

Research Article

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The mid-term clinical outcomes of total knee arthroplasty in the management of end-stage hemophilic arthropathy

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ABSTRACT

Objective: This study aimed to evaluate the mid-term clinical outcomes of total knee arthroplasty (TKA) in the management of end-stage hemophilic arthropathy.

Methods: Eleven patients (15 knees) undergoing TKA with stiff knees were retrospectively evaluated. TKA was performed in all patients without additional surgical interventions such as posterior capsular release, hamstring release, synovectomy, VY quadricepsplasty, or tibial tubercle osteotomy. All patients were evaluated for clinical and radiological results at follow-ups. Functional evaluation and pain status were assessed using the Knee Society Score and Visual Analogue Scale.

Results: The mean age at the time of operation was 40.8 ± 11.8 years (range = 30–64 years). The mean follow-up was 51.2 ± 20.6 months (range = 24–95). The mean flexion contracture significantly decreased from 17.6 ± 11.3 to 1.7 ± 2.8 degrees, and the mean maximum flexion increased dramatically from 55.6 ± 20.5 to 109.2 ± 16.2 degrees (P < 0.001). Statistical significant improvement in flexion and flexion contracture degrees continued up to the postoperatively 18 months. The mean Knee Society Score increased from 22.7 ± 2.4 points preoperatively to 87.8 ± 3.8 points at the last follow-up (P < 0.001). The mean cost of coagulation factor consumption and blood transfusion accounted for 78% of the total cost.

Conclusion: This study has shown that TKA is an effective treatment for relieving pain and improving both ranges of motion and quality of life in managing end-stage hemophilic arthropathy of the knee joint.

Level of Evidence: Level IV, Therapeutic Study

Introduction

Despite improvements in factor replacement therapy and developments in implant designs, total knee arthroplasty (TKA) remains a challenging procedure in end-stage hemophilic arthropathy.¹⁻³ Total knee arthroplasty performing in hemophilic patients is technically demanding due to the ankylosis, severe bone deformities, and poor bone quality. Therefore, it is difficult to perform an adequate surgical approach, deformity correction, and soft tissue balancing.^{4,5} Recent studies with midterm and long-term follow-up demonstrated promising results with high satisfaction level, significant improvement in knee function, better pain relief, and decreased complication rates.⁶⁻¹⁰ However, costs related to factor replacement and blood transfusion remain a problem.^{11,12}

Preoperative range of motion (ROM) is classically considered to be the most predictor of postoperative ROM following primary TKA and it has been shown that preoperative stiff knees were likely to have a limited postoperative ROM.^{13,14} Preoperative stiffness is a very common problem in end-stage hemophilic knees. Likewise, preoperative flexion contracture showed to be a good predictor for residual flexion contracture postoperatively.¹⁵ Despite advances in factor replacement therapy, there are studies showing that early aggressive and intensive postoperative physiotherapy may increase the risk of intra-articular bleeding in hemophilic knees.¹⁶ Also, it has been reported that hemophilic patients, through intensive postoperative therapy, may experience ROM improvements beyond a year and a half postoperatively.¹⁷ From this point, hemophilic knees could be unique. We think that satisfactory results can be obtained without additional surgical interventions such as synovectomy, V-Y quadricepsplasty, or aggressive soft tissue releases.

This study was performed to evaluate the midterm outcomes of TKA in end-stage hemophilic stiff knees. The clinical outcomes improved in the long-term with intensive physiotherapy after TKA without performing additionally surgical intervention.

Materials and Methods

Patients selection

Fifteen knees in 11 patients with end-stage hemophilic arthropaty were treated with TKA between May 2012 and April 2018. All the medical records were reviewed retrospectively. Patients with endstage hemophilic arthropathy were included in the study and only TKA was performed during one admission. Patients exclusion criteria were incomplete medical records or other surgical procedure interventions (total hip arthroplasty, ankle joint arhroplasty,

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or elbow joint arthroplasty). All procedures were performed by the senior author (S.K.). The study has been approved by an ethics committee (Ref no: 2018-281). A total of 15 total knee replacements consisted of 3 simultaneous bilateral, 7 unilateral, and 1 staged bilateral total knee replacements.

