

Risk factors associated with acute hip prosthetic joint infections and outcome of treatment with a rifampin-based regimen

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Background and purpose Acute prosthetic infection is a serious problem. We report factors related to the incidence of acute infection and results of combined joint debridement and prolonged rifampicin-based antibiotic therapy.

Patients and methods Between 1998 and 2004, 14 acute infections occurred after 819 primary hip arthroplasties. The association between patient-related and surgical factors and the risk of infection were analyzed. Infections were treated with multiple joint lavage, debridement, 2 weeks of antibiotic therapy, and then oral antibiotics for a minimum of 6 months.

Results There was a correlation between having a body mass index (BMI) of ≥ 30 , and also more than 2 co-morbidities, and an increased risk of infection. Diabetes was a potential risk factor. Following our regime of treatment, 11 of 14 patients retained their prosthesis. 2 of 3 who required resection arthroplasty underwent successful staged revision, while the third patient had no further surgery because of being deemed unfit.

Interpretation Primary joint replacement was salvaged in 11 of 14 patients. When successful re-implantation was included, 13 of 14 patients had a mobile prosthetic joint without further infection.

complicate implantation of a prosthesis such as a hip replacement, the results can be devastating (Schoifet and Morrey 1990, Wilson et al. 1990, Rand 1993, Knutson et al. 1994). The incidence of joint replacement infections is 0.5–5% (Poss et al. 1984, Grogan et al. 1986, Bengtson and Knutson 1991) and *Staphylococcus* species frequently predominate. It remains a challenge to eradicate such infections whilst retaining the prosthesis (Rand 1993, Tsukayama et al. 1996).

Debridement with retention of the prosthesis has been reported, with disappointing results (Schoifet and Morrey 1990, Brandt et al. 1997). Retrospective studies have suggested that removal of the prosthesis gives the best chance of eradication of the infection, and that staged re-implantation under prolonged antibiotic cover is a successful option for retaining long-term joint function. Long-term administration of suppressive antibiotics has, however, shown some efficacy when pathogen-targeted therapy is combined with surgical debridement. This approach is used when extensive surgery is not possible because of the patient's clinical status, or where a well-fixed prosthesis is difficult to remove (Drancourt et al. 1993, 1997, Stein et al. 1998, Zimmerli and Ochsner 2003). In 1998, our institution embarked on a protocol that combined extensive and repeated surgical debridement with targeted antimicrobial agents for the management of acute deep infections following hip replacement (Horan et al. 1992). We now report our analysis of

Surgical site infections occur at a rate of almost 3% (Jarvis 1996), and account for up to one-third of all nosocomial infections (Haley et al. 1985, Horan et al. 1993). When such infections

factors related to deep-seated joint infection and the outcome of management of joint prostheses from this series.

Patients and methods

Setting

Our study included patients from St. Vincent's Hospital in Melbourne, a 460-bed university-affiliated tertiary referral center. Each year, over 1,700 in-patients undergo orthopedic surgery at our institution, and of these, several hundred patients undergo primary joint replacement of the hip.

Definition

Prosthetic joint infections were defined as those with 2 or more positive deep-sample cultures for bacteria or 1 positive culture with purulence surrounding the joint at operation. This included all patients who incurred an infection up to 1 year after hip replacement surgery at our institution.

Patients

Patients in this study underwent primary hip joint replacement surgery between January 1998 and April 2004. No patient had undergone prior surgery to their hip. Epidemiological data related to hip replacement were collected in a prospective database. Analysis of outcomes following the institution of our regime for treatment of acute infections was performed on these data. Date of last review was August 1, 2005. If a patient had more than one episode of infection, only the first episode was considered. As a quality control measure, all patients who undergo total joint replacement are followed up regularly for at least 10 years with face-to-face interviews, and information regarding their surgery and outcomes is collected and noted in the patient history. Regular review and reporting of postoperative infection complies with the recommendations of the Australian Council of Health Care Standards for reporting specialty-specific indicators of performance.

There were 819 elective primary hip replacement procedures performed over this period, on 442 female patients and 377 male patients. The median age of the patients was 68 (18–96) years. The median was 28 (15–53).

