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Outcomes of Revision Total Knee Arthroplasty After Methicillin-resistant Staphylococcus aureus Infection

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Abstract

Background The incidence of infection by methicillin-resistant Staphylococcus aureus (MRSA) in total knee arthroplasty (TKA) is becoming a more frequent concern, as increased morbidity following TKA has been reported for infections by resistant organisms. This study investigates whether MRSA infections are associated with decreased functional scores.

Questions/purposes We therefore compared the functional scores, operative times, and rates of reinfection of revision TKA following MRSA infection versus other indications for revision.

Methods We retrospectively reviewed charts of 101 patients (103 knees) who underwent mobile bearing TKA revision from January 2003 to September 2006, with a minimum clinical followup of 2 years in 45 knees (44%). We obtained the following indices: WOMAC, Activities of Daily Living Score (ADLS), SF-36, and Knee Society scores (KSS). Three groups of revisions were compared: MRSA infection (n = 6), non-MRSA infection (n = 9), and aseptic failure (n = 30). The three groups were similar in demographics and comorbidities.

Results The MRSA (166 minutes) and non-MRSA groups (149 minutes) had longer operative times than the aseptic group (121 minutes). With numbers available, there were no differences in ROM, WOMAC, ADLS, KSS, and SF-36, with MRSA separate or combined with all infections. Infection recurrence between MRSA-infected knees and non-MRSA-infected knees was similar.

Conclusions While our study was underpowered to detect functional differences between MRSA-infected knees and non-MRSA-infected knees it does add data to the literature. Knees revised for infection have longer operative times and more frequent infection after revision. The reason for increased operative times is unclear.

Level of Evidence Level III, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

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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; our ethical board did not require informed consent for participation in the chart review portion of this study. Informed consent for participation in the study was obtained for those patients participating in the clinic visit portion of the study.
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Introduction

Infection in TKA is a serious complication causing considerable morbidity for the patient and, in the most severe cases, can even lead to loss of life or limb. Of the approximately 300,000 primary TKAs performed in the Unites States every year, approximately 1% to 4% become infected depending on a variety of factors, including the immune status [21, 29] and comorbidities of the patient [3, 19, 24, 33], the intraoperative time [24], and the proper use of prophylactic antibiotics [8, 15]. Treatment of acute joint sepsis can potentially be salvaged with aggressive débridement and antibiotic therapy [4, 7, 17, 28]. Chronically infected joints, however, generally require two-stage treatment with removal of the infected prosthesis, treatment with intravenous and local antibiotics, and replantation once infection is eradicated [4, 10, 16]. Several studies have reported functional score differences among patients undergoing revision TKA for prosthetic failure and those undergoing revision TKA for primary TKA infection [2, 6, 31]. Barrack et al. and Wang et al. described decreased knee society scores after revision TKA for septic indications relative to revision for aseptic reasons [2, 31]. In a comparative study, Ghanem et al. demonstrated revision TKA for septic and aseptic indications had similar WOMAC and SF-36 scores [6].

Methicillin-resistant Staphylococcus aureus (MRSA) infections are a growing problem with serious effects on mortality, morbidity, and economics [1, 5, 12, 25]. Engemann et al. demonstrated a 1.19-fold increase in cost associated with MRSA surgical site infection compared with methicillin-sensitive S. aureus [5]. Similarly, MRSA infections of joint arthroplasties have been recognized as a growing problem, prompting many orthopaedic surgeons to delay surgery if a nasal swab is positive for MRSA [27]. Kilgus et al. demonstrated a lower rate of retention of the revision TKA (with no future need for surgery) either after irrigation and débridement or after two-stage reimplantation following infection with resistant organisms [14]. Rates of retention were also studied in later studies, and the rate tended to be higher [9, 16, 20, 26, 30]. We have observed one common response of the joint to MRSA sepsis is hypertrophic scarring, and we presume this process causes increased technical difficulties in joint replantation and worse functional scores.

The purposes of this study are to (1) compare the functional scores of the three groups of TKA revisions: MRSA-infected, non-MRSA infected, and aseptic revisions, as well as a secondary aim of comparing all septic revision to all aseptic revisions; (2) compare the operative times between the three groups of TKA revisions; and (3) compare rates of reinfection between patients in our study.

