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Two-Year Outcome of Early Deep MRSA Infections After Primary Total Knee Arthroplasty

A Joint Registry Review

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Abstract: The aim of this study is to determine the success rate in eradication of early methicillin-resistant *Staphylococcus aureus* (MRSA) prosthetic joint infection. Rate of prosthesis retention and functional outcome between patients with prosthesis retention and prosthesis revision were compared. All patients who underwent primary total knee arthroplasty between May 1998 and September 2008 at our institution developing early deep MRSA infection were included. Patient demographics, time from infection to initial arthrotomy, successful eradication of infection and functional outcome of patients with a knee prosthesis at 2 years were studied. Open arthrotomy, debridement, and change of liner successfully treated 33.3% of infections. All remaining infections went onto treatment with 2-stage revision with a success rate of 88%. Overall 92% of patients had a well-functioning knee prosthesis at 2 years. **Keywords:** MRSA, prosthetic joint infection, survival, functional outcome.

The management of deep prosthetic joint infection is a major challenge to orthopedic surgeons [1]. The incidence of prosthetic joint infection in total knee arthroplasty ranges from 1% to 2% [2,3]. The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) surgical site infections is on an upward trend [3-6] and account for 30% to 60% of infections. Studies conducted to date have all been retrospective with conflicting results regarding the outcomes of infections. However, patients with MRSA joint infections do appear to have a prolonged hospital stay, increased costs, morbidity, mortality, and worse outcome [7-14]. Success rates at treating MRSA infection have been reported to be as low as 16% to 18% [9,14].

Acute infection is classically defined as that presenting within 30 days from the index operation [15-18]. It is often difficult to ascertain the duration of symptoms from patients and even infections debrided within 2 weeks from onset have variable success rates ranging from 8% to 83% [16,19]. Recent studies have redefined infections occurring within 3 months from the index operation as early infection [2,5].

The aim of this study is to assess the outcome of early MRSA infections following primary total knee arthroplasty. A successful outcome meant eradication of infection in a patient with a functional knee prosthesis at 2 years after treatment.

Materials and Methods

All patients who underwent primary total knee arthroplasty (TKA) between May 1998-September 2008 at the Singapore General Hospital (SGH) were considered for the study. Inclusion criteria were patients who developed an MRSA associated deep prosthetic joint infection (PJI), as defined by Centers for Disease Control guidelines [20], within 3 months from primary TKA. Diagnosis of deep prosthetic joint infection was made if the infection extended into the knee joint and involved deep tissues, or had either purulent discharge from the joint or a positive culture from the joint aspirate [21]. Patients with radiographic evidence of loosening of the prosthesis or osteitis were excluded. Previous studies have shown that patients with radiographic evidence of component loosening or evidence of osteitis were

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contraindications to debridement and component retention [14,22].

Parameters noted were patient demographics, comorbidities, diagnosis for which total knee arthroplasty was done, time from infection to initial arthrotomy, success rate in eradication of infection with joint debridement and change of liner, or staged reimplantation.

Protocol of Treatment for PJI

There is a standard treatment protocol in SGH for all early PJI cases without evidence of loosening of implant or osteitis after diagnosis was made. All patients underwent open joint debridement, irrigation and polyethylene liner exchange with component retention (ODCR), as a first-line operation. Joint debridement was carried out with 9 L (3 bags of 3 L each) of pulsed lavage. Liner exchange was done to allow access to the back of the knee for a more thorough lavage and also to clean the dead space between the poly and tibia tray. If synovium is necrotic, it is debrided. The wound is closed watertight over a large bore drain. The drain is kept on average 4-5 days till the incision wound is dry and drainage is less than 50 mL/d. All patients were comanaged with the infection disease physician and a full course of intravenous antibiotics, of minimum 6 weeks duration depending on response to treatment, were administered through a peripherally inserted central catheter. Antibiotics were selected according to the intra-operative culture results. Physiotherapy was withheld till the wound was dry.

Response to treatment was assessed clinically and through hematological markers (blood white cell count, erythrocyte sedimentation rate and C-reactive protein). Patients that failed to respond to ODCR and antibiotics were treated with prosthesis removal and insertion of antibiotics impregnated cement spacer. All cement spacers contained gentamycin and were static spacers. A second-stage reimplantation was considered if successful eradication of organisms was achieved with normalization of blood white cell count, erythrocyte sedimentation rate, and C-reactive protein. Patients were deemed to have eradication of infection if there was no clinical or biochemical evidence of infection after stopping antibiotics. A white blood cell count of less than 10.0×109/L, erythrocyte sedimentation rate less than 20 mm/h, and C-reactive protein less than 8.8 mg/L were used as cutoff values to determine infection clearance. A preoperative joint aspiration before reimplantation was not routine. Cases with persistent/uncontrolled infections despite prosthesis removal or those with poor soft tissues were managed with salvage procedures (permanent excisional arthroplasty, arthrodesis, or above knee amputation).

