

Evaluation of Preoperative Cultures Before Second-Stage Reimplantation of a Total Knee Prosthesis Complicated by Infection

A COMPARISON-GROUP STUDY*

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Abstract

Background: Two-stage reimplantation has proven to be highly successful in the treatment of patients with infection at the site of a total knee arthroplasty. However, up to 20 percent of patients have a recurrence of infection following this treatment. The purpose of our study was to determine whether aspiration of the affected joint and culture of the specimen, performed before reimplantation and after discontinuation of antibiotic therapy, would help to identify patients who might have a recurrent infection.

Methods: We prospectively followed sixty-nine patients who were treated for a culture-proven deep infection at the site of a total knee arthroplasty. Group I consisted of thirty-five patients who were treated with removal of the prosthetic components and irrigation and débridement of the joint, followed by six weeks of antibiotic therapy and reimplantation of a prosthesis. Group II was composed of thirty-four patients who were treated with removal of the components and irrigation and débridement of the joint, six weeks of antibiotic therapy, and then repeat culture four weeks after the antibiotic course had ended. If the culture was negative, the patient was managed with a second-stage reimplantation of a prosthesis. If the culture was positive, the protocol was repeated, beginning with irrigation and débridement. The two groups were similar with regard to male-to-female ratio, age, preoperative Knee Society scores, time since primary surgery, types of infectious organisms, duration of symptoms, duration of follow-up, and number of previous revisions. All of the patients were evaluated clinically with use of the objec-

tive scoring system of the Knee Society and were followed with serial radiographs. Success was defined as no infection and a functional prosthesis, with a Knee Society score of at least 75 points at the last (thirty-six-month-minimum) follow-up evaluation.

Results: Of the thirty-five patients in Group I, five (14 percent) had recurrence of infection. One of the patients was managed with a successful second-stage revision, three were managed with arthrodesis of the knee, and one continued with chronic antibiotic suppressive treatment. Of the thirty-four patients in Group II, three (9 percent) had a positive culture after the course of antibiotics. The protocol was repeated for all three, and they subsequently had a successful second revision. One other patient (3 percent) in Group II, who had a negative culture, had a recurrent infection and was eventually managed with arthrodesis of the knee.

Conclusions: Prerevision cultures, grown after discontinuation of antibiotic treatment and before reimplantation of the components, helped to identify the patients with infection at the site of a total knee arthroplasty in whom the infection might recur. The performance of aspiration and cultures resulted in a substantial improvement in the clinical outcome.

Two-stage revision arthroplasty^{1-3,9,12,17,20,26,28} appears to be the most successful treatment for late hematogenous, deep infection. The first stage consists of irrigation and débridement of the infected joint with removal of the prosthesis. Often, an antibiotic-loaded cement spacer is used to increase available levels of antibiotics and to prevent contracture of the joint space. The patient is subsequently treated with a course of intravenous antibiotics (usually six weeks) and then is returned to the operating room for implantation of the prosthesis. This strategy has proven reliable in the treatment of infections at the sites of total knee arthroplasties, with successful eradication of 80 to 100 percent of the infections in series of twenty to sixty patients^{15,17,26,28}. Despite this success, between 3 and 20 percent of patients managed with two-stage revision have a recurrence of the infection. In most series reported in the literature, the prosthesis was reimplanted without the performance of additional cultures of specimens from the joint before

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TABLE I
COMPARISON OF POSTOPERATIVE PARAMETERS OF THE TWO TREATMENT GROUPS*

Parameter	Group I (N = 35)	Group II (N = 34)	P Value†
Duration of follow-up‡ (<i>mos.</i>)	68 (36-114)	58 (36-91)	NS
No. of patients with recurrent infection	5 (14%)	1 (3%)§	<0.05
No. of procedures per patient‡	2.7 (2-4)	2.8 (2-4)	NS
No. of patients with Knee Society score ≥ 75 points	32 (91%)	33 (97%)	NS
Knee Society score of infection-free knees‡ (<i>points</i>)	86 (80-95)	88 (64-98)	NS

*Culture of the aspirate and culture of the affected joint were performed before reimplantation and after discontinuation of antibiotic therapy in Group II but not in Group I.

†NS = not significant.

‡The values are given as the mean, with the range in parentheses.

§Three patients had a recurrent infection before reimplantation, and the joints were debrided.

the discontinuation of antibiotic therapy^{26,28}.