Patients and Methods

We retrospectively reviewed all 101 patients (103 knees) who underwent a mobile bearing revision of a primary TKA at the University of Pittsburgh Medical Center from January 2003 to September 2006. All patients who received a mobile bearing joint for revision TKA (LCS Revision femur, MBT tibia; DePuy Orthopaedics, Warsaw, IN) were included in the study whether for a septic or aseptic etiology. We excluded one patient who did not have a mobile bearing joint used for revision during this period. Of the 103 revision TKAs, 56 had a revision procedure for an aseptic indication, and 47 underwent revision for a septic cause. Of the 47 septic knees, 10 had MRSA-positive cultures. Of the 101 patients (103 knees) at the start of the study, we excluded 27 patients (27 knees) because of one of the following "end points": death, severe dementia, amputation of the affected leg, rerevision, or fusion. These included one patient with severe dementia, one fusion, 15 rerevisions, nine deaths, and one patient with an above-knee amputation (MRSA-infected). Of the remaining 74 patients (76 knees) after exclusions, 11 patients were lost to followup (did not reply to requests through the postal service or to phone calls) when contacted for the specialized research visit starting in June 2008. Of the remaining 63 patients (65 knees) after exclusions and those lost to followup, 12 patients (12 knees) refused to participate, and eight patients (eight knees) were contacted, were willing to participate, but did not make any visits to the clinic. Forty-three patients (45 knees, 59% of the eligible 76 knees) remained after 27 patients were excluded, 11 patients were lost to followup, 12 patients refused to participate, and eight did not make any clinic visits; for those these 43 patients (45 knees), we had a minimum clinical followup of 2 years (average, 3.3 years; range, 2 to 5.7 years). Of these 45 knees, six had a MRSA infection, nine had non-MRSA infections, and 30 had aseptic indications. The average age across the three groups was similar. Likewise, there was no difference in gender, body mass index (BMI), or comorbidities (Table 1). In order to recognize any bias in our data due to having just 59% followup in the eligible knees, we compared demographics, comorbidities, and 6-month ROM between those patients who did not participate versus those patients who either met end points or did participate; the only difference in any of these measures was the BMI was higher in those patients who had followed up at the specialized research visit (Table 2). We obtained prior Institutional Review Board approval for both the chart review and the specialized clinic visit.

Serum erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were examined, and arthrocentesis was performed preoperatively if effusion was present. Cultures were taken, both aerobic and anaerobic, and were

Table 1. Patient demographics, comorbidities, and ROM at 6 months and grouped by indication for revision

Number, demographics, and characteristics of patients	MRSA	Non-MRSA	Aseptic	p Value
Patients, number	9	37	55	—
Knees, number	10	37	56	—
Age, mean years (SD, number)	71.3 (9.1, 10)	63.0 (1.3, 37)	67.4 (1.1, 56)	0.11
Female gender, number	4	20	30	0.77
Male gender, number	6	17	26	0.77
Body mass index, mean kg/m^2 (SD, number)	38.3 (12.7, 6)	30.7 (7.5, 21)	34.2 (7.3, 39)	0.18
Number of comorbidities, mean (number)	2.0 (10)	2.43 (37)	1.77 (56)	0.123
6-month total ROM (SD, number)	85.0 (30.8, 6)	102.8 (19.3, 18)	101.5 (23.5, 29)	0.41
6-month extension (SD, number)	−11.7 (14.7, 6)	−2.4 (3.8, 18)	−3.1 (6.8, 28)	0.28
6-month flexion (SD, number)	96.7 (21.6, 6)	105.4 (17.5, 18)	103.8 (18.8, 28)	0.62

MRSA = patients revised after a methicillin-resistant Staphylococcus aureus infection; non-MRSA = patients revised after a non-MRSA infection; Aseptic = patients revised for noninfectious etiologies.