Success was defined as a patient with a functional knee prosthesis and successful eradication of infection. At 2 years of follow-up, overall success rate and success rate with ODCR was determined. For patients with persistent infection after ODCR, the rate of successful staged revision of implants was also determined. Unsuccessful outcome was defined as failure to eradicate joint infection requiring salvage surgery ie permanent excision arthroplasty, arthrodesis, or amputation. Functional outcome was assessed for patients with a knee prosthesis in terms of range of motion of the knee, Knee Society Scores (KSS) and SF-36 scores at 2 years of follow-up.

Statistical Methods

SPSS (SPSS, Chicago, IL) was used to perform statistical analysis. The success rate with initial joint debridement and change of liner or staged revision as well as functional scores for patients with a knee prosthesis at 2 years were analyzed. Patients with prosthesis retention versus prosthesis removal were compared in terms of demographics, comorbidities, time from infection to initial arthrotomy and debridement. Chi-square tests were used to compare ratios and independent *t* tests were used to compare means. $P < .05$ was considered to be significant.

Results

A total of 8212 knees had primary TKA at SGH during the study period. Thirty-nine cases developed PJI during this period, which gives the overall infection rate of 0.5%. There were 27 cases of early PJI following primary total knee arthroplasty with 12 cases being MRSA positive. These 12 cases were included for the study. The mean age of patients in the study was 69.9 (SD 6.1) with the majority being females (9 of 12). All patients had osteoarthritis of the knee. None of the MRSA were resistant to vancomycin.

The mean time from diagnosis of infection to washout was 10.5 (SD 6.0) days and 9.4 (SD 6.9) days for patients with prosthesis retention and prosthesis removal

Table 1. Patient Demographics and Surgical Details of Patients

	Prosthesis Retention (n = 4)	Prosthesis Removal (n = 8)	*P*
Mean age (SD)	70.3 (3.1)	69.8 (7.3)	.90
Gender			.16
Male	0	3 (37.5%)	
Female	4 (100%)	5 (62.5%)	
Comorbidities			.23
Nil	3 (75%)	4 (50.0%)	
Diabetes mellitus	0 (20%)	3 (37.5%)	
Renal impairment	0 (0%)	1 (12.5%)	
Diabetes mellitus and renal impairment	1 (25%)	0 (0%)	
Mean time to arthrotomy from diagnosis of infection in days (SD)	10.5 (6.0)	9.4 (6.9)	.79
Mean number of surgeries required (SD)	2.8 (0.5)	4.1 (1.6)	.12

Table 2. Patient Characteristics, Number of Operations, Antibiotics and Time to Re-Implantation

Patient	Prosthesis Removed or Retained	Time to ODCR From Primary Surgery	Time to ODCR From Infection In Days	Total Number of Operations	Intravenous Antibiotics Treatment	Oral Antibiotics Suppression	Time to Re-Implantation From First Arthrotomy
1	Removed	85	2	3	Vancomycin		9 months
2	Removed	38	13	4	Vancomycin		3 months
3	Removed	44	20	6	Vancomycin	Clindaycin and fusidic acid	27 months
4	Removed	17	2	7	Vancomycin	Rifampicin and Fusidic acid	14 months
5	Removed	71	7	3	Vancomycin		10 months
6	Retained	54	13	2	Teicoplanin (allergic reaction to Vancomycin)		
7	Retained	20	9	1	Vancomycin		
8	Removed	17	6	3	Vancomycin	Rifampicin and Fusidic acid	24 months
9	Retained	35	3	1	Vancomycin		
10	Removed	16	7	4	Linezolid (allergic reaction to Vancomycin)	Rifampicin and Fusidic acid	9 months
11	Retained	46	17	2	Vancomycin	Rifampicin and Fusidic acid	
12	Removed	52	18	3	Vancomycin	Rifampicin and Fusidic acid	Patient refused reimplantation

respectively. The difference was not statistically significant. All patients were treated with intravenous vancomycin as first line. Two patients developed allergic reaction to Vancomycin and were treated with either Teicoplanin or Linezolid according to the recommendation by the infection disease physician. The minimum duration of intravenous antibiotics was for 6 weeks. Oral antibiotics suppression was used in some cases.

In terms of surgical outcome, all patients had successful eradication of infection. The success rate of ODCR as first-line treatment was 33.3% (4 of 12 patients). The remaining 8 patients proceeded to implant removal and insertion of antibiotics spacer. Seven of the 8 patients had a successful second-stage re-implantation. The mean time to reimplantation was 13.7 months. One patient refused a reimplantation even though infection was successfully cleared.