Variables gathered for analysis included date of surgery, age, sex, diagnosis, type of implant, surgical approach, operating time, co-morbidities (cardiovascular, respiratory, renal, endocrine, gastrointestinal, neurovascular, vascular, oncological, hematological, urological, rheumatological, psychiatric, anticoagulation status, smoking status, height, weight, pre- and postoperative hemoglobin), transfusion rate, use of drain tube, amount drained from drain tubes, type of anesthesia, length of stay, complications, urinary catheterization, intraoperative antibiotic type, dose and duration, date of infection, duration of symptoms, surgical treatment for infection, number of washouts, date of lavage, intravenous antibiotics, outcome of treatment, organisms isolated, and oral antibiotics.

Diagnosis

The antecedent diagnoses leading to hip replacement included osteoarthritis (664), avascular necrosis (64), inflammatory arthritis (32), developmental dislocation of the hip (24), perthes (12), conversion from fractures of the femoral neck (8), and others (15).

Medical co-morbidities

The major co-morbidities were cardiovascular ($n = 466$), gastrointestinal ($n = 169$), endocrine ($n = 123$) and respiratory ($n = 118$). Almost one-third of patients ($n = 266$) had more than 2 medical co-morbidities. Most patients were non-smokers ($n = 640$). Diabetes was noted in 87 patients.

Surgery

Primary joint replacement surgery was conducted in a positive-pressure operating room with 24 air exchanges per hour. Patients received perioperative prophylactic antibiotics consisting of 1 g of intravenous cephalothin at the time of surgery and continued 8 hrly for 24 h afterwards. All patients received a urinary catheter, which was inserted in the operating room just before surgery and usually withdrawn after 48 h. Gentamicin was given intravenously as a single dose prior to insertion and removal of the urinary catheter. Anesthesia consisted of general and regional anesthesia in 79 and 740 patients, respectively. Epidural catheters were removed after 48 h.

The median operating time was 100 (50–295) min. The anterolateral approach was used in 699 patients and the posterior approach was used in 120 patients. There were 277 totally cemented, 158 totally cementless, and 384 hybrid (cemented stem, cementless acetabulum) hip replacement procedures. In 134 of the 661 cemented cases antibiotic loaded cement was used.

Blood transfusion

The median preoperative hemoglobin level was 136 (91–181) g/dL and the median postoperative hemoglobin level was 99 (54–153) g/dL. 308 patients received a postoperative transfusion and the median transfusion was 2 (1–10) units of packed cells. 2 patients required 7 and 10 units of packed cells, 1 for bleeding esophageal varicies, and 1 patient required coronary artery bypass in the immediate postoperative period.

Suction drains

Postoperative low-pressure suction drains were inserted in 744 patients, and all fluid output was collected in sterile containers and measured regularly over a 24–48-h period. The median total drainage was 355 (0–2,840) mL. Drains were removed between 24 and 48 h postoperatively, once drainage had reduced to 10 mL or less per h for a 6-h period.

Patients were mobilized starting on the day after surgery. The median total length of stay in the hospital was 6 (2–40) days. The median length of stay for the 215 patients who were transferred to a rehabilitation unit was 10 (2–46) days.

Microbiology

Microbiological studies were performed on intraoperative soft tissue samples and swabs obtained at the time of joint washout and debridement. These included direct microscopic examination of leukocytes and bacteria, as well as aerobic and anaerobic cultures. Sensitivity testing was also performed against a panel of antibiotics.

Follow-up

The median follow-up of patients was 42 (16–91) months. 21 patients had died during follow-up. The median follow up for these 21 patients was 71 (24–89) months.

Statistics

The differences and similarities between categorical groups were compared using the chi-squared test. Continuous variables were compared using the Mann-Whitney non-parametric rank sum test. A p-value of 0.05 and less was considered significant for all statistical tests. Data were stored and analyzed using Access (Microsoft, Redmond, WA) and SigmaStat for Windows version 3.0.1 (SPSS Inc., Chicago, IL).