Table 2. Demographics, comorbidities, and early motion are compared between those with followup versus those without followup

Number and characteristics of patients	Had followup	No followup	p Value
Knees, number	45	35	—
Miles from hospital	34.8	35.6	0.90
Age, mean years (SD)	66.3 (10.2)	65.3 (12.0)	0.69
Female gender, number	24	12	0.17
Body mass index, mean kg/m^2 (SD)	36.3 (7.5)	30.7 (7.0)	0.018
Number of comorbidities, mean	2.2	1.9	0.42
6-month total ROM (SD, number)	102.3 (24.7)	99.6 (21.8)	0.74

Had followup = those patients who presented at a specialized research visit to have outcomes assessed; no followup = those patients who were lost to followup, refused followup, or did not respond to a request to followup at a specialized research visit.

considered negative if there was no growth at 7 days. Acid fast bacteria cultures and fungal cultures were taken and considered negative if there was no growth after 1 month. Acute infection was defined as one of the following: purulence of the synovial fluid or at the implant site; growth of the same organism from two or more cultures (either synovial fluid or intraoperative tissue). Chronic infection was defined as one of the following: pain at rest, along with ESR and CRP elevation and loosening of the implant; chronic draining sinus; growth of the same organism on two or more cultures [23, 34].

All patients with infection underwent a two-stage revision with removal of the infected joint and placement of an antibiotic-laden, nonarticulating, polymethylmethacrylate spacer. Intraoperative frozen section analysis for acute inflammation was used as a final check before replantation.

Postoperatively, all patients were seen by physical therapy when they reached the hospital floor and assisted to a chair on the same day as surgery. Within 24 hours, patients were seen again by physical therapy and taught to walk and weight bear, as tolerated, to and from the hospital room restroom and down the hallway. After 24 to 48 hours postoperatively, patients were taken to the main physical therapy department where a complete and standard ROM protocol was begun. The in-house physical therapy was supervised and usually took at least 2 hours per patient per day. At discharge, physical therapy was ordered for 2 weeks at home and then for 6 weeks as an outpatient. All patients revised for infection were treated with 6 weeks of parenteral antibiotics with two patients requiring long-term suppression with parenteral followed by oral antibiotics.

The followup routine for patients included clinic visits at 2 weeks, 1 month, 3 months, 6 months, 12 months, and then annual postoperative visits. Clinical examinations and ROM were assessed at each visit. Radiographs were taken and assessed during the immediate postoperative period and also at 2 weeks, 1 month, 3 months, 6 months, 12 months, and annually thereafter. Data were gathered using paper charts, electronic medical records, and relevant imaging modalities. Data were collected on patient demographics and comorbidities, including age, gender, height and weight, active smoking, hypertension, diabetes, history

Table 3. Results of outcome measures are compared by indication for revision

Outcome measurements	MRSA	Non-MRSA	Aseptic	p Value
Post-ROM on clinic day (SD, number)	94.3 (37.8, 7)	100.2 (28.6, 10)	111.4 (22.3, 30)	0.50
WOMAC (SD, number)	19.3 (22.2, 6)	23.3 (14.4, 8)	20.2 (17.2, 28)	0.76
SF-36 physical components score (SD, number)	37.9 (16.7, 6)	34.2 (12.8, 9)	37.0 (11.6, 30)	0.78
SF-36 mental components score (SD, number)	50.5 (15.6, 6)	59.1 (8.7, 9)	59.4 (6.8, 30)	0.55
Knee Society score physician (SD, number)	66.0 (35.8, 6)	83.7 (14.9, 9)	75.9 (18.3, 30)	0.49
Knee Society score patient, (SD, number)	44.2 (25.6, 6)	59.4 (22.3, 9)	65.0 (28.7, 30)	0.15
Activities of daily living, (SD, number)	67.6 (30.1, 6)	64.8 (17.5, 8)	72.6 (18.8, 29)	0.59

MRSA = patients revised after a methicillin-resistant Staphylococcus aureus infection; non-MRSA = patients revised after a non-MRSA infection; Aseptic = patients revised for noninfectious etiologies.

