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Haemophilic arthropathy: Long-term outcomes in 107 primary total knee arthroplasties

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ABSTRACT

Background: Arthropathy of the knee is a frequent complication in patients with severe bleeding disorders leading to considerable pain and disability. Total knee arthroplasty (TKA) provides marked pain relief. However, a modest functional outcome and a high number of complications due to prosthetic infection and loosening are reported. Data on long-term outcomes are scarce, and most case series include few patients. We have studied clinical outcomes and complications of TKAs with special emphasis on prosthetic survival and periprosthetic infection.
Methods: A consecutive series of 107 TKAs in 74 patients with haemophilic arthropathy were retrospectively reviewed. Follow-up was mean 11.2 years (range 0.8–33.1 years).
Results: Five- and 10-year survival rates, with component removal for any reason as the end point, were 92% and 88%, respectively. Twenty-eight TKAs were removed after median 10 years (range 0.8–28 years). The most common cause of failure was aseptic loosening (14 knees) and periprosthetic infection (seven knees). The overall infection rate was 6.5%. The mean postoperative drop in haemoglobin levels was 4.3 g/dL (range 0.5–9.4) with a significant difference between haemophilia A patients with and without inhibitor (6.3 g/dL (range 3.6–9.4) versus 3.7 g/dL (range 0.5–8.1) ($p < 0.001$). A painless knee was reported in 93% of the TKAs at the latest follow-up.
Conclusions: The medium and long-term results of primary TKA in a large haemophilic population show good prosthetic survival at five and 10 years with an excellent relief of pain. Periprosthetic infection is still a major concern compared to the non-haemophilic population.
Level of evidence: Level IV.

1. Introduction

Haemophilic arthropathy is a well known complication in patients with severe bleeding disorders as a result of recurrent haemarthrosis causing synovial inflammation and destruction of the articular tissue. Haemophilic arthropathy most commonly involves knees and ankles, and patients present with a painful joint with severe functional deficit often at a relatively young age if primary prophylaxis has not been provided from early childhood [1–3]. Total knee arthroplasty (TKA) provides marked pain relief, improves functional status and reduces the tendency to bleed in end-stage arthropathy [4–8]. TKA was first reported in patients with haemophilia in the mid-1970s [9,10]. The surgery is technically challenging because of soft tissue fibrosis, flexion contractures and poor bone quality. Even though TKA is known to effectively relieve pain in haemophilic arthropathy, many authors have reported a modest functional outcome and a high number of complications due to prosthetic infection and loosening [11–13]. Data on long-term outcomes are still scarce, and most case series include few patients.

The aim of this retrospective study was to review medium and long-term results in 107 consecutive primary TKAs in patients with severe bleeding disorders treated at a single institution. We studied clinical outcomes and complications with special emphasis on prosthetic survival and periprosthetic infection.

2. Patients and methods

From December 1979 to April 2011, 110 primary TKAs were performed in 77 patients with severe haemophilia A and B (factor VIII/IX activity <1%), moderate haemophilia A and B (factor VIII/IX activity 1–5%), severe FVII deficiency and von Willebrand disease type 3. A chart review was performed in January 2013. We excluded one patient who died soon after surgery and two patients who had emigrated. This leaves 107 TKAs in 74 patients (70 men and four women) to be included for further analysis. Thirty-three patients underwent bilateral TKA, but only two were in the same surgical session.

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The haemophilia comprehensive care centre at Oslo University Hospital is the only haemophilia centre in Norway, and all elective orthopaedic surgery in Norwegian patients with severe bleeding disorders is performed at Oslo University Hospital. The patients are seen at the haemophilia centre yearly by a haematologist/paediatrican, a physiotherapist and an orthopaedic surgeon when indicated. After approval from the hospital's Data Protection Official for Research, the patients' medical records were retrospectively reviewed. We registered demographic data, type and severity of the haemophilia, HIV status, HCV status, type of prosthesis, pre- and postoperative ranges of motion (ROM), pre- and postoperative levels of haemoglobin (Hb), complications, periprosthetic infection, implant survival and time and cause of death, if applicable. In the case of revision surgery with removal of components, time of revision was defined as follow-up endpoint. We used the lowest Hb level from the operative day to postoperative day seven as postoperative Hb level. Periprosthetic infection was classified into early or late with symptoms presenting less or more than four weeks after arthroplasty, respectively, according to the classification by Segawa and Tsukayama [14].

The haemophilia patients received factor replacement as a preoperative bolus infusion followed by a continuous infusion of factor concentrate according to the institution's protocol, targeting a factor VIII (FVIII) level of 70% perioperatively and the first three postoperative days followed by a FVIII level of 50% the next three days and tapered down to 30% the next three days from January, 1996. Between 1979 and 1996, they received repeated bolus injections as described previously [4]. The inhibitor patients were treated with repeated injections with bypassing agents, primarily activated prothrombin complex concentrate, as described previously [15]. The patients with von Willebrand disease received von Willebrand factor containing concentrate and the ristocetin cofactor activity (VWF:RCo) was kept above 50% during the peri- and postoperative phase. The FVII deficient patients received rFVIIa replacement therapy according to the institutional protocol [16].