Results

14 patients had deep infections of their total hip replacements. Median time to diagnosis of infection was 14 (5–102) days. 3 patients developed wound infections after a fall affecting the surgical side. 1 patient developed a wound infection following an acute myocardial infarction within days of surgery. None of the other 10 patients had any antecedent events recorded. None of the 14 patients had had previous surgery to their operated hip.

Correlation of host-related and surgical factors with infection

Possible correlations between patient-related or surgical factors were investigated in those who did and did not develop deep infections (Table 1). The median BMI for patients with infections (33 (22–42)) was higher than for those without infections (28 (15–53), $p = 0.01$). Patients with a BMI of ≥ 30 had a higher incidence of infection. The incidence of infection when BMI was 30 or above was 10 in 299 patients, as compared to 4 in 520 patients with a BMI of < 30 .

Patients with more than 2 co-morbidities were more likely to develop infections. There was a strong trend involving patients with diabetes mellitus: they were more likely to develop deep infections, although this trend was just above the level of statistical significance ($p = 0.08$). Age, smoking, and preoperative hemoglobin levels were not associated with a higher incidence of infection. There was no difference in the median length of stay in hospital following the index surgery in patients with or without joint infections.

We found no difference between operating times for patients who did or did not develop infection.

Table 1. Clinico-pathological characteristics of patients with and without joint infection after primary hip replacement

Variable	Infection	No Infection	P-value
Age (years)			
median	71	68	0.6
range	60–79	18–96	
Sex			
Male	8	369	0.4
Female	6	436	
BMI			
median	33	28	0.01
range	22–42	15–53	
< 30	4	516	0.01
≥ 30	10	289	
Co-morbidities			
Median (range)	3 (1–7)	2 (0–9)	0.07
≤ 2	6	523	
> 2	8	282	0.02
Diabetes			
Yes	4	83	0.08
No	10	722	
Smoking			
Yes	2	89	0.9
No	12	716	
Cardiovascular			
Yes	10	456	0.4
No	4	349	
Gastrointestinal			
Yes	5	164	0.3
No	9	641	
Operation time (min)			
median (range)	95	100	0.8
range)	50–190	50–295	
Implant			
Cementless	2	271	0.8
Cemented	6	378	
Hybrid	6	156	0.7
Approach			
Lateral	12	687	0.7
Posterior	2	118	
Drain tube			
Yes	13	731	0.8
No	1	74	
Drainage (mL)			
median	360	350	0.8
range	80–1130	0–2840	
Anesthesia			
Spinal	13	727	0.9
GA	1	78	
Preoperative hemoglobin			
median	133	136	0.4
range	99–147	91–181	
Transfusion (U)			
median (range)	2 (1–4)	2 (1–10)	0.5
Yes	7	302	
No	7	503	

BMI: body mass index; GA: general anesthesia.

We could not find a significant correlation between development of infection and the type of fixation of the prosthesis, the surgical approach, the use of postoperative drains, or the amount of drainage. There was no correlation between the incidence of infection and either pre- or postoperative hemoglobin levels, or the amount of transfusion.

Microbiological studies

Intraoperative specimens from 9 of the 14 patients with joint infections yielded cultures of methicillin-resistant organisms (Table 2). 4 of these patients also had mixed infections. 3 patients had sensitive staphylococcal infections, and 1 of them also had a β -hemolytic *Streptococcus*. One other patient had an *E. coli* infection, and another patient had a group b streptococcal strain cultured from intraoperative specimens.

Treatment outcomes

Surgery. Diagnosis for an acute joint infection was in all cases heralded by the onset of wound and para-incisional erythema, induration, pain, and wound discharge. On clinical diagnosis, all patients underwent at least 2 formal arthrotomies of the joint (2–3 days apart) followed by aggressive debridement of the infected soft tissue and washout of the joint under high-pressure mechanized pulsatile lavage with 10–12 L of physiological saline on each occasion. In some patients, this regime was performed on 3 occasions.