of malignancy, heart disease, and lung disease. Data were collected on operative times, and outcomes after surgery were recorded. From the medical records, data were abstracted on ROM generating a database that showed the changes in ROM throughout the course of recovery. This database included measurements made after the revision until 2 years of followup was obtained. To gather data not available in the medical record, all patients not meeting an end point (74 patients) were asked to come back for a followup appointment. At this appointment, outcome data were collected using the following forms and questionnaires: WOMAC, SF-36 [32], Knee Society score (KSS) [11], and Activities of Daily Living (ADLs) [13]. Patients also underwent a physical examination to determine knee ROM and stability and underwent radiographic examination if due for their annual radiographs. These radiographic examinations were used to determine the KSS, for which varus and valgus measurements were needed. These functional assessments were obtained on 45 of the 76 knees (59%) that underwent revision TKAs, 30 of which were performed for aseptic loosening and the remainder being the result of infection. Of the 15 septic knees, six had MRSA identified as the causative organism, whereas the remaining nine had organisms other than MRSA.

Descriptive analysis, including mean, SD and univariate statistics were used to describe the three patient groups we looked at in this study: aseptic revisions, MRSA-negative septic revisions, and MRSA-positive septic revisions. The same approach was used to compare those patients who did and did not return for followup at the specialized research visit. Analysis of variance (ANOVA) was used to compare demographic data among the three treatment groups and between those patients who did and did not have followup at the two year research visit. The Kruskal-Wallis test was used to compare continuous, nonparametric variables, including the WOMAC, SF-36, KSS, and ADLs, and operative times between the three treatment groups. The Mann-Whitney rank-sum test was used to compare the two treatment groups when all infections were grouped together.

Results

We observed no differences between the three treatment groups at final followup for the following indices: WOMAC, ADLs, SF-6, or KSS (Table 3). When all infections were grouped together and compared with the aseptic group, no differences were found.

Intraoperatively, the average operative times were 166 minutes for the MRSA septic group, 149 minutes for the non-MRSA septic group, and 121 minutes for the aseptic group. The MRSA-septic group had operative times that were longer ($p = 0.001$) . Likewise, the non-MRSA-septic group had operative times that were longer ($p = 0.012$) than the aseptic group. There was no difference between operative times in the MRSA-infected and non-MRSA-infected groups.

Among 10 knees infected with MRSA, no knees had MRSA reinfection after revision. One knee (10%) did become infected with coagulase-negative S. aureus, and this patient underwent an above-knee amputation. Among the 37 non-MRSA septic knees, seven knees had reinfection after revision (18.9%). Irrigation and débridement was used for treatment in five of these knees, and one of these went on to require tibiofemoral arthrodesis. Two of these reinfected knees had superficial infections, and they were managed medically. No amputations were necessary in this group. Of the 56 knees revised for aseptic reasons, two knees had superficial infections (3.6%). Both of these infected knees were managed medically. No irrigation and débridement, amputation, or arthrodesis was used to manage these infections.

Discussion

Methicillin-resistant S. aureus is a growing problem in health care with deleterious effects on patient mortality and morbidity as well as healthcare economics [1, 5, 12, 25]. The field of orthopaedic surgery has not been spared this problem, and efforts to reduce infection are in use

throughout the United States and the world [18, 22]. Total joint reconstruction is no exception. Concerns regarding the decreased retention of the total joint after infection with antibiotic resistant organisms have been studied, with demonstration that such infections can be difficult to manage [14]. In our own experience, these infections can be both difficult to manage and be associated with increased scarring intraoperatively. This led us to ask the question whether these infections might be associated with decreased functional outcome scoring, in addition to presenting difficult infection management issues. We also explored issues related to study limitations as well as reinfection concerns.

We recognize several limitations. First, we included only 43 patients (with 45 of the 103 knees) in our functional assessments. Another 27 patients (27 knees) were ineligible for inclusion because they had met end points, and 31 patients were lost to followup or refused to participate in the study. For many of these patients, a study visit was viewed as an "extra" visit, and many chose not to participate, perhaps as a result of difficulties with driving distances and expense or perhaps as a result of general discontent with their outcomes. Although it is possible patients did not participate as a result of dissatisfaction with their outcomes, we found no indication from the record and 6-month followup that there was a difference between patients with and without final followup. The second major limitation was that we had a low number of patients. A post hoc power analysis for the functional scores revealed that for greater than 80% power to detect differences, assuming an alpha level of 0.05 and an effect size equal to the difference in the outcome measure between the groups, a cohort composed of between 35 (KSS) and 1000 (ADLs) MRSA subjects would be required. Given the lack of power for functional scoring, the risk of accepting the null hypothesis (that there is no difference in functional scores between the MRSA group and other groups) when the null hypothesis is not true (a type II error) is large. Therefore, in terms of functional scoring, this study does not allow definite conclusions to be made.