In our study, we examined the role of preoperative cultures performed at least four weeks after antibiotic therapy had been discontinued. Patients with positive cultures were treated with more irrigation and débridement and a second course of antibiotics; revision was performed only when preoperative cultures were negative. The goal of our study was to see whether this approach reduced the morbidity and increased the successful outcome of treatment of infection at the site of a total knee arthroplasty when compared with a standard method of two-stage reimplantation without culture before the reimplantation.

Materials and Methods

Sixty-nine consecutive patients with a deep infection following total knee arthroplasty that was treated with two-stage revision arthroplasty between January 1, 1989, and December 31, 1993, were prospectively followed. The deep infections developed from one to ninety-seven months after the index knee arthroplasty. Demographic information such as preoperative history, operative findings, and postoperative course were obtained from hospital and outpatient records and recorded. In addition, preoperative and postoperative radiographs, nuclear medicine scans, laboratory findings, and culture results were reviewed. Anteroposterior and lateral radiographs were made annually to check for progressive radiolucencies or migration of the prosthesis. The patients were divided into two groups depending on the treatment protocol, which was selected solely on the basis of the preference of one of the two senior surgeons (M. A. M. or D. S. H.) and not on the basis of the severity of the infection or any other factors. The patients in Group I were managed by one surgeon, and the patients in Group II were managed by the other surgeon. The objective clinical rating system of the Knee Society¹⁴ was used to follow the patient's clinical course, and the radiographic scoring system of the Knee Society⁶ was used to assess postoperative radiographs.

Study Groups

Group I consisted of thirty-five knees treated with removal of the components, irrigation and débridement of the joint, six weeks of intravenous antibiotics, and reimplantation of a total knee prosthesis. Group II was composed of thirty-four knees treated with removal of the components, irrigation and débridement, six weeks of intravenous antibiotics, and cultures of material obtained from one knee-joint aspiration performed four weeks after completion of the antibiotic therapy. If the culture was negative after two weeks, the patient underwent reimplantation. If the culture was positive, the patient was managed with repeat irrigation and débridement of the joint and then was reentered into the protocol. The operative procedure was similar for all

of the patients. The joint was extensively debrided of all grossly infected tissue; the débridement included a complete synovectomy. The components were removed, and the bone surfaces were aggressively curetted. A cement spacer impregnated with two grams of tobramycin (one gram per pack of cement) was placed loosely into the joint, and the wound was closed over two suction drains. For all of the patients, intravenous antibiotics were chosen after consultation with the infectious disease service. Antibiotic levels were carefully monitored, and a bactericidal titer of at least 1:8 was maintained for the six-week course. As mentioned, the treatment protocol was determined preoperatively solely by the preference of the attending surgeon.

Demographics

Group I consisted of seventeen men and eighteen women. The mean age of the patients at the time of infection was sixty-four years (range, forty-six to eighty years). The mean time from the index arthroplasty until the diagnosis of infection was thirty-three months (range, two to ninety-seven months). The mean duration of symptoms until diagnosis was forty-eight days (range, one to 138 days). There were thirty-one primary and four revision arthroplasties. All knees had a late deep infection proven on culture. The mean duration of follow-up was sixty-eight months (range, thirty-six to 114 months).

Group II consisted of sixteen men and eighteen women. The mean age of the patients at the time of infection was sixty-nine years (range, fifty-six to eighty-two years). The mean time from the index arthroplasty until the diagnosis of infection was thirty-five months (range, one to eighty months). The mean duration of symptoms until the diagnosis was fifty-six days (range, four to 322 days). There were thirty primary and four revision arthroplasties. All knees had a late deep infection proven on culture. The mean duration of follow-up was fifty-eight months (range, thirty-six to ninety-one months).

There was no significant difference between the two groups in terms of the male:female ratio, age, preoperative Knee Society score, time from the index arthroplasty until the diagnosis of infection, types of infectious organisms, duration of symptoms before diagnosis, number of previous revisions, or duration of follow-up ($p > 0.05$).