Surgery was performed in a standard operating room with vertical laminar air flow. The patients were placed in a supine position and the standard parapatellar medial incision in a bloodless field was used. The types of prosthetic components used are shown in Table 1. The operations were performed by five surgeons during the study period. Between 1979 and 2000, the patients did not receive prophylactic antibiotics. From the year 2000, all patients received prophylactic systemic antibiotics at induction and three additional doses within 24 h after surgery. No anti-thrombotic prophylaxis was used throughout the study period. The patients started active exercises on the first postoperative day and full weight bearing was allowed from day one.

2.1. Statistical analysis

Descriptive statistics were computed with SPSS for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). Kaplan–Meier survivorship analysis was performed to determine prosthetic survival rates. Prosthetic failure was defined as removal for any reason. The Student's *t*-test was used to compare continuous variables and the chi-squared test or Fisher's exact test was used to compare categorical variables. A two-sided p-value of <0.05 was considered significant.

Table 1
Types of total knee prosthesis used (n = 107).

Prosthesis	Numbers (%)	Time period
Richards Maximum Contact (RMC)	9 (8%)	1979–1989
Guepar	1 (1%)	1980
Attenborough	2 (2%)	1985–1988
Tricon M	4 (4%)	1985–1991
Tricon C	7 (7%)	1989–1991
Tricon IIC	37 (35%)	1991–1998
Profix	12 (11%)	1998–2004
Genesis	9 (8%)	1998–2001
NexGen	26 (24%)	2005–2011

3. Results

The mean age of the patients at the time of surgery was 41 years (range 20–82 years). Fifty-eight patients had haemophilia A (78%), nine patients haemophilia B (12%), four patients von Willebrand disease (5.4%) and three patients severe FVII deficiency (4%) (Table 2). Seven patients were HIV-positive and 52 (70%) patients were HCV antibody positive. Twenty of the 74 patients (29 joints) had died by the end of the study, at a mean of 11.4 years (range 2.2–29.7 years) after primary surgery. The causes of death were AIDS-related complications, amyotrophic lateral sclerosis (ALS), malignant melanoma, alcoholism, leukaemia, hepatitis C virus (HCV)-related hepatic cirrhosis, hepatic carcinoma, pancreatic cancer, pulmonary cancer, thyroid cancer, intracerebral haemorrhage, postsurgical bleeding after fracture surgery and bowel ischaemia. Three died from unknown causes. The mean follow-up for the whole cohort was 11.2 years (range 0.8–33.1 years).

3.1. Prosthetic survival

Of the 107 TKAs, 28 (26%) prostheses were removed after a mean of 10 years (range 0.8–28 years); 14 because of aseptic loosening, seven because of periprosthetic infection, three because of pain, three because of severe instability and one because of recurrent haemarthrosis. The 14 TKAs that were reoperated because of loosening were removed after mean 12.2 years (range 2.1–28 years). With the exception of the TKAs removed because of infection, all the knees were treated with a stemmed revision arthroplasty. In addition, four patients had an osteosynthesis because of a periprosthetic fracture without removing the TKA. The five- and 10-year survival rate, with component removal for any reason as the end point, was 92% and 88%, respectively (Fig. 1, Table 3). Forty-three patients (58 TKAs) were alive with the primary TKA in place at a mean of 12.4 years (range 1.8–33.1 years).

3.2. Prosthetic infections

Two patients suffered an early periprosthetic infection due to *Staphylococcus aureus* and *Acinetobacter baumannii*, respectively. Both patients were initially treated with soft-tissue debridement and retention of the prosthesis without success however. The prostheses were removed, and in one patient a successful knee arthrodesis was later performed, whereas in the other the infection persisted. In addition, late periprosthetic infection was recorded in four patients (five knees) with removal of the prosthesis after a mean of 7.2 years (range 1.3–10.8 years). *S. aureus* was grown from four knees and *Streptococcus vestibularis* from one knee. In three patients, an arthrodesis was successfully performed, and one patient eventually had an above-knee amputation performed. One patient developed a late infection with *S. aureus* in both knees, and he suffered chronic infection after removal of the prostheses. This patient as well as two other patients who developed late periprosthetic infections were injection drug abusers. Overall, 7/107 TKAs were complicated by infection (6.5%). Infection occurred in one HIV-positive patient. There was no difference in infection rates between patients with or without HIV ($p = 0.47$).

3.3. Haemorrhage

The mean drop in haemoglobin levels after surgery was 4.3 g/dL (range 0.5–9.4) ($n = 57$). There was a significant difference in haemoglobin drop between patients with haemophilia A with and without inhibitor (6.3 g/dL (range 3.6–9.4) versus 3.7 g/dL (range 0.5–8.1) ($p < 0.001$)). In 5/57 TKA procedures, postoperative blood transfusion was required, median 1 (1–2) unit. No fatal bleedings were observed. One patient had recurrent haemarthrosis postoperatively and was eventually reoperated because of loosening nearly three years after the index operation.

3.4. Function

Due to the retrospective design of this study, data on total ROM before and after surgery were available in only 50 TKAs. Mean total ROM was 70° (range 5–125) preoperatively and 79° (range 15–115) at the latest follow-up. The difference was not significant ($p = 0.07$). Severely limited ROM led to postoperative manipulation under anaesthesia in three knees and arthroscopic or modified open lysis in another three. One patient had

Table 2
74 patients with haemophilia undergoing TKA.

		Patients	Inhibitor present
Haemophilia A	Moderate	2	
	Severe	56	5
Haemophilia B	Moderate	2	
	Severe	7	
FVII deficiency		3	
von Willebrand disease		4	

TKA: total knee arthroplasty.