activities due to the joint damage known as hemophilic arthropathy.[3] Therefore, the affected haemophilia patients may need joint arthroplasty potentially at a younger age. This joint destruction can affect other structures, such as the capsule, synovial tissue, ligament, and tendon, leading to joint deformity, joint pain, function abnormity, soft tissue hematoma, and capsular fibrosis.[4]

Although arthropathy of the hip is less common than other joints (e.g., knee, elbow, or ankle) in people with hemophilia, this induces more functional impairments due to tribulation and loss of movement.[5,6] In this arthropathy, satisfactory clinical results following arthroplasty were discussed.

However, some post-operative complications, such as aseptic loosening, infection, and arthrofibrosis were also mentioned during the disease period.[7] In this regard, the present study was designed as a review of the related literature on THA and its consequences among hemophilia patients [Figure 1].

Indications for total hip arthroplasty in hemophilia patients

The hip is the main weight-bearing joint of the lower limb. Due to the congruent nature of the hip joint concerning other joints, conservative treatments have only temporary influence and thus seem to be less effective than interventional approaches. However, scheduling surgical approaches in moderate to severe grades in hip arthropathy is preferred for obtaining proper long-term outcomes. On the other hand, the hip joint is influenced by hemorrhage due to hemophilia because of the lack of synovial tissue and the lower chance for injury.[8-10]

Hemophilic hip arthropathy indications for THA are debilitating pain and useless joint; however, such arthropathy remains unresponsive to conservative therapies.[2,11] In this regard, the association of wide arthrofibrosis, flexion contractures, and deformities with poor bone quality in hemophilic arthropathy makes THA a complicated surgery.[12,13]

The main contraindication of joint replacement in such patients is an active infection. Other contraindications are local skin problems and comorbidities, such as HIV or liver diseases, that would affect post-operative outcomes.[14-16]

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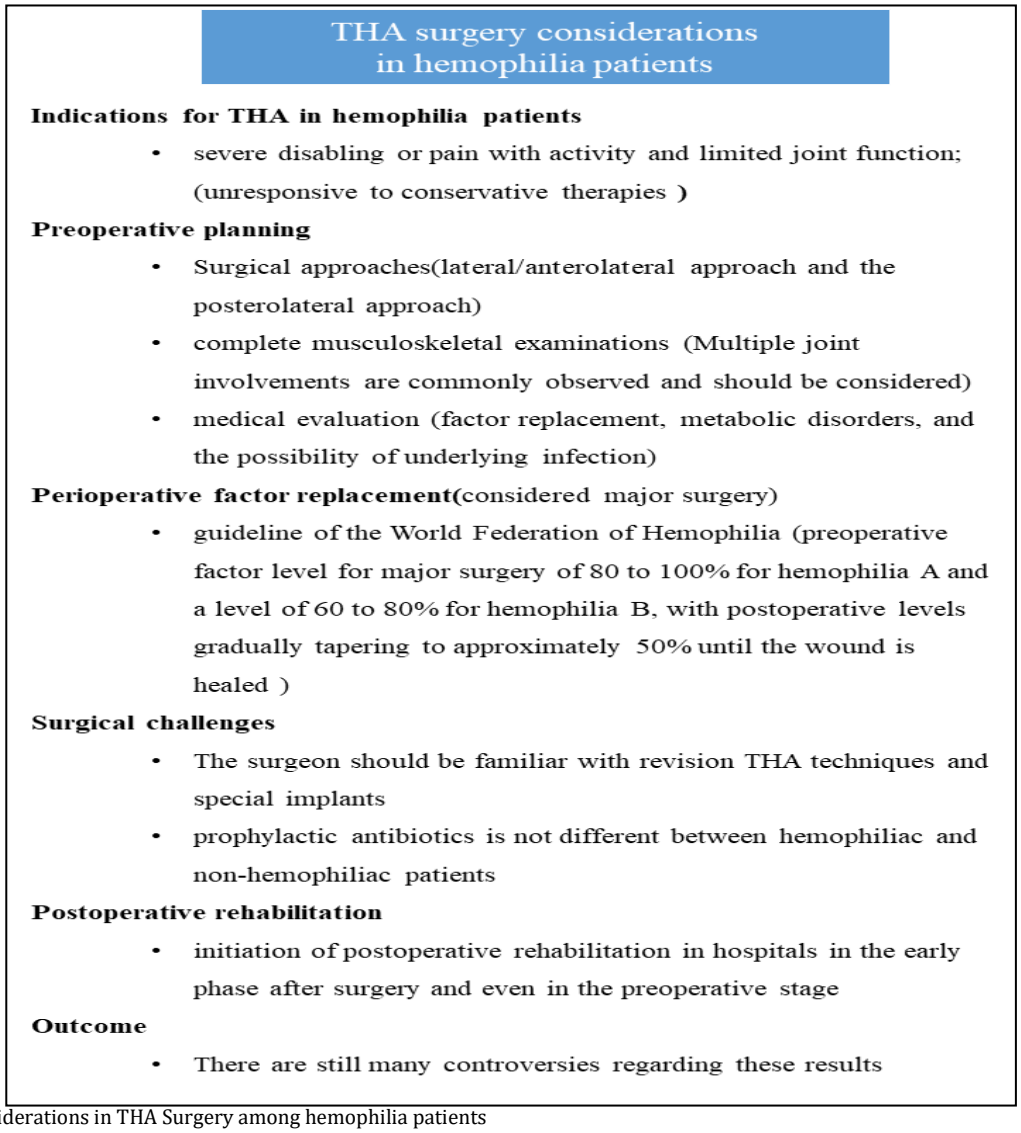