Treatment

At the time of reimplantation, all patients had careful débridement of the affected joint, removal of the cement spacer, and reinsertion of a knee prosthesis. All prostheses were fixed with cement impregnated with antibiotics (tobramycin, one gram per pack). If a patient was found to be free of infection at the time of reimplantation (with negative gram stains and specimens that were completely free of polymorphonuclear leukocytes), no antibiotics were given. If a knee was found to have a persistent infection (polymorphonuclear leukocyte counts of ten or more cells per high-power field), it was debrided again, another course of antibiotics was given, and the patient was reentered into the protocol. The patients were followed with yearly physical and radiographic examinations, and data from the most recent follow-up evaluation were recorded as the final re-

TABLE II
PATIENT DATA FOR GROUP I

Case	Gender, Age at Infection (yrs.)	Time from Index Op. to Diagnosis (mos.)	Type of Arthroplasty	Findings on Culture	Durat. of Symptoms Prior to Diagnosis (days)	Outcome	Knee Society Score at Final Follow-up (points)	Durat. of Follow-up (mos.)
1	M, 64	37	Primary	<i>S. aureus</i>	54	Success	84	60
2	F, 62	42	Primary	<i>Strep. pneumoniae</i>	1	Success	87	48
3	F, 58	23	Primary	β -hemolytic strep.	24	Success	80	56
4	F, 56	2	Primary	β -hemolytic strep.	4	Failure	64	36
5	M, 46	6	Primary	<i>S. aureus</i>	77	Success	80	40
6	F, 59	23	Primary	<i>S. aureus</i>	45	Success	93	65
7	M, 63	22	Primary	<i>S. aureus</i>	78	Failure	82	51
8	F, 60	8	Primary	<i>S. aureus</i>	44	Success	80	92
9	M, 58	5	Revision	<i>E. coli</i>	53	Success	86	60
10	M, 64	24	Primary	<i>S. aureus</i>	22	Success	94	92
11	M, 57	4	Primary	Mixed gram-negative organisms	49	Success	90	61
12	F, 62	83	Primary	<i>Strep. viridans</i>	8	Failure	58	69
13	M, 55	48	Primary	<i>S. epidermidis</i>	79	Success	81	70
14	F, 74	43	Revision	<i>S. aureus</i>	47	Success	90	69
15	M, 67	61	Primary	<i>S. epidermidis</i>	36	Success	80	56
16	F, 68	40	Primary	<i>S. aureus</i>	130	Success	94	57
17	M, 75	49	Primary	<i>S. aureus</i>	18	Success	85	68
18	F, 64	97	Primary	<i>P. aeruginosa</i>	74	Success	84	89
19	M, 76	24	Primary	<i>S. aureus</i>	138	Success	86	60
20	F, 63	63	Primary	<i>Enterococcus</i>	9	Failure	61	57
21	M, 66	35	Primary	<i>S. epidermidis</i>	120	Success	81	85
22	M, 70	44	Revision	<i>S. aureus</i>	53	Success	80	114
23	F, 80	61	Primary	<i>K. oxytoca</i>	8	Success	92	70
24	M, 71	22	Primary	<i>S. aureus</i>	62	Failure	95	88
25	M, 66	20	Primary	<i>S. aureus</i>	49	Success	95	69
26	F, 65	6	Primary	<i>S. aureus</i>	80	Success	90	66
27	M, 71	12	Revision	<i>S. aureus</i>	9	Success	81	86
28	F, 72	42	Primary	<i>S. epidermidis</i>	20	Success	87	96
29	M, 73	29	Primary	<i>S. epidermidis</i>	49	Success	85	92
30	F, 64	18	Primary	<i>P. mirabilis</i>	76	Success	83	84
31	M, 65	3	Primary	<i>S. aureus</i>	10	Success	88	47
32	F, 52	33	Primary	<i>S. epidermidis</i>	51	Success	89	52
33	F, 53	63	Primary	<i>S. aureus</i>	20	Success	87	68
34	F, 54	17	Primary	<i>S. aureus</i>	19	Success	90	44
35	F, 65	46	Primary	<i>S. epidermidis</i>	50	Success	83	64

sults in this report. The reimplantation was considered a success when the objective Knee Society score was 75 points or more and the patient was free of infection at the time of the most recent follow-up.

Data Analysis

The primary issue was whether performing preoperative aspiration and culture had a significant effect on the rates of reinfection and successful clinical outcomes following two-stage revision arthroplasty. The null hypothesis suggested that performing preoperative aspiration and culture would have no effect on the rate of reinfection or on the final clinical outcome. Differences in frequencies of infection between Groups I and II were analyzed with the chi-square test. Differences in Knee Society scores were analyzed with the two-tailed Student t test.

