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Treatment of Periprosthetic Knee Infection With a Two-stage Protocol Using Static Spacers

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Abstract

Background Two-stage exchange arthroplasty is a standard approach for treating total knee arthroplasty periprosthetic joint infection in the United States, but whether this should be performed with a static antibiotic spacer or an articulating one that allows range of motion before reimplantation remains controversial. It is unclear if the advantages of articulating spacers (easier surgical exposure during reimplantation and improved postoperative flexion) outweigh the disadvantages of increased cost and complexity in the setting of similar rates of infection eradication.

Questions/purposes The purposes of this study were (1) to determine the ultimate range of motion; and (2) to determine the proportion of patients who remained free of infection at a minimum 2 years after treatment with static antibiotic spacers as part of a two-stage revision TKA for the treatment of periprosthetic joint infection.

Methods Between 1999 and 2011, we treated 121 patients with chronically infected TKAs, of whom three had medical comorbidities precluding a two-stage exchange, four had died before 2-year followup for reasons other than the surgical intervention, and seven were lost to followup. The remaining 107 patients (109 knees; 53 men and 54 women) were treated using a two-stage approach with static spacers and are evaluated here at a mean of 3.7 years (range, 2.0–9.8 years); no patients were treated with articulating spacers during this study period. Twenty-five percent (27 of 109) of the organisms isolated the first-stage procedure were resistant to methicillin and/or vancomycin. Median age at the time of reimplantation was 67 years (range, 42–89 years). Range of motion was measured by an independent physical therapist with a standard goniometer. Knee Society knee and function scores were calculated before the first stage and at the 2-year mark. Because many of these patients were treated before consensus definitions

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
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of infection were established, we made the diagnosis of infection (and established that a patient was believed to be free of infection) using the approaches prevalent at that time, which generally included presence of a sinus tract communicating directly with the implant, two positive tissue cultures, or a combination of cultures, fluid analysis, and serology.

Results Postoperatively, 67 knees had full extension and no patients had a flexion contracture > 10°. Median flexion was 100° (range, 60°–139°). Thirty-nine knees had postoperative flexion > 120°. Ninety-four percent of patients were clinically free of infection at last followup.

Conclusions Our two-stage exchange protocol with static spacers yielded comparable flexion and infection eradication when compared with other recent studies that have used articulating spacers. The large proportion of resistant organisms is alarming. Future multicenter studies should compare static with articulating spacers and should evaluate both cost and efficacy, because our study suggests that adequate range of motion can be achieved without the added cost of the articulating spacer.

Level of Evidence Level IV, therapeutic study.

Introduction

One of the most devastating reasons for revision TKA is periprosthetic joint infection (PJI), representing 16% to 27% of all revision TKAs in recent series [2, 4, 6, 16, 17, 21, 22]. Although various surgical approaches for eradicating infection are used around the world, two-stage exchange arthroplasty is the gold standard for treating TKA PJI in the United States. The general protocol involves removal of all components, thorough débridement, and placement of an antibiotic-laden cement spacer with subsequent extended intravenous and sometimes oral antibiotics. Revision arthroplasty is then conducted after presumed eradication of infection.

Although there is much variation, antibiotic cement spacers fall into two general categories, either static or articulating. There is controversy about whether static or articulating antibiotic spacers are superior to one another.

Emerging data suggest that articulating spacers offer comparable rates of infection eradication, improved postoperative flexion, and easier surgical exposure when compared with static spacers, albeit at a higher cost and complexity [8, 10, 14, 20, 23]. By contrast, potential advantages of static spacers include lower cost, ease of implantation, and facilitation of wound immobilization whereby tenuous soft tissues, bone deficiency, and extensor mechanism compromise may be better managed. By contrast, because restoration of ROM is one of the most critical factors associated with patient satisfaction [18], those in favor of articulating spacers tout the theoretical advantages of easier surgical approaches at the time of reimplantation and superior postreimplantation ROM [5]. In any case, the supposed benefits of using an articulating spacer remain unsubstantiated by available studies beyond 2-year followup [5]. The recent 2013 Musculoskeletal Infection Society (MSIS) international consensus meeting on PJI endeavored to address these issues. Using the Delphi method, over 400 delegates from 52 countries critically assessed the available scientific data to create recommendations and guide therapeutic regimens. Using the available data, the consensus results indicated a "…non-significant trend in ROM improvement with articulating versus non-articulating spacers" at minimum 2 years followup (82% agreement) and "…the type of spacer does not influence the rate of infection eradication with the use of articulating or non-articulating spacers in the knee" (89% agreement) [5]. It appears imperative that further investigation into restoration of functional ROM and effective eradication of infection in two-stage exchange arthroplasty for PJI be undertaken to further delineate the most efficient means of treatment.