Figure 1. Considerations in THA Surgery among hemophilia patients

Overall, pain is the most common indication of THA. In hemophilic hip arthropathy, there is a limited joint range of motion; thus, walking is limited due to pain. The stage of the disease plays a significant role in hip arthropathy treatment. Patient's quality of life, symptoms severity, previous medical interventions, and accessible resources are other important factors influencing the treatment.[1] In hemophilia patients, radiographic findings are far worse than physical examinations, and therefore, medical doctors should be aware that they do not base their treatment on radiological evidence.[17] Despite the favorable results, surgeons should note that THA in relatively young patients holds the risk of cup and stem loosening and late infections in immunocompromised patients.[18] Based on previous studies; there are no definitive indications for THA in hemophilia patients. It seems that hip arthroplasty is usual in patients that did not respond to non-operative treatments.[1, 17]

Pre-operative planning

Aiming to increase the level of satisfaction with the outcome of the operation, precise care was provided by medical experts (e.g., orthopedic/hemophilia treatment center team) consisting of the nurse, social worker, and physical therapist. Despite such measures, the post-operative complication rate has been significantly higher in hemophilic patients.[19-21]

Total hip arthroplasty in hemophilic patients could be performed by two surgical approaches: the lateral/anterolateral approach or the posterolateral approach, which is based on the surgeon's preference. It is well-known that the lateral approach is easier and has a lower risk of instability than the posterolateral approach. On the other hand, the posterolateral approach is more conservative and has no muscular impairment. Limping may occur in lateral approach due to abductor muscle

harm.[22, 23]

Similar to other diseases, complete musculoskeletal examinations should be done as pre-operative assessments in these candidates. Multiple joint involvements are commonly observed and should be considered to have the correct planning.[22] Before executing any procedure on a hemophilia patient, a comprehensive assessment must be performed about the perioperative factor replacement, metabolic disorder, and the possibility of underlying infection.[23, 24]

Factor replacement before surgery

Factor substitution for THA in these patients acts as a serious pattern in preventing hematoma, hemarthrosis, and other side effects. The argument on the description of major or minor surgeries in hemophilia is ongoing. Overall, THA is considered a major surgery.[25] Prophylaxis can slow the natural course of hemophilic arthropathy. However, due to high costs, prophylaxis is not possible for all of them. Some researchers offer a level of 120% for factors VIII and IX for induction of anesthesia, an extra 40% after 4 h in the surgery room, a level of 60-80% for 72 h after surgery, 50% for 2 weeks, 30-40% for one month, and 40% before each physical therapy session up to 6 weeks after surgery.[26] The World Federation of Hemophilia guideline suggests 80 to 100% for hemophilia A and a level of 60 to 80% for hemophilia B factor level before major surgeries and tapering it to approximately 50% for wound healing (over two weeks). For major surgeries, this guideline also recommended separating the factor level based on the level of feasibility of resources.[1] The factors have different half-lives; factors VIII and IX standard types have half-lives of 8-12 and 18-24 h, and factor replacement could be done in two ways. 1) the starting dosage (patient's weight (in kg) multiplied by the considered increase level for factor VIII (as a whole, such that the desired level of 100 percent is entered as 100) multiplied by the volume of injection (for factors VIII and IX, this equals 0.5 and 1, respectively)) and subsequent doses are given at intervals of one half-life of the injected product for that patient, which is described below. These further doses are usually half of the initial dose and are infused at almost one half-life of the product. The required dose is considered based on the current and the desired level of the factor. 2) First dose (calculated similarly to the previous option) followed by ongoing injection of 4 IU/kg/h and 6 IU/kg/h for factors VIII and IX. Although in the second option, the monitoring of factor level is required less frequently, factor activity levels should be checked periodically, with the interval determined by the previous level, dose adjustments, and clinical bleeding. Factor half-life and hemostasis could be affected by the variation of individual pharmacokinetics; therefore, monitoring is important to determine the subsequent doses in both methods.[27-29]