Antibiotic regime. 11 patients received perioperative vancomycin-based intravenous antibiotic regimes prior to isolation of the infective agents, and 3 patients received a cephalosporin-based antibiotic regime. Intravenous antibiotics were commenced intraoperatively at the initial washout, after all tissue samples and swabs were taken. After 2 weeks of intravenous antibiotics, 12 of 14 patients were placed on rifampicin-based regimes, while 2 others received clindamycin and ciprofloxacin alone. Fusidic acid was added to rifampicin in 11 cases (Tables 2 and 3).

Outcome

Complete suppression was defined as (1) lack of clinical signs and symptoms of infection, (2) C-reactive protein level less than 5 mg/L, and (3) absence of radiographical signs of loosening or

Table 2. Organism, antibiotic, duration of therapy, and outcome

Patient	Organism ^a	Antibiotic ^b	Initial ESR/CRP ^c	Latest ESR/CRP ^c	Duration (months)	Follow-up ^c (months)	Outcome
1	<i>E. coli</i>	Cip	43/11	17/<5	indefinite	61	Retained
2	MRSA	Cip, Rif	63/148	66/36	24	30	Retained
3	MRSA	Rif, Fus	42/212	64/8	6	21	Girdlestone
4	MSSA/B-hemo., strep. sens.	Rif, Cip, Aug	86/297	22/16	12	15	Retained
5	MSSA	Rif, Fus	71/170	10/<5	18	37	Retained
6	Gp B Streptococcus	Clin	96/175	20/8	indefinite	31	Retained
7	MRSA/Enterococcus	Rif, Fus, Pen	70/94	23/<5	6	38	2 stage rev.
8	MRSA, MRSE, <i>E. faecalis</i>	Rif, Fus, Clin, Amox	33/7	40/21	24	35	Retained
9	MRSA	Rif, Fus	62/38	46/6	20	24	Retained
10	MRSE/coag. neg. Staphylococcus/Klebsiella	Rif, Fus, Aug	16/18	15/8	4	14	Retained
11	MSSA	Rif, Fus	123/316	11/<5	18	18	Retained
12	MRSA/Enterobacter aerogenes	Rif, Fus	35/244	40/9	12	17	Retained
13	MRSA	Rif, Fus	63/439	66/36	Indefinite	17	2 stage rev.
14	MRSE	Rif, Fus	123/316	11/<5	12	17	Retained

^a MRSA: Methicillin-resistant *Staphylococcus aureus*;
MRSE: Methicillin-resistant *Staphylococcus epidermidis*;
MSSA: Methicillin-sensitive *Staphylococcus aureus*;
E. faecalis: *Enterococcus faecalis*;
E. coli: *Escherichia coli*.

^b Cip: Ciprofloxacin (500 mg 12-hourly); Rif: Rifampicin (300 mg 8-hourly); Fus: fusidic acid (500 mg 8-hourly);
Aug: Augmentin DF (1 g 8-hourly); Clin: clindamycin (300 mg 6-hourly); Pen: penicillin (1 g 6-hourly);
Amox: amoxicillin (1 g 8-hourly).

^c ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

^d After cessation of antibiotics.

infection at 18 months. Treatment failure was defined as the absence of complete suppression, and relapse was defined as the reappearance of infection caused by the same isolate that had caused the original infection, regardless of the timing of this secondary infection.

After completing our protocol of lavage, debridement, and antibiotics, 11 of the 14 patients with infected joints did not require any further surgery and thus retained their original prostheses. The median follow-up time from debridement for this group was 23 (14–61) months.

Of the 3 remaining patients, 1 had an immediate girdlestone's arthroplasty without subsequent re-implantation because of unfitness for surgery, relating to an ongoing neurological condition. This patient's infection remains suppressed 21 months after excisional arthroplasty. 1 patient had an immediate girdlestone's arthroplasty and developed a pulmonary embolism, delaying revision to a joint replacement for 12 months. This patient remains free of infection 38 months later.

A third patient failed treatment and required a girdlestone's arthroplasty 3 months after treatment of infection was commenced. This was followed by re-implantation of a prosthesis 4 months later, and this patient remains infection-free after 17 months. Other than 1 patient who refused further oral antibiotics after 4 months, all patients had a minimum of 6 months of oral antibiotics (Table 2). Primary joint replacement was salvaged in 11 of 14 patients, and, including successful re-implantation, 13 of 14 patients had a mobile prosthetic joint without further infection.