Results

Group I (Tables I and II)

Of the thirty-five patients in Group I, thirty (86 percent) had no recurrence of infection. These patients all had a well functioning prosthesis and were free of infection at the most recent follow-up evaluation. Of the five patients (14 percent) who had a recurrence of infection, one was managed with repeat delayed exchange arthroplasty. At the time of the last (fifty-one-month) follow-up, this patient had retained the second revision prosthesis, was free of apparent infection, and had a Knee Society score of 82 points. Three of the other pa-

TABLE III
PATIENT DATA FOR GROUP II

Case	Gender, Age at Infection (yrs.)	Time from Index Op. to Diagnosis (mos.)	Type of Arthroplasty	Findings on Culture	Durat. of Symptoms Prior to Diagnosis (days)	Outcome	Knee Society Score at Final Follow-up (points)	Durat. of Follow-up (mos.)
1	M, 70	34	Primary	<i>S. epidermidis</i>	29	Success	84	58
2	M, 67	60	Primary	<i>S. epidermidis</i>	30	Success	85	48
3	F, 62	1	Primary	<i>S. aureus</i>	4	Success	87	68
4	F, 56	2	Primary	<i>P. mirabilis</i>	15	Success	84	60
5	M, 63	46	Revision	<i>S. epidermidis</i>	16	Success	91	91
6	F, 65	36	Primary	<i>S. aureus</i>	3	Success	93	67
7	F, 64	22	Primary	<i>S. aureus</i>	62	Failure	64	48
8	M, 61	74	Primary	<i>S. epidermidis</i>	30	Success	92	36
9	F, 60	4	Revision	<i>S. aureus</i>	50	Success	89	62
10	M, 69	27	Primary	<i>S. aureus</i>	160	Success	86	58
11	M, 58	54	Primary	<i>S. epidermidis</i>	20	Success	76	69
12	M, 68	24	Primary	<i>S. aureus</i>	64	Success	89	56
13	F, 68	30	Primary	Mixed gram-negative organisms	4	Success	90	36
14	M, 59	6	Primary	<i>S. aureus</i>	60	Success	87	68
15	M, 69	23	Primary	<i>Strep. viridans</i>	52	Success	90	60
16	F, 70	3	Primary	<i>S. aureus</i>	58	Success	90	76
17	M, 70	15	Revision	<i>K. oxytoca</i>	83	Success	91	59
18	F, 59	76	Primary	<i>S. aureus</i>	108	Success	77	59
19	M, 64	20	Primary	<i>S. aureus</i>	82	Success	87	90
20	F, 80	80	Primary	<i>S. epidermidis</i>	322	Success	97	58
21	M, 77	2	Primary	<i>S. aureus</i>	20	Success	94	74
22	F, 80	27	Primary	<i>S. aureus</i>	14	Success	95	57
23	F, 71	64	Primary	<i>S. epidermidis</i>	54	Success	78	36
24	M, 76	36	Revision	Group-B β -hemolytic strep.	98	Success	85	48
25	F, 82	24	Primary	<i>S. aureus</i>	86	Success	90	60
26	M, 79	76	Primary	<i>S. aureus</i>	29	Success	80	55
27	F, 69	36	Primary	<i>S. epidermidis</i>	4	Success	95	59
28	F, 78	48	Primary	<i>S. aureus</i>	20	Success	95	36
29	F, 72	62	Primary	<i>Strep. viridans</i>	85	Success	84	56
30	M, 75	34	Primary	<i>E. coli</i>	86	Success	98	78
31	F, 74	50	Primary	<i>S. aureus</i>	3	Success	80	60
32	F, 68	40	Primary	<i>S. epidermidis</i>	48	Success	80	36
33	M, 69	34	Primary	<i>P. aeruginosa</i>	89	Success	88	57
34	F, 74	9	Primary	<i>S. aureus</i>	30	Success	89	48

tients who had recurrent infection had successful arthrodesis of the knee²⁴. One patient continued with chronic antibiotic suppression and did not undergo removal of the revision prosthesis. The mean time to reinfection was four months (range, two to six months). All reinfections were from the organism that had caused the initial infection, although in three of the five patients the sensitivities of the organism to antibiotics had changed. The mean postoperative Knee Society score associated with successful clinical outcomes was 86 points (range, 80 to 95 points). The mean knee flexion at the time of the latest follow-up in the patients with initial eradication of

the infection was 95 degrees (range, 30 to 122 degrees), and the mean extension was -5 degrees (range, 0 to -10 degrees).

Group II (Tables I and III)

Of the thirty-four patients in Group II, thirty-one (91 percent) had a negative culture after the course of antibiotics had ended. These patients were managed with second-stage total knee arthroplasty after the negative culture was obtained. Thirty of the thirty-one patients were free of infection and had a functioning prosthesis at the time of the last follow-up. One patient

had a recurrent infection after the second-stage revision; the infection was caused by *Staphylococcus aureus*; this was different from the initial infecting organism, which was a streptococcus species. This patient eventually had a knee arthrodesis²⁴. The three patients (9 percent) who had a positive culture were managed with six weeks of intravenous antibiotics after more operative débridement. All three had the same infecting organisms as they had had preoperatively, although the sensitivities to antibiotics had changed. The three patients subsequently had a negative culture and a successful revision arthroplasty.