Data collection and measurements

Preoperative function and postoperative outcomes were quantitatively measured at the preoperative visit, as well as at 1, 6, 12, 18, and 24 months postoperatively. Knee ROM was measured by an independent observer using digital goniometer (Baseline digital goniometer, 12-1027; NY, USA). The patients' functional status was evaluated with the Knee Society Score preoperatively and at subsequent follow-up.¹⁰ The Knee Society Score is based on a total of 100 points. It is divided into 3 categories, namely pain, ROM, and instability. The scores above 85 were graded as excellent, 70-84 as good, 60-69 as fair, and below 60 as poor.

Preoperative and postoperative follow-up radiographs taken routinely were obtained. Patient demographics, gender, and age were summarized in Table 1. Postoperatively factor consumption, blood transfusion rates, and the length of hospital stay were recorded. Postoperative and at the time of follow-up radiographs were judged with regard to evaluation of the alignment of the leg and signs of loosening of the prosthesis (Figure 1).

Surgical procedure and perioperative management

All operations were performed under general anesthesia with a pneumatic tourniquet applied to the thigh. A standard midline incision was used and a medial parapatellar arthrotomy was performed. To obtain adequate exposure, fibrous adhesions in the patellofemoral area and the suprapatellar pouch were debrided. Patellofemoral ankylosis was osteotomized with a saw to mobilize the patella in 2 patients. Freehand patellofemoral osteotomy was performed from the patella by providing enough patellar height that would not increase the risk of patellar fracture and from the femur that would not cause notching. After the main osteotomy was performed, appropriate corrections were applied with guides. In cases of tibiofemoral ankylosis, a 2-2.5 cm wedge of bone was excised from the joint level, and the posterior cortex osteotomy was completed by osteoclasis. Following this, the knee was carefully flexed and the bony preparation was completed. Posterior cruciat ligament was routinely resected and posterior cruciate ligament-substituting prostheses were implanted with cement. In all patients, cemented cruciate-substituting posterior-stabilized knee prosthesis (NexGen, Zimmer, Warsaw, IN, USA) was used. None of the patellae had been resurfaced in this group of patients, but patelloplasty was performed. At the stage of evaluation with trial implants, attention was paid to residual flexion deformity. When required, additional distal femoral resection was performed. None of the patients had performed additonal surgical intervention such as synoviectomy, posterior capsular release, hamstring release, tibial tubercle osteotomy, or V-Y quadricepsplasty. In our clinic, we routinely keep

HIGHLIGHTS

- Achieving satisfactory functional results following total knee arthroplasty remains a problem despite improvements in treatment protocols.
- This study was performed to evaluate the midterm outcomes of TKA in endstage hemophilic stiff knees.
- In the present study, TKA resulted in high patient satisfaction together with pain relief, improved functional scores, and decreased flexion contracture. The results suggest that TKA is an effective treatment for end-stage hemophilic arthropathy of knee joint providing good clinical outcome.

Table 1. Patients demographics		
Number of patients	11	
Number of knees	15	
Age (years)	40.8 ± 11.8	
Gender (M/F)	11/0	
Hemophilia type (A/B)	7/4	
BMI (kg/m²)	24.8 ± 2.1	
HIV/HCV/HBV	0/1/2	
Hospital stay (days)	7.2 ± 1.9	
Follow-up (months)	51.2 ± 20.6	

away from additional surgical interventions as much as possible in patients with hemophilic arthropathy. After the cemented prothesis implantation, tourniquet deflation and homeostasis were performed before the wound closure. Postoperative drains were used routinely.

Prophylactic antibiotic was adminstered within 24 hours after surgery. Drainage was removed 24-48 hours after surgery. Hemoglobin was measured preoperatively and postoperatively. Blood transfusions were applied in patients whose hemoglobin levels were less than 7 g/dL or less than 10 g/dL with anemic symtpoms. Tromboprophylaxis regimen was applied for deep venous trombosis by given low-molecular-weight heparin and weared compressive elastic stockings.

The perioperative factor substitution regimen was prescribed by hemophilia experts from the Department of Hematology. All patients received clotting factor replacement therapy according to the World Hemophilia Foundation guidelines.¹⁹ Preoperatively, all patients received factor replacement to maintain factor level of 80%-100% until postoperative day 3 and then maintained factor level of 40%-50% until the discharge. The protocol was modified depending on the patient's factor levels, wound status, and pharmacokinetic parameters such as half-life or optimal dose.

