Orthopaedics & Traumatology: Surgery & Research 101 (2015) 147–150

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www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Original article

Simultaneous bilateral total knee arthroplasty in severe hemophilia: A retrospective cost-effectiveness analysis

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ARTICLE INFO

Article history:
Received 26 June 2014
Accepted 23 December 2014

Keywords:
Hemophilia A
Simultaneous total knee arthroplasty
Cost-benefit analysis
Bilateral knee replacement

ABSTRACT

Introduction: Simultaneous bilateral total knee arthroplasty (TKA) is proposed in the general population as an alternative to staged bilateral TKA and has the advantage of reducing costs with equivalent complication rates. The aim of this study was to evaluate the cost-effectiveness of this alternative in a population of patients with severe hemophilia.
Hypothesis: Simultaneous bilateral TKA is less expensive than staged bilateral TKA.
Materials and methods: We performed a retrospective case control study in patients with severe hemophilia A to compare the direct costs of coagulation factors, the length of hospital stay and sick leave as well as the clinical outcome (KKS) of simultaneous bilateral TKA (group 1; G1: 5 patients) and staged bilateral TKA (group 2; G2: 12 patients).
Results: The mean cost of coagulation factors was 65,880 € in G1 and 139,000 € in G2 ($P < 0.001$). The length of the hospital stay (24 days vs 44 cumulative days, respectively) and sick leave (105 days vs 183 cumulative days, respectively) was significantly reduced in G1. There was no significant difference in clinical outcome at the final follow-up. One patient in G2 had a late knee infection.
Discussion: Simultaneous bilateral TKA in severe hemophilia is associated with lower costs than staged bilateral TKA with equivalent clinical results.
Level of evidence: Level 3, case control study.

1. Introduction

In the general population, simultaneous bilateral total knee arthroplasty (TKA) has sometimes been associated with certain risks including increased morbidity [1] with, in particular, an increase in myocardial infarction and thromboembolic events [2] or perioperative confusion [3] in patients over the age of 80 or ASA 3 or 4 [3,4]. Continuous improvement of perioperative management has reduced the number of adverse events so that certain authors have re-evaluated the controversial issues associated with this procedure, and recent studies have not reported any increase in complications in selected patients [5–8].

TKA is a well-tolerated and effective technique in patients with severe hemophilia (factor VIII < 1%) with good long-term results [9–11]. Moreover, the episodes of hemarthrosis are reduced and thus there is a decrease in the consumption of coagulation factors, which are very expensive [12].

In patients with severe hemophilia, TKA is usually indicated when the patient is in his thirties [13,14]. Because lesions are usually bilateral, in young patients without comorbidities other than the causal disease, simultaneous bilateral TKA is indicated, so the patient can return to his professional activities as quickly as possible.

The simultaneous bilateral procedure also has the advantage of limiting the consumption of coagulation factors, resulting in a significant reduction of costs because these factors are expensive, and because of the quantities necessary in patients with severe hemophilia.

The goal of this study was to compare the direct costs of coagulation factors during simultaneous bilateral TKA compared to staged bilateral TKA in patients with severe hemophilia. We also evaluated the length of the hospital stay, the length of sick leave and the clinical outcome.

Hypothesis: simultaneous bilateral TKA is less expensive than staged bilateral TKA in patients with severe hemophilia.

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http://dx.doi.org/10.1016/j.otsr.2014.12.010
1877-0568/

2. Materials and methods

This retrospective study was performed in a University Hospital Center (CHU de Bicêtre, AP–HP, Kremlin-Bicêtre) between 2006 and 2013 and included patients with severe hemophilia with an incapacitating bilateral hemophiliac arthropathy. All patients in whom both knees were operated on were included in the study. Five patients underwent simultaneous bilateral TKA (group 1, G1) and twelve patients underwent staged bilateral TKA (group 2, G2). Patients in G1 were eligible for simultaneous bilateral TKA because they had symmetric involvement at the time of the initial consultation, followed by a discussion between the surgeon (VM) and the referring hematologist (TL) and the patient's consent to undergo a serious operation. Inclusion in G1 or G2 was not consecutive. The mean age at surgery was 33.5 years old (23–39 years) in G1 and 37.2 years old for the first operation (27–54 years old) in G2. The mean delay between the 2 procedures in G2 was 21.5 months (range: 6–74 months). The mean follow-up was 4.8 years in G1 and 4.1 years after the second operation in G2. The two groups were comparable for age, Knee Society Score (KSS) and preoperative range of motion (Table 1). There was no difference between any of the two knees in the same patient.

2.1. Factor replacement therapy

Factor replacement therapy was adapted to each patient according to weight, with daily adjustment by the Reference Center for the Treatment of Hemophilia (Centre de référence pour le traitement de l'hémophilie) (CRTH, CHU de Bicêtre) for at least 21 days. The targeted residual FVII activity levels or the clinical target in patients receiving an inhibitor were the same for G1 as those for unilateral TKA.

