Total Knee Arthroplasty in Hemophilic Arthropathy

Am J Orthop. 2015 December;44(12):E503-E507

Authors:
Rodríguez-Merchán EC

Author Affiliation | Disclosures

E. Carlos Rodríguez-Merchán, MD, PhD

Author’s Disclosure Statement: The author reports no actual or potential conflict of interest in relation to this article.

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Chronic hemophilic arthropathy, a well-known complication of hemophilia, develops as a long-term consequence of recurrent joint bleeds resulting in synovial hypertrophy (chronic proliferative synovitis) and joint cartilage destruction. Hemophilic arthropathy mostly affects the knees, ankles, and elbows and causes chronic joint pain and functional impairment in relatively young patients who have not received adequate primary prophylactic replacement therapy with factor concentrates from early childhood.1-3

In the late stages of hemophilic arthropathy of the knee, total knee arthroplasty (TKA) provides dramatic joint pain relief, improves knee functional status, and reduces rebleeding into the joint.4-8 TKA performed on a patient with hemophilia was first reported in the mid-1970s.9,10 In these cases, the surgical procedure itself is often complicated by severe fibrosis developing in the joint soft tissues, flexion joint contracture, and poor quality of the joint bone structures. Even though TKA significantly reduces joint pain in patients with chronic hemophilic arthropathy, some authors have achieved only modest functional outcomes and experienced a high rate of complications (infection, prosthetic loosening).11-13 Data on TKA outcomes are still scarce, and most studies have enrolled a limited number of patients.

We retrospectively evaluated the outcomes of 88 primary TKAs performed on patients with severe hemophilia at a single institution. Clinical outcomes and complications were assessed with a special focus on prosthetic survival and infection.

Patients and Methods

Ninety-one primary TKAs were performed in 77 patients with severe hemophilia A and B (factor VIII [FVIII] and factor IX plasma concentration, <1% each) between January 1, 1999, and December 31, 2011, and the medical records of all these patients were thoroughly reviewed in 2013. The cases of 3 patients who died shortly after surgery were excluded from analysis. Thus, 88 TKAs and 74 patients (74 males) were finally available for evaluation. Fourteen patients underwent bilateral TKAs but none concurrently. The patients provided written informed consent for print and electronic publication of their outcomes.
We recorded demographic data, type and severity of hemophilia, human immunodeficiency virus (HIV) status, hepatitis C virus (HCV) status, and Knee Society Scale (KSS) scores. KSS scores include Knee score (pain, range of motion [ROM], stability) and Function score (walking, stairs), both of which range from 0 (normal knee) to 100 (most affected knee). Prosthetic infection was classified (Segawa and colleagues) as early or late, depending on timing of symptom onset (4 weeks after replacement surgery was the threshold used).

Patients received an intravenous bolus infusion of the deficient factor concentrate followed by continuous infusion to reach a plasma factor level of 100% just before surgery and during the first 7 postoperative days and 50% over the next 7 days (Table 1). Patients with a circulating inhibitor (3 overall) received bypassing agents FEIBA (FVIII inhibitor bypassing agent) or rFVIIa (recombinant factor VII activated) (Table 2). Patients were not given any antifibrinolytic treatment or thromboprophylaxis.

Surgery was performed in a standard surgical room. Patients were placed on the operating table in decubitus supinus position. A parapatellar medial incision was made on a bloodless surgical field (achieved with tourniquet ischemia). The prosthesis model used was always the cemented (gentamicin bone cement) NexGen (Zimmer). Patellar resurfacing was done in all cases (Figures 1A–1D). All TKAs were performed by Dr. Rodríguez-Merchán. Intravenous antibiotic prophylaxis was administered at anesthetic induction and during the first 48 hours after surgery (3 further doses). Active exercises were started on postoperative day 1. Joint load aided with 2 crutches was allowed starting on postoperative day 2.
Mean patient age was 38.2 years (range, 24-73 years). Of the 74 patients, 55 had a diagnosis of severe hemophilia A, and 19 had a diagnosis of severe hemophilia B. During the follow-up period, 23 patients died (mean time, 6.4 years; range, 4-9 years). Causes of death were acquired immune deficiency syndrome (AIDS), liver cirrhosis, and intracranial bleeding. Mean follow-up for the full series of patients was 8 years (range, 1-13 years).