In addition, isometric quadriceps exercises were started in the early postoperative period. Physiotherapy was carefully coordinated with factor replacement and intravenous patient-controlled analgesia. Each physiotherapy session was matched to the patients' status to avoid exacerbation of pain or wound condition. Individualized home exercise programs were then provided upon discharge, and, in some cases, outpatient physiotherapy was initiated. Outpatient physical therapy was initially prescribed for 4 weeks postoperatively and tailored to the specific patient's needs and ROM. Physical therapy exercises typically included isometrics for the quadriceps, hamstrings and gluteal muscles, active and passive knee ROM exercises, selfpatellar mobility, and progressive resistive lower extremity exercises as the patient progressed. The total cost for patients was calculated, including perioperative physiotherapy costs. None of the patients required manipulation under anesthesia.

Statistical analysis

The statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Version 22.0 (IBM SPSS Corp., Armonk, NY, USA) statistical analysis software. Normal distribution was defined by the Shapiro–Wilk test. All values were calculated as the mean and the standard deviation. The preoperative and postoperative comparisons were performed using repeated measures analysis of variance and P < .05 was considered statistically significant. The sample size calculation was performed on the basis of the evidence available at the time, which indicated long-term improvements after TKA in hemophilic



Figure 1. a.f. Pre- and postoperative radiographs of the left knee of a 34-year-old hemophilic patient with patellofemoral ankylosis in 20° flexion. Preoperative anteroposterior (a) and lateral (b) radiograph of the knee showing patellofemoral ankylosis in 25° of flexion. Anteroposterior (c) and lateral (d) view taken immediately after operation and showing restored joint space and prosthesis alignment. Radiographic results (e, f) were satisfactory without any complications or additional surgeries 4 years postoperatively.

arthropathy.¹⁷ The calculation resulted in a sample size of 15 knees with a power of 80% and a significance level of .05 using G*Power software (version 3.1.9.2 Dusseldorf University, Dusseldorf, Germany).

Results

The mean age at the time of operation was 40.8 ± 11.8 years (range: 30-64) years). The mean follow-up was 51.2 ± 20.6 months (range; 24-95). Seven patients had a factor-VIII deficiency (residual factor activity <1%) and 4 (residual factor activity <2%) had a factor-IX deficiency. None of patient had inhibitors against clotting factor. None of our patients were positive for the human immunodeficiency viruses. One patient was positive for the hepatitis C virus and 2 patients for the hepatitis B virus.

The preoperative ROM was 60° or less in all patients with stiff knees preoperatively. Both flexion and flexion contracture degrees statistically significant improvement continued up to 18 months postoperatively. However, with measurements at 18 and 24 months postoperatively, time points were not significantly different. It was observed that degrees of flexion and flexion contracture reached a plateau after the 18 months postoperatively. From 18 months postoperatively, the knee ROM at the point of plateau was significantly higher than preoperative measurements. The average flexion contracture significantly decreased from $17.6^{\circ} \pm 11.3^{\circ}$ to $1.7^{\circ} \pm 2.8^{\circ}$ (P < .001), and the average maximum flexion significantly increased from $55.6^{\circ} \pm 20.5^{\circ}$ to $109.2^{\circ} \pm 16.2^{\circ}$ (P < .001). The mean values of range of flexion and flexion contracture at various time points are detailed in Table 2 and Figure 2.

The average Knee Society Score increased from 22.7 ± 2.4 points preoperatively to 87.8 ± 3.8 points at the last follow-up visit (P < .001). Nine knees were graded as excellent and 2 as good. The average Visuel Analog Scale score descreased from 8.7 ± 0.1 points preoperatively to 1.2 ± 0.2 points at the last follow-up (P < .001).

The mean length of hospital stay was 7.2 \pm 1.9 days (range: 5-11 days). The mean blood loss as measured from the drains in the unilateral performed group and the bilateral group was 356 cc and 723 cc, respectively. The mean blood transfusion requirement was

Duration	Flexion Degrees (Mean ± SD)	P	Flexion Contracture Degrees (Mean ± SD)	P
Pre-op	55.6 ± 20.5		17.6 ± 11.3	
1 month	70.3 ± 18.2	< 0.001*	12.3 ± 10.1	< 0.001*
6 months	92.6 ± 19.4	< 0.001*	6.5 ± 9.1	< 0.001*
12 months	102.1 ± 15.5	< 0.001*	4.2 ± 5.2	< 0.01*
18 months	108.5 ± 16.8	= 0.008*	2.1 ± 3.3	= 0.007*
24 months	109.2 ± 16.2	n.s.ª	1.7 ± 2.8	n.s. ^b

^aNo significant difference between 18 and 24 months (P=.24). ^bNo significant difference between 18 and 24 months (P=.58).