Barrack et al. reported patients undergoing revision TKA for septic indications had lower Knee Society clinical scores, lower function score, and had more trouble returning to daily activities than patients who had revision for aseptic reasons [2]. We presumed patients with MRSA infections would have diminished functional scores owing to what we qualitatively perceived as an increased scar response to MRSA infections. Contrary to what we presumed, however, we found no differences in functional scores, and a post hoc power analysis revealed that our study was underpowered to detect these differences. Therefore, with the numbers available, we can make no clear conclusions based on the results of this study. In a comparative study to Barrack et al. [2], Ghanem et al. found patients with knees revised for infections achieved functional, pain, and mental health scores similar to those achieved by patients revised for aseptic reasons [6]. In our study, when all infections were grouped together, we did not observe any difference in outcome score measures. The

Table 4. A comparison of functional outcome scores for this study and previous studies

Study	Outcome Measure				
	SF-36		WOMAC*		Knee Society Score†
Barrack et al. [2]					
- Aseptic	Not included		Not included		135
- Septic					115
Ghanem et al. [6]					
- Aseptic	Physical-53	Mental-65	Function-19	Pain-6	Not included
- Septic	Physical-53	Mental-66	Function-26	Pain-6	
Laudermilch et al. [current study]					
- Aseptic	Physical-37	Mental-59	Composite score-20		Total score-139
- Non-MRSA septic	Physical-34	Mental-59	Composite score-23		Total score-134
- MRSA septic	Physical-38	Mental-50	Composite score-19		Total score-110
Wang et al. [31]					
- Aseptic versus septic	No data given, stated clinical outcomes were less favorable in chronic infections. In this study, they used a modified Knee Society Score to measure clinical outcomes.				

*The composite score is an average of the pain, stiffness, and physical function. The study from Ghanem et al. [6] did not include the measures for stiffness.

† The knee society score has two components (each with 100 possible points), one based on the provider's assessment and the other based on patient responses. It is not clear how Barrack et al. [2] combined these, although it may be that the scores for these two components were added together. Wang et al. [31] stated the Knee Society Score was modified, but did not give details of the modification.

results of our study were compared to these and other studies (Table 4).

In regard to operative times, we found a longer surgical time for MRSA replantations and non-MRSA replantations than for one-stage revisions for aseptic loosening. While this does demonstrate increased time needed for the operation, we believe this increased time may reflect increased irrigation times, and not necessarily increased time due to hypertrophic scarring.

We found similar rates of reinfection with non-MRSA-infected knees and the MRSA knees. The percentage of recurrence for MRSA-infected knees was lower than, although similar to, that reported in 2007 by Mittal et al. [16], which included antibiotic-resistant organisms. The reason for these similar rates is unclear. Although non-antibiotic resistant infections may present fewer challenges for eradication, the MRSA infections may have been eradicated at a similar rate due to more aggressive irrigation and débridement, and proper use of antibiotics. However, as stated previously, operative times were not different for MRSA septic and non-MRSA septic knees, perhaps indicating that the aggressiveness of the irrigation and débridement was similar.

The treatment of prosthetic joint sepsis, especially from MRSA, is a difficult, time-consuming, exacting process. This study was underpowered to detect differences in functional outcome scores. However, it did demonstrate numerical score values that add to the existing literature (Table 4). It also suggested that operative times for revisions performed for infections tend to be longer than revisions performed for aseptic indications, although the specific reason for this increased time is still unclear. Furthermore, it suggests that aggressive and appropriate treatment of MRSA septic knees and non-MRSA septic knees may lead to similar rates of infection eradication.

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