Discussion

Infection following joint replacement is a devastating outcome, with a mortality in elderly patients that approaches 8% (Powers et al. 1990, Saccante 1998). Guidelines for minimizing infections are well established (Hanssen and Rand 1998) and these include preoperative optimization of patients'

Table 3. Intravenous antibiotic treatment following diagnosis

Patient no.	Type	Dose (g)	Frequency	Days of treatment
1	vancomycin	1	daily	3
	kefzol	1	8-hourly	7
	Revision:			
	vancomycin	1	12-hourly	14
2	vancomycin	1	12-hourly	28
3	vancomycin	1	12-hourly	14
4	vancomycin	1	daily	14
5	vancomycin	1	12-hourly	14
	ceftriaxone	1	daily	7
6	penicillin	1.8	6-hourly	7
7	vancomycin	1	daily	14
8	vancomycin	1	12-hourly	10
	timentin	3.1	6-hourly	7
9	flucloxacillin	1	6-hourly	5
	vancomycin	1	12-hourly	14
10	cephazolin	2	8-hourly	10
11	flucloxacillin	1	6-hourly	10
12	vancomycin	1	12-hourly	5
	penicillin	2.4	4-hourly	7
	flucloxacillin	2	4-hourly	14
	cephazolin	3	6-hourly	7
13	cephalothin	2	6-hourly	2
	ampicillin	2	6-hourly	20
14	dicloxacillin	2	6-hourly	5
	cephazolin	2	8-hourly	3
	ceftriaxone	2	daily	7

health, preserving intraoperative sterile procedures, prophylactic use of antibiotics, and postoperative prevention of complications or trauma. Our overall rate of deep infection for hip arthroplasty is 1.7%, which compares favorably with other series (Poss et al. 1984, Grogan et al. 1986, Bengtson and Knutson 1991, Hanssen and Rand 1998) where infection rates as high as 5% have been reported.

Obesity is a common condition that seems to be overrepresented in patients presenting for elective orthopedic surgery. In one study, almost one-quarter of patients presenting for disc surgery, hip arthroplasty, knee arthroplasty, and arthroscopy were classified as obese (Bostman 1994). We observed in our study group that there was a strong correlation between obesity and infection, patients with a BMI greater than 30 having a significantly increased risk of deep infection (10 of 299 patients). There have been very few reports on the relationship between obesity and wound infections in orthopedics, however (Karunakar et al. 2005).

In one study, Fleischmann et al. (2005) observed an inverse relationship between subcutaneous tissue oxygenation and infection. They went on to demonstrate that obese patients had a significantly reduced degree of tissue oxygenation compared to non-obese controls and that this difference could be accentuated in the setting of surgery, thus increasing the risk of obese patients developing wound infection.

Obesity may also influence the incidence of infection in other ways. For example, excessive wound blood loss is common in obese patients at surgery (Bowditch and Villar 1999, Karunakar et al. 2005) and blood collections in the wound may be infected. However, there is controversy as to whether or not drainage of these collections by the routine use of wound drains lowers the risk. Some studies have reported no difference in outcome whether or not a wound drain was used (Hadden and McFarlane 1990, Kim et al. 1998). In another study, the use of a drain resulted in a higher postoperative transfusion rate (Hallstrom and Steele 1992). In our study we found no difference in the incidence of infection whether drains were used or not, but we did observe that patients with a drain tube in place were more likely to require a transfusion.

There was a positive correlation between the incidence of diabetes in our patients and the incidence of wound infection. This correlation, however, was not statistically significant. Nonetheless, a strong correlation between diabetes and infection has been shown in the literature (Menon et al. 1983, Malone et al. 2002), and it is likely that this relationship reflects the poor healing capacity of tissue that has poor microvasculature (Sivan-Loukianova et al. 2003). In this regard, the lower oxygen tension known to exist in the subcutaneous tissue of obese patients (Fleischmann et al. 2005) may well contribute to the microangiopathy of diabetes.