2.2. Surgical procedure

All procedures were performed without a tourniquet by anteromedial approach with a V-Y quadricipital plasty in case of severe stiffness. Prostheses (Ceragyr or Hermes–Ceraver, Roissy, France) were cemented with antibiotic-loaded cement (Palacos Genta–Heraeus Medical GmbH, Wehrheim, Germany). There was no patellar resurfacing (Fig. 1). The incision was closed on Redon drains and a pressure dressing was applied. The patients were given locoregional analgesia via a unilateral or bilateral femoral perineural catheter. Rehabilitation began on postoperative day 1 with the help of a physical therapist and continuous passive motion by arthromotor alternating from one knee to the other in G1. The drains were removed a mean 5 days after surgery (range: 3–10 days) in both groups.

2.3. Evaluation

The main judgment criteria were the direct costs of replacement factors determined by the dose received during the initial hospital stay. The purchase price of these drugs in 2013 by the General Agency for Medical Products (AGEPS: Agence générale des produits de santé–AP–HP, Paris) was 720 € for 1000 UI of factor VIII (Helixate® – CSL Behring or Advate® – Baxter) and 608 € for 1 mg of factor VII (Novoseven® – Novo Nordisk). The length of the hospital stay and the date of the return to work were recorded, using the sum of the stays for both operations in G2. Evaluation of function was obtained by the pre- and postoperative Knee Society Score (KSS – former version [15]) until the final follow-up. Results were the sum of the mean right and left knee scores on one hand and the function score on the other. Severe adverse events included death, surgical revision due to infection, hemarthrosis, fracture or loosening.

Table 1
Comparison of populations before surgery.

	Group 1 ($n=5$)	Group 2 ($n=12$)
Age (years)	33.5 (23–39)	37.2 (27–54)
Presence of inhibitors	1	0
KSS (knee score)	13 (0–27)	14.6 (0–28)
KSS (function score)	22 (0–45)	23.7 (0–50)
Range of motion	43° (0–50)	47° (10–65)

KSS: Knee Society Score.

2.4. Statistical analysis

The statistical analysis was performed with BiostaTGV software – Inserm, France. Comparison of the costs of replacement therapy during hospitalization, the length of the hospital stay and sick leave were performed with the Wilcoxon–Mann–Whitney test. $P<0.05$ was considered to be significant.

3. Results

During the hospital stay a mean 91,500 UI (65,880 €) of factor VIII was administered per person to patients without circulating antibodies in G1 compared to 193,250 UI (or 139,000 €) of factor VIII in G2 ($P<0.01$). The cost of replacement therapy was 766,000 € (1260 mg de Novoseven®) for the patient with circulating antibodies (Table 2). The mean length of the hospital stay was 24 days (range 21–26) in G1 and the cumulative hospital stay was 44 days in two hospital stays in G2 (range 39–50) ($P<0.01$). The patient returned to work after a mean 105 postoperative days (range 90–120) in G1 and after a mean 183 cumulative days in G2 (range 150–210) ($P<0.01$). Three patients in G1 received a transfusion during their hospital stay and 9 in G2 ($P=0.6$). No severe adverse events were observed during the initial hospital stay. There were no early revision surgeries during hospitalization. One patient in G1 underwent manipulation under anesthesia for stiffness on postoperative day 60, which did not improve in one of the two knees. There were no infections or other complications in G1. In G2, one case of infection of the prosthesis and two hemarthroses required surgical treatment. The mean KSS at the final follow-up was 158.4 for G1 and 155.6 for G2 ($P=0.6$). All patients who underwent simultaneous TKA stated that they were satisfied and would repeat the operation, but they described the first postoperative week as very difficult, with nearly total dependency.

4. Discussion

Simultaneous bilateral TKA is a serious operation that is indicated in patients with severe hemophilia due to the bilateral involvement, which is extremely incapacitating in young patients. In the general population, Reuben et al. observed a decrease of 36% in the cost of simultaneous bilateral TKA compared to two staged operations [16]. Odum et al estimated that the hospital costs of simultaneous bilateral TKA were 45,000 $ compared to 72,000 $ for a series of 2 operations [17].

In patients with severe hemophilia presenting with involvement of both knees, the cost of replacement therapy for simultaneous bilateral TKA is nearly twice as inexpensive as that for staged bilateral TKA. The savings are even greater in patients with inhibitors, for whom the cost of replacement therapy is especially high: the estimated cost in the literature of a single TKA in these cases is more than 850,000 $ [12] which is comparable to the results in our study. The total length of the hospital stay was also nearly twice as short and the sick leave was also significantly reduced. The