Descriptive statistical analysis was performed with SPSS Windows Version 18.0. Prosthetic failure was regarded as implant removal for any reason. Student t test was used to compare continuous variables, and either χ² test or Fisher exact test was used to compare categorical variables. P < .05 (2-sided) was considered significant.

**Results**

Prosthetic survival rates with implant removal for any reason regarded as final endpoint was 92%. Causes of failure were prosthetic infection (6 cases, 6.8%) and loosening (2 cases, 2.2%). Of the 6 prosthetic infections, 5 were regarded as late and 1 as early. Late infections were successfully sorted by performing 2-stage revision TKA with the Constrained Condylar Knee (Zimmer). Acute infections were managed by open joint débridement and polyethylene exchange. Both cases of aseptic loosening of the TKA were successfully managed with 1-stage revision TKA using the same implant model (**Figures 2A-2D**).

Mean KSS Knee score improved from 79 before surgery to 36 after surgery, and mean KSS Function score improved from 63 to 33. KSS Pain score, which is included in the Knee score, 0 (no pain) to 50 (most severe pain), improved from 47 to 8. Patients receiving inhibitors and patients who were HIV- or HCV-positive did not have poorer outcomes relative to those of patients not receiving inhibitors and patients who were HIV- or HCV-negative. Patients with liver cirrhosis had a lower prosthetic survival rate and lower Knee scores.
Discussion

The prosthetic survival rate found in this study compares well with other reported rates for patients with hemophilia and other bleeding disorders. However, evidence regarding long-term prosthesis survival in TKAs performed for patients with hemophilia is limited. Table 3 summarizes the main reported series of patients with hemophilia with 10-year prosthetic survival rates, number of TKAs performed, and mean follow-up period; in all these series, implant removal for any reason was regarded as the final endpoint. Mean follow-up in our study was 8 years. Clinical outcomes of TKA in patients with severe hemophilia and related disorders are expected to be inferior to those achieved in patients without a bleeding condition. The overall 10-year prosthetic survival rate for cemented TKA implants, as reported by the Norwegian Arthroplasty Register, was on the order of 93%. Mean age of our patients at time of surgery was only 38.2 years. TKAs performed in younger patients without a bleeding disorder have been associated with shorter implant survival times relative to those of elderly patients. Thus, Diduch and colleagues reported a prosthetic survival rate of 87% at 18 years in 108 TKAs performed on patients under age 55 years. Lonner and colleagues reported a better implant survival rate (90% at 8 years) in a series of patients under age 40 years (32 TKAs). In a study by Duffy and colleagues, the implant survival rate was 85% at 15 years in patients under age 55 years (74 TKAs). The results from our retrospective case assessment are quite similar to the overall prosthetic survival rates reported for TKAs performed on patients without hemophilia.

Rates of periprosthetic infection after primary TKA in patients with hemophilia and other bleeding conditions are much higher (up to 11%), with a mean infection rate of 6.2% (range, 1% to 11%), consistent with the rate found in our series of patients (6.8%). This rate is much higher than that reported after primary TKA in patients without hemophilia but is similar to some rates reported for patients with hemophilia. In our experience, most periprosthetic infections (5/6) were sorted as late.