We therefore asked (1) what is the ultimate ROM; and (2) what is the proportion of patients who remained free of infection at a minimum 2 years after treatment with static antibiotic spacers as part of a two-stage revision TKA for the treatment of periprosthetic joint infection?

Patients and Methods

This was a retrospective case series performed with institutional review board approval. Between 1999 and 2011, we treated 121 patients with chronically infected TKAs, of whom three had medical comorbidities precluding a two-stage exchange, four had died before 2-year followup for reasons other than the surgical intervention, and seven were lost to followup. The remaining 107 patients (109 knees; 53 men and 54 women) were treated using a two-stage approach with static spacers and are evaluated here at a mean of 3.7 years (range, 2.0–9.8 years); no patients were treated with articulating spacers during this study period.

Demographics including patient age, sex, body mass index, and etiology of arthritis were recorded prospectively into our local register. ROM was recorded by a clinical physical therapist (SI) with a standardized goniometer. Knee Society scores (KSS) were calculated before the first stage and at the 2-year mark. Our colleagues in infectious disease comanaged our patients with regular clinical evaluation and physical examination, serial infectious laboratory monitoring, and guided titration of antibiotic regimens.

Because these patients were treated, in many instances, before the MSIS definitions for infection [19] were established, we made the diagnosis of infection (and established that a patient was believed to be free of infection) using the approaches prevalent at that time, which generally included presence of a sinus tract communicating directly with the implant, two positive tissue cultures, or one positive culture and three of the following: elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), elevated synovial fluid white blood count (WBC) and elevated synovial fluid polymorphonuclear cell percentage, positive histologic analysis of periprosthetic tissue (> five polymorphonuclear cells in five high-powered fields), or gross purulence in the joint. Patients were considered free of infection at last followup if the soft tissue envelope had healed and the knee was functioning satisfactorily.

Patients diagnosed with infection underwent a standardized treatment protocol. An aspiration of the affected joint was performed under sterile technique before the incision. Tissue samples were taken during resection and submitted for culture and pathology evaluation. Implants were removed followed by meticulous débridement of bone and soft tissues. A static antibiotic spacer was then fashioned using combinations or monotherapy with vancomycin, gentamycin, and tobramycin-impregnated polymethylmethacrylate and implanted. Patients were admitted as inpatients and received routine postoperative care. Intravenous antibiotics were subsequently administered and titrated per culture speciation. Treated patients were placed on antibiotics for at least 6 weeks followed by an antibiotic holiday of at least 2 weeks with subsequent aspiration and laboratory testing for inflammatory markers before undertaking second-stage reimplantation arthroplasty. All prostheses reimplanted were approved for this use by the US Food and Drug Administration.

An integral feature of our institutional protocol for addressing PJI is the involvement of our colleagues in infectious disease. Two attending physicians with subspecialty training in infectious disease with interest in musculoskeletal infection help direct management of our patients with PJI. These physicians assisted in following the clinical progression of each patient with regular laboratory and clinical assessment and titrated our therapeutic antibiotic regimens. Patients were transitioned to oral antibiotics if appropriate. Patients were followed regularly in our multidisciplinary clinic for a minimum of 2 years.

Additionally, our clinic incorporates an independent experienced physical therapist to guide rehabilitation and functional treatments. As part of the routine pre- and postoperative clinical visits, knee ROM was measured with a standard goniometer. ROM data were then entered into our database and used to calculate KSS. Preoperative knee ROM data were available on 74 knees. Preoperative ROM values were lacking in others because the same independent observer (our physical therapist) was not always available in the hospital to make these ROM measurements, because many were urgent hospital-to-hospital transfers from other centers. In addition, accurately quantifying ROM some patients with knee sepsis can be difficult as a result of patient guarding from intense pain.

Outcomes for ROM and effective infection eradication rates were determined following a standardized protocol. Assessment of preoperative ROM, interval status after two-stage exchange ROM, and ROM at 2-year followup was measured and recorded by an independent physical therapist using a standard goniometer. These values were incorporated to calculate KSS before undergoing spacer placement and then at 2 years after revision surgery. Our physical therapists provided tailored ROM and strengthening exercise instruction to each patient.