The mean postoperative Knee Society score for all of the knees in Group II was 87 points (range, 64 to 98 points). At the time of the final follow-up, the mean knee flexion in the patients with initial eradication of the infection was 98 degrees (range, 63 to 130 degrees), and the mean extension was -4 degrees (range, 0 to -12 degrees).

There were no signs of loosening, on the most recent postoperative radiographs, of any of the surviving prostheses in either group. No prosthesis had migrated compared with the position seen on postoperative radiographs. Three revision femoral components showed partial, nonprogressive radiolucent lines anteriorly (in zone 1) on the lateral radiograph. Two prostheses had partial, nonprogressive radiolucent lines under the medial tibial tray (in zones 1 and 2) on the anteroposterior radiograph.

Discussion

The optimum treatment for an infection complicating total knee arthroplasty continues to be controversial. An ideal treatment would entail a minimum of surgical procedures, an acceptable level of joint function during the treatment, and a high rate of success. Each method represents a tradeoff between the success rate and the morbidity of the treatment itself. Protocols that include retention of the affected components seek to reduce the need for additional surgical treatment and the period of disability. These procedures include arthroscopic irrigation and débridement^{8,25}, open irrigation and débridement^{4,5,18,22,23}, as well as one-stage revision arthroplasty^{7,10,11}. Unfortunately, the high rates of reinfection seen with these methods have been disappointing.

Two-stage revision arthroplasty is the most commonly reported alternative. This method involves removal of the prosthesis followed by at least six weeks of antibiotics. Studies of two-stage revision have demonstrated the most consistent and successful results. Windsor et al.²⁸ reported a success rate of 97 percent (thirty-two) of the thirty-three knees treated. Borden and Gearen⁴ reported success in ten of eleven knees treated with two-stage revision. Even with these uniformly successful results, reinfections do occur. The most likely source of reinfection is bacteria retained in the joint following the first-stage débridement. Bac-

terial resistance, inadequate débridement, or a new infection may account for persistence of infection in some cases.

Rationale for Prerevision Cultures

Despite the superior clinical results obtained with two-stage arthroplasty in a number of centers, there may be modifications that can improve this method. Preoperative cultures may be a sensitive way of detecting persistent infection. A number of recommendations have been made regarding these cultures¹⁶. Insall et al.¹³ recommended that antibiotic therapy be stopped and then cultures be performed before revision arthroplasty. Other authors have recommended that cultures be performed while the patient is receiving antibiotic therapy or have believed that there should be no aspiration at all before a revision procedure²⁶⁻²⁹. Any joint that becomes reinfected following revision may have harbored bacteria that were suppressed by the antibiotic course. These joints show few or no clinical signs of continued infection, and intraoperative sampling may not be helpful because of low bacterial counts. Allowing four weeks off antibiotics before culture of specimens from the joint gives any bacteria present an opportunity to proliferate and potentially to be detected by culture of the aspirate. This technique also allows a period for clinical symptoms from bacterial proliferation, if present, to manifest themselves. The disadvantage of repeat cultures is a delay in definitive operative treatment as well as the prolonged morbidity associated with a minimally functioning knee joint. Many patients with an infection at the site of a prosthesis are often those who are least able to tolerate a long period of relative immobility^{19,21}. In the current study, there were no significant differences between groups with regard to the most recent follow-up scores of the knees with successful reimplantation; this finding indicates that the delay in treatment had no long-term effects.

One weakness in our study is the lack of randomization of the patients. The patients were managed according to the protocol of the two senior surgeons, and differences in their approaches may account for the reported results. However, all of the patients were managed with similar operative techniques, operating-room teams, equipment, and assistant surgeons. Since all six recurrences happened after less than one year of follow-up, the minimum three-year follow-up used in this study should have been adequate to detect all persistently infected joints.

Two-stage revision arthroplasty was found to be an effective method for treating infection after total knee arthroplasty. This study suggests that prerevision cultures, after the discontinuation of antibiotic treatment, should be performed in all patients treated with this procedure. With identification of continuing infection, the morbidity associated with recurrent infection may be avoided and the number of surgical procedures may be reduced.

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