In the presence of inhibitors (neutralizing alloantibody against infused factor), factor injection is challenging, as inhibitors make the factors useless.[28] It is essential to recognize inhibitors in pre-operative assessments. A bypassing product is the choice for a patient with a titer > 5 Bethesda unit with a high responding inhibitor and needs for a major surgery like total knee arthroplasty. These products include recombinant activated factor VII (rFVIIa) and activated prothrombin complex concentrates (aPCCs), such as factor eight inhibitor bypassing agent (FEIBA) contains an activated form of a downstream clotting factor in the coagulation cascade. For patients with a positive inhibitor of hemophilia A, both of these products could be selected; however, for hemophilia B, rFVIIa is the preferred agent because it does not contain factor IX when some people with hemophilia B with an inhibitor may have the experience of reaction upon exposure to factor IX. Both of these bypassing factors are prothrombotic; therefore, prudence about venous thromboembolism (VTE) occurrence should be taken, especially about aPCCs (FEIBA).[30] When rFVIIa is injected 90 to 120 mcg/kg every 2-3 h until hemostasis is attained and then at 3 to 6 h intervals after hemostasis has been restored, FEIBA is given 50 to 100 units/kg every 6 to 12 h, not to exceed 100 units/kg/dose or 200 units/kg/day. The dosing is adjusted by the clinical response instead of laboratory testing. This protocol continues for minimum of 48 to 72 h for major surgeries and is followed by a taper gradually increasing dosing interval. Other options may be considered when the bleeding cannot be stopped by one of these factors. Another treatment option for inhibitor-positive hemophilic patients (>5 Bethesda unit) with life-threatening bleeding is plasmapheresis.[29, 31]

Challenges in surgery

Total hip arthroplasty in hemophilic patients is complicated due to deformed anatomy, malformations, osteopenia, contractures in soft tissue, and atrophia in muscles. Consequently, familiarity with revision THA techniques and special implants is obligatory for surgeons.[15-19] Before surgery, a complete examination of knee, hip, and ankle should be done because multiple joints involve in this disorder may change the surgical planning. To investigate deformity and bone loss, pre-operative radiographic assessment should be done.

The use of prophylactic antibiotics is similar between hemophiliac and non-hemophiliac patients that should be started pre-operatively with the administration half an hour before the operation. The antibiotic of choice is the first-generation cephalosporin; however, vancomycin or clindamycin could be used in case of sensitivity to cephalosporins.[32-36] In addition, using cement is recommended by authors.[32, 37,38]

Another challenging point is the risk of bleeding. However, there is some disparity in the related literature about the increased risk of bleeding in these patients. Löfquist et al. showed that the mean blood loss was 900 ml (a range of 400-2900 ml) and concluded that undertaking simultaneous bilateral THA and the existence of inhibitors may increase the risk of blood loss. However, the definition of normal blood loss has previously been challenging to define.[39] Miles et al. found no increased risk for bleeding or transfusion requirement in such a group of patients and found post-operative blood loss comparable to that seen in people undergoing THA due to Degenerative Joint Disease (DJD).[40]

Sikkema et al. found no incremental risk for hemorrhage or hematoma in THA among hemophilic patients. In addition, Haberman et al. also demonstrated that blood loss did not exceed the normal distribution.[41, 42]

Moreover, hemoglobin decrease is mentioned to be a better indicator of blood loss than an intraoperative assessment of bleeding volume. However, Howe et al. showed that clinically estimated blood loss is correlated well with the actual change in perioperative hemoglobin levels in patients undergoing major orthopedic surgery.[43] Huang et al. showed that tranexamic acid in total joint replacement in hemophiliac patients caused less perioperative and hidden blood loss, transfusion, a lower ratio of post-operative knee swelling and pain, lower levels of inflammatory biomarkers, better function, increase in range of motion (ROM), as well as reduction of pain intensity.[44] However, hemophiliac patients need to improve their lifestyles to improve their destructive pain.[45]

Post-operative rehabilitation

There is a lack of comprehensive studies on the effectiveness of rehabilitation after arthroplasty in hemophilic people. However, the authors suggest beginning rehabilitation in hospitals in the early phase after surgery and even before surgery. Stephensen et al. demonstrated that rehabilitation before and after surgery might be effective in the recovery of hemophiliac patients undergoing orthopedic surgeries, especially in patients with co-morbidities.[46] Santavirta et al. revealed the impact of physical therapy and inpatient rehabilitation sessions on pain and disability.[47] Panotopoulos et al. recommended that intensive physical therapy should be started after surgery, and patients should be mobilized with crutches for six weeks.