Despite the well-known detrimental effects of smoking on wound healing (Towler 2000, Burns et al. 2003, Freiman et al. 2004, Wong et al. 2004, Izadiand Ganchi 2005, Zimmerman et al. 2005), we were surprised to find that there was no correlation between smoking and wound healing in our study group. We regard this result with some caution because of the low number of infected cases, in a setting where smokers only represented a small proportion of the entire group.

We found no significant difference in infection rates between patients who had surgery through the posterior approach or the anterolateral approach. Few studies have reported specifically on the incidence of infection after posterior or anterior approaches to the hip. A Cochrane review of surgical approaches for hemiarthroplasty of the hip failed to identify with any clear indication which approach was associated with a greater risk of infection (Parker and Pervez 2002).

The commonest infective organisms are the staphylococcal species, which include *Staphylococcus aureus* and *Staphylococcus epidermidis*. These may be the leading infective organism in 19–33% (12 of 63 and 17 of 51 cases) and 12–40% (6 of 51 and 25 of 63 cases), respectively (Inman et al. 1984, Schmalzried et al. 1992). Acute early infections that occur in the first 3 months are most commonly caused by *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Streptococcus* species (Inman et al. 1984). Most of our infections occurred in the first 3 months, and these cases should be regarded as early acute infections. However, we have also considered the situation where the surgery itself may increase the vulnerability of the prosthesis to infection, as in the creation of a locus minoris with possible seeding, for example, following dental manipulation, urinary tract infections, bowel infections, and trauma. We believe that increased vulnerability may last up to 1 year after surgery; hence our selection of this inclusion period. Polymicrobial infections may be as high as 19% of infected cases (Berbari et al. 1998), and this amounted to 5/14 of our cases. In our series, *Staphylococcus* species accounted for 12 of 14 cases. Of the 12 staphylococcal infections, 10 organisms were methicillin-resistant *Staphylococcus aureus* in 8 cases, *epidermidis* in 1 case, and mixed *aureus/epidermidis* in one case). This strongly suggests that a nosocomial infection was likely in the 10 patients with resistant *Staphylococcus*.

Excisional arthroplasty combined with a staged prosthetic revision and targeted oral antibiotic therapy remains the norm for treatment of acute infections of the hip (Lieberman et al. 1994). Successful preservation of joint function can be achieved in up to nine-tenths of patients following this regime (Lieberman et al. 1994). Recently, however, there has been an emergence of more conservative treat-

ment with an attempt at preserving the primary prosthesis through aggressive soft tissue debridement and prolonged antibiotic therapy (Segreti et al. 1998, Zimmerli and Ochsner 2003). This latter approach may be suitable for patients who are not fit for major revision surgery, for those who decline further major surgery, or when the implant is firmly fixed. If the regime of conservative prosthesis-sparing surgery is combined with appropriate antibiotics and this leads to successful eradication or suppression of infection, then perhaps the same regime may be a valid alternative for the management of acute prosthetic infections per se.

Our study has demonstrated that prosthesis survival (median 2 (1–5) years) is quite possible following early, aggressive debridement and lavage, and the use of pathogen-targeted oral antibiotics. We were ultimately able to suppress or cure infection in all 14 patients, with preservation of joint function in 13 patients with acute prosthetic infections. This is in line with the findings of others (Segreti et al. 1998, Zimmerli et al. 1998, Pavoni et al. 2004). Only 1 of our 14 patients can be classified as a treatment failure, as this patient required further surgery to remove the prosthesis after initial debridement—and antibiotics failed to prevent septic loosening.

Our success, however, contrasts with the work of Schoifet and Morrey (1990) who reported a low rate of success (23%) after treatment with debridement and prosthetic retention in total knee replacements. These authors concluded that the major causes of failure were a longer duration of infection before initial debridement (36 days in failed cases compared to 21 days in retained cases), infection with *Staphylococcus aureus*, and the presence of penicillin-resistant *Staphylococcus aureus*. Although the authors used antibiotics that were chosen on the basis of the sensitivity of the organism, they did not specify the exact antibiotic used or whether combinations of antibiotics were utilized. This is important information, because there were 8 penicillin-resistant *Staphylococcus* strains cultured in the 24 patients in the series who failed their regime of debridement and prosthetic retention, and in none of these was the antibiotic regimen stated clearly.