Table 3. Long-Term Prosthetic Survival Rates for Total Knee Arthroplasties (TKAs) Performed in Patients With Hemophilia

<table>
<thead>
<tr>
<th>Study</th>
<th>10-Year Survival Rate, %</th>
<th>TKAs, N</th>
<th>Mean Follow-Up, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silva &amp; Luckf</td>
<td>83</td>
<td>90</td>
<td>7.8</td>
</tr>
<tr>
<td>Wang et alf</td>
<td>83</td>
<td>40</td>
<td>11.8</td>
</tr>
<tr>
<td>Chevalier et alf</td>
<td>88</td>
<td>72</td>
<td>7.8</td>
</tr>
<tr>
<td>Zinga et alf</td>
<td>85</td>
<td>43</td>
<td>8.6</td>
</tr>
<tr>
<td>Goddard et alf</td>
<td>89</td>
<td>70</td>
<td>9.2</td>
</tr>
<tr>
<td>Westberg et alf</td>
<td>92</td>
<td>107</td>
<td>11.2</td>
</tr>
</tbody>
</table>

Table 4. Rates of Periprosthetic Infection After Primary TKA in Patients With Hemophilia

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silva &amp; Luckf</td>
<td>8.8%</td>
</tr>
<tr>
<td>Wang et alf</td>
<td>8.5%</td>
</tr>
<tr>
<td>Chevalier et alf</td>
<td>8.5%</td>
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<tr>
<td>Zinga et alf</td>
<td>8.5%</td>
</tr>
<tr>
<td>Goddard et alf</td>
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<tr>
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<td>8.5%</td>
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</table>
Late infection is a major concern after TKA in patients with hemophilia, and various factors have been hypothesized as contributing to the high prevalence. An important factor is the high rate of HIV-positive patients among patients with hemophilia—which acts as a strong predisposing factor because of the often low CD4 counts and associated immune deficiency, but different reports have provided conflicting results in this respect. We found no relationship between HIV status and risk for periprosthetic infection, but conclusions are limited by the low number of HIV-positive patients in our series (14/74, 18.9%). Our patients’ late periprosthetic infections were diagnosed several years after TKA, suggesting hematogenous spread of infection. Most of these patients either were on regular prophylactic factor infusions or were being treated on demand, which might entail a risk for contamination of infusions by skin bacteria from the puncture site. Therefore, having an aseptic technique for administering coagulation factor concentrates is of paramount importance for patients with hemophilia and a knee implant.

Another important complication of TKA surgery is aseptic loosening of the prosthesis. Aseptic loosening occurred in 2.2% of our patients, but higher rates have been reported elsewhere. Rates of this complication increase over follow-up, and some authors have linked this complication to TKA polyethylene wear. Development of a reactive and destructive bone–cement interface and microhemorrhages into such interface might be implicated in the higher rate of loosening observed among patients with hemophilia.

In the present study, preoperative and postoperative functional outcomes differed significantly. A modest postoperative total ROM of 69° to 79° has been reported by several authors. Postoperative ROM may vary—may be slightly increased, remain unchanged, or may even be reduced. Even though little improvement in total ROM is achieved after TKA, many authors have reported reduced flexion contracture and hence an easier gait. However, along with functional improvement, dramatic pain relief after TKA is perhaps the most remarkable aspect, and it has a strong effect on patient satisfaction after surgery.

Our study had 2 main limitations. First, it was a retrospective case series evaluation with the usual issues of potential inaccuracy of medical records and information bias. Second, the study did not include a control group.

**Conclusion**

The primary TKAs performed in our patients with hemophilia have had a good prosthetic survival rate. Even though such a result is slightly inferior to results in patients without hemophilia, our prosthetic survival rate is not significantly different from the rates reported in other, younger patient subsets. Late periprosthetic infections are a major concern, and taking precautions to avoid hematogenous spread of infections during factor concentrate infusions is strongly encouraged.
Key Info

Figures/Tables

References

References


Multimedia

Product Guide

- STRATAFIX™ Symmetric PDS™ Plus Knotless Tissue Control Device
- STRATAFIX™ Spiral Knotless Tissue Control Device
- BioComposite SwiveLock Anchor
- BioComposite SwiveLock C, with White/Black TigerTape™ Loop

Citation

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