Table 3. Functional Outcome of Patients with Prosthesis Retention versus 2 Stage Prosthesis Revision

2-Year Results	Prosthesis Retention	Prosthesis Removal	*P*
Mean Extension/degrees (SD)	−1 (1.7)	0 (3.2)	.63
Mean Flexion/degrees (SD)	103.3 (17.1)	82.0 (52.7)	.53
Mean KSS (SD)	87.0 (9.7)	77.8 (14.8)	.37
Mean SF1/Physical function (SD)	61.7 (20.2)	36.7 (36.8)	.32
Mean SF2/Physical role function (SD)	100.0 (0.0)	33.3 (51.6)	.07
Mean SF3/Bodily pain (SD)	94.7 (9.2)	66.8 (25.8)	.12
Mean SF4/General health (SD)	72.0 (22.9)	65.0 (30.2)	.74
Mean SF5/Vitality (SD)	77.5 (17.1)	84.0 (15.2)	.89
Mean SF6/Social function (SD)	100 (0.0)	50 (54.7)	.17
Mean SF7/Emotional role (SD)	100.0 (0)	100.0 (0)	–
Mean SF8/Mental health (SD)	82.7 (18.0)	77.8 (14.8)	0.31

Between patients with successful implant retention and those who subsequently had implant removal, there was no difference in terms of age, gender, comorbidities, time to washout and number of surgeries (Table 1). Table 2 summarizes the patient's antibiotics usage, time to arthrotomy and time to re-implantation. There was no statistical difference in range of motion or functional outcome between patients with prosthesis retention and those who had 2-stage revision of implants at 2 years (Table 3). There was a trend to having better SF-2 (physical role function) in patients who had prosthesis retention as compared to patients with prosthesis removal ($P = .07$).

Discussion

Methicillin-resistant *S aureus* is becoming an increasingly prevalent organism in periprosthetic joint infections [23,24]. In our study, 44% (12 of 27) of early infections following primary total knee arthroplasty was caused by MRSA. With increasing prevalence of antibiotics usage, this is not surprising. It is thus important for orthopedic surgeons to be familiar with MRSA prosthetic joint infections and have a protocol in place to deal with infections by drug-resistant organisms. Surgical outcome should be known so that patient's expectations can be managed.

Despite the worry about treating antibiotic resistant *S aureus* [25], we have found patients with MRSA infection of the knee following primary total knee arthroplasty can be successfully eradicated with our protocol. All our patients were successfully cured of MRSA joint infection.

Initial debridement with arthrotomy, washout, change of liner and component retention eradicated a third of infections successfully. This is better than the previously reported success rate of only 18% with ODCR [14]. Although recent literature have reported successful outcome of one stage revision for patients with MRSA infection [26], there are advantages to performing ODCR as a first-line treatment. Open debridement with our protocol can be carried out by orthopedic surgeons in an urgent scenario and does not involve any specialized equipment or staff. Bone stock is also preserved as the well fixed implants are not removed making future revision easier. Two-stage revision can also result in a prolonged period of disability which is avoided with component retention.

Unfortunately, two-thirds of patients with MRSA infected total knee arthroplasty will require removal of implants to completely eradicate the infection. Both the surgeon and the patients should be aware of this statistic. In the scenario where ODCR fails, our paper advocates a 2-stage revision rather than placing false hopes on prolonging the intravenous antibiotics treatment. When we followed the protocol through, we managed to eradicate all MRSA infections successfully.

In terms of functional outcome, there is no difference in patients with prosthesis retention or a 2-stage re-implantation. Surgeons should not hesitate to remove implants should ODCR fail as the primary goal should be to eradicate infection. With careful soft tissue and extensor mechanism preservation, acceptable functional outcome can be obtained with re-implantation. Studies have shown similar outcome can be obtained between MRSA and non-MRSA infected total knee arthroplasty [24].

As with all previously published prosthetic joint infection studies involving resistant organisms, the cohort size is inherently small. This is the main limitation of the study. There are only 27 patients with early prosthetic joint infections of which 12 are infected with MRSA. Even though there is no statistical difference between the functional difference and range of motion, patients with prosthesis retention had about 20° more flexion than those with prosthesis removal. A larger study may be more sensitive to detect any statistical difference.

In conclusion, MRSA prosthetic joint infections occurring within 3 months from index surgery, without loosening of components, can be effectively treated using our protocol. Initial open arthrotomy, debridement, and change of liner can eradicate one-third of MRSA infections offering advantages of less complicated surgery, component retention and preservation of bone stock. However, should this fail, prosthesis removal and insertion of antibiotics impregnated cement spacer can eradicate remaining infections effectively. A second-stage reimplantation can be considered once infection is completely eradicated to give good functional outcome.

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