Physical therapy after arthroplasty requires several months of dedication to the program. Patients can expect a good outcome by regular attending in therapy sessions and working independently at home. In that case, the potential problems could be detected early, and appropriate intervention could be implemented more quickly.[48,49] Rodriguez-Merchan concluded intensive rehabilitation was started on the third day after surgery and continued twice a day during the hospital stay.[50] Kleijn showed that physiotherapy management is crucial in any invasive procedure, regardless of any joints involved. Pre- and post-operative physiotherapies, as part of care, are needed to reach the optimal functional outcome and, consequently, lead to an optimal quality of life for people with hemophilia.[51] Various studies addressed that proper hemostatic coverage during rehabilitation is crucial.[52] There are challenges among scholars to define appropriate outcomes.

Outcomes

In the first THA surgery performed on a hemophilic patient in 1967, cryoprecipitate was used to control bleeding.[53] previously, the multidisciplinary process for managing patients with severe arthropathy of hip joint undergoing THA with modern implants showed excellent results the surgery in hemophilic patients than in non-hemophilic accompanied by a lower rate of complications. Previous studies shared information about previous generation of hip joint surgeries that most surgeons used cemented monoblock prosthesis, quite long stems, metal-on-polyethylene (MOP) couplings and small diameter heads. Recently, surgeons use modular cementless implants with bioactive surfaces for more osseointegration, with ceramic-on-ceramic (COC) or ceramic-on-polyethylene (COP) bearings associated with using larger femoral heads and shorter stems.[54-58] Although metal-on-metal (MOM) cups were used for a short time, due to several reports on their potential local and systemic biological squeals, their using was limited.[59] With these changes from past until now, longer survival rates and better results are desired, allowing these young people to keep their primary implant for a longer duration and, in the case of revision, making the surgery easier.[4] Considering that THA's preliminary results in hemophilic arthropathy are incentives, the challenging topic is the survival and functional outcomes of cementless THA in such patients. The evidence emphasized that newer cementless implants showed better results in survivorship than cement or hybrid implants. Infection and revision surgeries were the topic of many recent outcome studies that have focused on medium to long-term outcomes.[2,11] In a retrospective cohort study by Kaseb et al. with the aim of assessing the efficiency of the direct anterior approach in patients with hemophilia, they could demonstrate significant improvement of Harris Hip Score followed by rare procedural complications, including dislocation, local infection or needing transfusion.[60] In a study conducted by Mann et al. an equivalent blood loss with THA for DJD was reported.[1] However, another study reported a higher risk of hemorrhage with a 900 ml mean blood loss.[12] Nelson et al. showed that 7.6% of his patients in the study (3/39 patients) were involved in hematoma formation.[13] However, in none of the mentioned studies, the hemoglobin reduction was considered an indicator of blood loss. These results make THA a good option in hip arthropathy of hemophilicpatients, while special attention should be paid to its complications.

Complications

Due to particular features of hemophilic patients, such as bleeding risk, younger age, pre-operative restricted ROM, deformed structures, and high adverse effects, it is essential to pay attention to multiple challenges for THA in these patients before, during, and after surgery. Miles et al. demonstrated that no complications occurred in THA of the cementless group in hemophilia patients; however, Yoo et al., Carulli et al., and Lee et al., described lower rates of loosening, infection, and revision after cementless fixation.[4,11,12] Reasons for higher complications, such as infection, periprosthetic fracture, bleeding and neurovascular injury are higher bleeding diathesis, poor bone quality, bone loss, fibrosis of soft tissue and atrophy of muscles, and flexion contracture.[50] Sikkema et al. evaluated the results of joint replacement therapy in hemophilic and non-hemophilic patients and demonstrated a significantly higher rate of hemarthrosis; however, a similar rate of infection following groups leaded to an excellent implant survival in this group.[61]

Traditionally, the VTE rate after THA was estimated to be 45%-57%.[62] However, in patients with hemophilia, the DVT or Pulmonary Embolism (PE) amount has only been minimally addressed. Girolami et al. claimed that in hemophilia A patients with inhibitors, the main risk factor for thrombosis was the administration of FEIBA as an anti-inhibitor coagulant complex or rFVIIa concentrates, while injection of prothrombin complex concentrates was the main hemophilia B treatment.[63] Regarding the mentioned debates, DVT after surgery could be attributed to prothrombin complex concentrates hemophilia B patients. While the American College of Chest Physicians and the American Academy of Orthopedic Surgeons have set guidelines for thromboembolic prophylaxis in the general population, no such care was set for hemophilic people. As a final note, the favorable outcomes at the end of follow-up indicated that with experienced operative skills and appropriate post-operative care, increased blood loss in hemophilia patients has no apparent negative result on the prosthesis survivorship in the general population.

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