SD, standard deviation.



Figure 2. a, b. Knee range of motions statistically significant improvement continued up to the 18 months postoperative time point. Trendline charts show that flexion (a) and flexion contracture (b) degrees reached a plateau after the 18 months postoperative time point. For both flexion and flexion contracture degrees, there was no significant difference between 18 and 24 months (P=.24 for flexion and P=.58 for flexion contracture).

 0.81 ± 0.9 unit. The average factor replacement administration during hospitalization was 32 727 \pm 18 618 units. The mean total hospital charges was US \$8335.36 in unilateral TKA and US \$11 177.91 in bilateral TKA for hemophilia patients. The mean cost of coagulation factor consumption and blood transfusion accounted for 78% of the total cost.

Only 1 patient of hemarthrosis was observed. The case was treated by continued factor replacement and conservative therapy. We did not have any other complications such as skin necrosis, blisters, superficial and deep wound infections, nerve injury, and septic or aseptic loosening.

Discussion

Total knee arthroplasty is a good option for management of end-stage hemophilic arthropathy.²⁰ However, arthrofibrosis, bone deformities, quadriceps contracture, and poor bone quality in patients with end-stage hemophilic arthropathy adversely affect the outcomes of TKA surgery.²¹ In the present study, TKA resulted in high patient satisfaction together with pain relief, improved functional scores, and decreased flexion contracture.

Stiffness is a common concern seen in end-stage hemophilic arthropathy that affects postoperative ROM. Atilla et al¹⁵ reported midterm outcome of 21 knees treated by TKA in hemophilic patients and found that a residual contracture postoperatively was more likely present in knees with significant flexion contracture preoperatively. Strauss et al²² evaluated 23 TKAs in hemophilic stiff knees and found that 65.2% of patients had good or excellent Knee Society Functional Scores. They reported that the clinical outcome is inferior compared to nonstiff knees reported in the literature.²² Kamath et al¹⁷ presented 24 TKAs in hemophilic patients and showed encouraging results at a mean follow-up of 50 months. They showed that the mean flexion contracture improved from -10.5° preoperatively to -5.1° at final follow-up. They emphasized the effectiveness of soft tissue stretching with physiotherapy and showed a significant gain in flexion between 12 months and the final follow-up. Similarly, Silva et al²³ evaluated 90 TKAs in 68 hemophilic patients and showed that the average flexion arc improved from 59° to 69° in the early postoperative phase and then to 75° at the latest follow-up of 2 years. It has been reported that the greatest improvement in knee ROM occurred during the first 12 weeks after TKA for primer osteoarthritis.²⁴ Zhou et al²⁵ found that the recovery in knee ROM plateaus no later than 12 months post-TKA in primer knee osteoarthritis. In our study, there was no significant improvement in ROM in the early postoperative period, while significant improvement was observed in the long-term. In our study, statistically significant improvement both in flexion and flexion contracture degrees continued up to 18 months postoperatively. The potential and possibility for later improvements in ROM should be kept in mind. Early additional surgical interventions may be prevented with intensive and organized physiotherapy sessions.

Total knee arthroplasty is a effective procedure for chronic hemophilic arthropathy to relive pain and improve function. It may be technically more demanding than in nonhemophilic patients because of poor bone quality, bone deformity, and extensive fibrosis. Improvements in surgical techniques and implant designs and current hemophilia medical treatment algorithms have improved the functional and clinical scores of patients who underwent total knee replacement surgery.²⁶ Recent studies have noted much success with knee arthroplasty with hemophilics. Atilla et al¹⁵ reported that functional knee score increased from 27.9 points preoperatively to 79.4 points postoperatively. Heeg et al²⁷ reported that functional knee score increased from 36.8 points preoperatively to 80 points postoperatively. In another study, the average clinical knee score improved from 36 points to 73 points in the late postoperative phase.²⁸ The patients in our study saw a comparable improvement with both functional and clinical knee scores. In the present study, the procedure resulted in high patient satisfaction and in a significant improvement of knee function.