Pertinent patient data points were entered into an encrypted Excel Database (Microsoft, Redmond, WA, USA). Proprietary program applications were used to generate results for median age, body mass index, and ROM in our sample.

One hundred seven patients (109 knees) were included in the study. There were 53 men and 54 women. Median age at the time of reimplantation was 67 years (range, 42–89 years). Median body mass index was 29 kg/m^2 (range 20–56 kg/m^2). Indications for primary TKA were 67 (62%) knees for osteoarthritis, 27 (25%) knees for posttraumatic arthritis, and 15 (14%) knees for inflammatory arthritis (Table 1).

Staphylococcus species and *Streptococcus* species were the most common organisms isolated, representing 77 (71%) patients in total. *Staphylococcus* species alone represented 51% of patients (56 knees). Resistance to methicillin and/or vancomycin was detected in 27 of 109 (25%) of the organisms isolated from infected knees at the time of resection arthroplasty. Twenty of 27 (74%) of cultures yielded methicillin-resistant *Staphylococcus aureus* as the offending bacteria (Table 2). Sixty-eight knees received intravenous vancomycin either alone or in conjunction with other therapies as the initial treatment antibiotic. Patients received antibiotics postoperatively for a median of 11 weeks (range, 5–20 weeks). Only one patient received antibiotics for less than 6 weeks and only two patients did not undergo a 2-week antibiotic holiday before reimplantation surgery. Eradication of PJI before reimplantation was confirmed with laboratory evaluation of ESR, CRP, WBC, and repeat aspiration.

Results

Extension improved from a preoperative median of −5.0° (range, 0°–80°) to a median of 0° (range, 0°–35°) at latest

Table 1. Patient demographics

Sex	Mean age (years)	Mean body mass index (kg/m^2)	First TKA indication
Female (N = 54)			Osteoarthritis 67 (62%)
	67 (range, 42–89)	29 (range, 20–56)	Posttraumatic 27 (25%)
Male (N = 53)			Inflammatory 15 (14%)

Table 2. Organism isolates

Organism	Number of knees
Staphylococcus species	56 (51%)
Streptococcus species	21 (19%)
Methicillin-/vancomycin-resistant	27 (25%)
Methicillin-resistant *Staphylococcus aureus*	20/27 (74%)

Table 3. Range of motion

Motion	Before the first stage	2-year followup
Extension (degrees)	Median −5 (range, 0–80)	Median 0 (range, 0–35)
Full extension	34/74 knees (46%)	67/109 (62%)
Flexion (degrees)	Median 90 (range, 0–115)	Median 100 (range, 60–139)

followup. Sixty-seven knees had full extension at latest followup. Flexion improved from a preoperative median of 90° (range, 0°–115°) to a median of 100° (range, 60°–139°) at latest followup. At latest followup, one knee had a flexion contracture > 10°. Thirty-nine knees had postoperative flexion ≥ 120° (Table 3).

One hundred two of 109 knees (94%) were deemed free from infection clinically at latest followup. Knee Society knee scores improved from a preoperative median of 36 (range, 24–48) to a postoperative median of 86 (range, 65–98). Knee Society function scores improved from a preoperative median of 32 (range, 22–45) to a postoperative median of 85 (range, 61–97).

Discussion

One of the most devastating reasons for revision TKA is PJI, which has been found responsible for 16% to 27% of all revision TKAs in recent investigations [2, 17, 21, 22]. PJI has also been implicated as the primary culprit in early revision (< 2 years) [13, 17, 22]. Although various methods are used, two-stage exchange arthroplasty with an interim articulating or static antibiotic-laden bone cement spacer remains the gold standard for treating PJI in the United States. However, the indications for choosing articulating over static spacers remain unclear. In recent reports, it appears articulating spacers offer comparable rates of infection eradication, improved postoperative flexion, and easier surgical exposure when compared with static spacers, albeit at a higher cost and complexity [3, 15, 20, 23], and it has been noted that restoration of ROM is one of the most critical factors associated with patient satisfaction [18]. Importantly, however, some of the supposed benefits of articulating spacers remain unsubstantiated by the available literature at 2-year and greater followup [5]. Proponents of static spacers argue the low cost, ease of implantation, and facilitation of wound immobilization whereby tenuous soft tissues, bone deficiency, and extensor mechanism compromise may be addressed [7]. We therefore sought to evaluate our results using static spacers to treat patients with chronically infected TKAs with particular attention to ROM and infection eradication at a minimum followup of 2 years.