Pain was evaluated by a Visual Analog Scale (VAS) and given a score from 0 to 10, from no pain to very severe pain. In a recent study, 50 TKA cases in 41 hemophilic patients were evaluated and the mean VAS score decreased significantly from 7.9 points to 1.8 points.²⁹ In our study, pain was considerably reduced in all patients. Visual Analog Scale score was 8.7 points preoperatively and decreased to 1.2 points. Thus, knee arthroplasty offers excellent pain relief. With advancements in technology in prostheses and coagulation factor replacement, patients have reported better pain relief.³⁰

Despite these significant improvements in patient satisfaction and knee scores, many complications were observed in hemophilic patients who underwent knee arthroplasty.⁷ The most common complications are hemarthrosis, hematoma, infection, and implant loosening.⁷ Among them, hemarthrosis is the most common complication seen in end-stage hemophilic arthropathy patients undergoing TKA.³¹ Low factor levels, factor inhibitor development, and the presence of fragile synovial tissues can cause hemarthrosis.³² This is also a problem for intensive physiotherapy. Postoperative physiotherapy can cause recurrent bleeding, but subsequent fibrosis may occur if physiotherapy is not performed properly. The combination of stiffness, intensive physiotherapy, recurrent bleeding, subsequent fibrosis, and stiffness can result in a vicious circle. Increased stiffness seen in the case of hemarthrosis may cause unsatisfactory results in ROM. In our study, only 1 patient had hemarthrosis.

Additional surgical interventions such as posterior capsular release, hamstring release, synovectomy, V-Y quadricepsplasty, or tibial tubercle osteotomy were not performed, which are generally recommended and performed.^{8,15,22,33-36} Patella resurfacing was not performed in any knees and patelloplasty consisting of articular surface smoothing and patella rim denervation was done. In our study, we observed a significant increase in ROM with appropriate postoperative physiotherapy in hemophilic patients who underwent TKA, without performing additional surgical interventions. Physiotherapy is the most important component to a patient's success. Rehabilitation should address restoration of ROM into flexion and extension, muscular strengthening, and restoration of patients' proprioceptive performances.³⁷ In a study, it was emphasized that the effectiveness of intensive physiotherapy lasted 2-4 months which resulted in less pain and stiffness.³⁸ In another study, it was observed that organized physiotherapy was more effective in patients who underwent it for 1 month than in patients who underwent it only for 1-2 weeks.³⁹ We performed long-term rehabilitation protocols for all hemophilic patients who underwent TKA. In our study, those patients with the poorest ROM benefited the greatest from an intense postoperative rehabilitation course.

According to recent studies, increased costs and the risk of postoperative complications such as bleeding remain a major concern.^{11,12} Wang et al¹¹ reported that hemophilia patients have higher rates of postoperative transfusion, hospital costs, and increased length of stay. They revealed that the cost of coagulation factor consumption, blood transfusion, and hospital stay accounted for 92% of the total cost in the hemophilic TKA group. In our series, we also observed that residual knee flexion contracture after early postoperative phase was correlated with less bleeding episodes, transfusion, and factor consumption during the course of follow-up. In our series, the mean blood transfusion requirement and factor replacement administration were 0.81 ± 0.9 units and $32\ 727 \pm 18\ 618$ units, respectively. The mean cost of coagulation factor consumption and blood transfusion accounted for 78% of the total cost.

In our study, we observed that TKA without aggresive soft tissue release may reduce recurrent bleeding and achieve long-term improvements in knee function with no increased factor consumption, blood transfusion, and costs. These findings can encourage the performance of TKA without additional surgical intervention in endstage hemophilic arthropaty, but high-quality randomized controlled studies are required to confirm these results.

There exist some limitations in this study. First, this is a retrospective study with a limited number of patients. The absence of a control group such as early gained ROM with performed soft tissue release was second limitation. The relatively shorter follow-up is another limitation in this study.

In conclusion, midterm outcomes of TKA in hemophilic arthropathy appear to be satisfying with significant improvement of function and reduction in pain. This study concludes that TKA is an effective treatment for end-stage hemophilic arthropathy of knee joint providing better clinical outcome and improving quality of life. However, longterm outcomes require further evaluation.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Karadeniz Technical University (Ref No: 2018-281).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Author Contributions: Concept - M.K., S.K.; Design - M.K., A.E.O.; Supervision - S.K., M.K.; Materials - M.K., Ü.K.; Data Collection and/or Processing - M.K.; Analysis and/ or Interpretation - S.K., M.K., A.E.O.; Literature Review - M.K., A.E.O.; Writing - M.K., A.E.O.; Critical Review - S.K.

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