Our study had multiple limitations. A question in any retrospective study is that of selection bias; however, here, static spacers were used in 118 of 121 patients treated during the study period. The other three were treated with irrigation and débridement and insert exchange because they were deemed unfit for two major procedures. Second, we did not directly examine cost of individual implants or the overall cost of care, and without a contemporaneous control group, it would not be possible to do cost-effectiveness analysis. So although cost is a concern here, our study could not evaluate it. Third, the necessity of an extensile approach during reimplantation was not documented and thus metrics for ease of implantation were not available for review. Fourth, preoperative ROM data on many patients were never recorded. This is of limited importance here given that we did not aim to determine changes in ROM based on the treatment itself.

Using static spacers, we found ROM at a minimum of 2 years after surgery that was quite comparable to other studies that have used articulating spacers. Anderson et al. [1] retrospectively studied 25 knees with an articulating spacer that incorporated an autoclaved femoral component with a new polyethylene insert and reported similar ROM before (5°–112°) and after (2°–115°) the second surgical stage. Two systematic reviews have endeavored to elucidate differences in ROM with the use of static versus

Table 4. Comparison of results

Study	Number of knees	Static spacer	Articulating spacer	ROM static	ROM articulating	Mean Knee Society function static	Mean Knee Society function articulating	Cure percent static	Cure percent articulating
Current study	109	109	–	100° (median)	–	85	–	94	–
Voleti et al. [23]	1526	654	872	91° (mean)	101° (mean)	77	80	88	92
Pivec et al. [20]	1669	707	962	92° (mean)	100° (mean)	82	83	90	92

articulating spacers (Table 4). In 2013 Voleti et al. [23] compared seven Level III comparative studies and 32 Level IV case series and compared reinfection rates, ROM, functional scores, and complication rates. Articulating spacers yielded significantly greater range of knee motion after reimplantation (101° for articulating and 91° for static, $p < 0.001$); however, there was little difference in cure rates or functional scores. In 2014, Pivec et al. compared the results of 962 articulating spacers and 707 static spacers with mean 4 years followup. KSS were found to be similar, slightly favoring static spacers. ROM was improved in the articulating group (102° versus 90°) although no difference was found in reinfection, reoperation, or complication rates [20]. Although allowing knee ROM between stages may facilitate patient activity through a more mobile limb for the interval between stages, this has not been shown to provide consistent superior benefit at longer-term followup. The MSIS expert panel reviewed a total of 46 original articles and excluded case reports, review articles, and technical reports. The consensus indicated 89% agreement that "…articulating spacers provide better function than non-articulating spacers for the patient in between the stages of TKA. An articulating spacer is especially preferred for the patient who is likely to have a spacer in place for more than 3 months" [5]. However, at minimum of 2 years followup there was "…a non-significant trend in ROM improvement with articulating versus non-articulating spacers" (82% agreement) [5].

Our investigation found 102 of 107 (94%) treated knees were clinically free of infection. The MSIS consensus regarding elimination of infection indicated "…the type of spacer does not influence the rate of infection eradication with the use of articulating or non-articulating spacers in the knee" (89% agreement) [5]. Our results are similar to those observed in other investigations. Anderson et al. [1] retrospectively studied 25 knees with an articulating spacer that incorporated an autoclaved femoral component with a new polyethylene insert and reported that 4% of their patients developed reinfection [1]. Hofmann et al. demonstrated similar results in two series conducted in 1995 and 2005, but with a wide range of effective infection eradication with recurrence from 0% (1995) to 12% (2005) [11, 12]. Gooding et al. retrospectively reviewed 115 knees undergoing revision for chronic infection using a prefabricated articulating PROSTALAC spacer (Prosthesis of Antibiotic-Loaded Acrylic Cement; DePuy, Warsaw, IN, USA) and found eradication of infection in 101 (88%) of knees at last followup [9]. As discussed previously, two systematic reviews conducted by Voleti et al. and Pivec et al. failed to elucidate significant differences in the rate of long-standing infection eradication when comparing articulating and nonarticulating spacers [20, 23]. It appears both methods represent reasonable strategies for overall treatment of infection. However, concerns of cost, ease of reimplantation, preservation of the soft tissues, and maintaining an intact extensor mechanism remain pertinent.

Our study revealed consistently effective results in treating infection and preserving or improving postreimplantation ROM. Future multicenter studies should prospectively compare static with articulating spacers and should evaluate both cost and efficacy, because our study suggests that adequate ROM can be achieved without the added cost of an articulating spacer.

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