Another group from the same institution (Brandt et al. 1997) concentrated on patients whose knee

prostheses were only infected with *Staphylococcus aureus*, and once again they reported a high failure rate with the regime of debridement and prosthetic retention, 21 of 33 prosthetic infections. In 4 of the cases the infecting strain was penicillin-sensitive, and in 32 of cases it was oxacillin-sensitive. Thus, β -lactam drugs (cefazolin, nafcillin, oxacillin, and penicillin) were the mainstay of their treatment. Unlike our series, the patients of Brandt et al. were treated with intravenous antibiotics for a median of 28 days, and if chronic suppression was elected, cefadroxil and dicloxacillin were used in 60% and 27% of cases, respectively. The authors did not mention whether any of their organisms were antibiotic-resistant. In the light of their findings, one can only speculate about the efficacy of the choices of antibiotic in the series of Schoifet and Morrey (1990) and Brandt et al. (1997).

In contrast to these 2 studies, we were also able to show that resistant staphylococcal infections or mixed infections do not exclude the regime of debridement and prosthesis retention. In our series, 11 of the 14 patients were infected by methicillin-resistant *Staphylococcus aureus*, and we were able to eradicate this in all 11 cases—although 1 patient had permanent excision of the joint. Others have also demonstrated successful treatment of staphylococcal prosthetic infections (Drancourt et al. 1993, 1997, Stein et al. 1998, Zimmerli et al. 1998, Pavoni et al. 2004). Pavoni et al. successfully treated resistant and sensitive *Staphylococcus aureus* and *S. epidermidis* with combinations of antibiotics that included rifampicin, ciprofloxacin, minocycline, teicoplanin, and β -lactams. In a randomized, placebo-controlled, double-blind trial, Zimmerli et al. (1998) reported successful salvage in 12/12 patients with a combination of rifampicin and ciprofloxacin, but in only 7/12 patients when a regime of placebo and ciprofloxacin was used. Drancourt et al. (1993) also reported similar results with a salvage rate of 35 in 47 patients when a rifampicin-based combination was used. Another study (Drancourt et al. 1997) reported greater success of rifampicin with fusidic acid as compared to rifampicin and ofloxacin. The former combination may be preferable because of the rising incidence of quinolone-resistant organisms, and also because of the higher patient intolerance of quinolone antibiotics.

These series strongly suggest that rifampicin-based antibiotic combinations appear to be central to success against sensitive and resistant staphylococcal infections. The rationale for use of rifampicin is that this antibiotic retains its bactericidal activity against staphylococci that adhere to implants, and also reaches elevated intracellular and tissue concentrations. When combined with other antibiotics such as a quinolone, minocycline, or glycopeptides, emergence of resistance to rifampicin may be prevented (Clumeck et al. 1984, Chuard et al. 1991, Zimmerli et al. 1998). These combinations may also be efficacious against methicillin-resistant staphylococci, and they have been shown to be more effective than monotherapy in in vivo experimental models of foreign-body infections with staphylococci (Desplaces and Acar 1988, Tarasi et al. 2003).

There is disparity in the duration of treatment in the published literature. Soriano et al. (2006) referred to a relatively short treatment period of 2–3 months. In contrast, Zimmerli et al. (1998) recommended a minimum of 6 months. When we elected to follow our regime of treatment, we were influenced by the work of Zimmerli et al. (1998) and chose a minimum duration of 6 months. If the patient was frail, or if the organisms were mixed or particularly pathogenic, our choice was to prolong treatment. We recognize that there are toxicities associated with prolonged antibiotic treatment, so our patients were treated under the supervision of infectious diseases physicians.

Although the correct choice of antibiotic therapy is fundamental to successful treatment, the quality of surgical debridement itself cannot be stressed enough. The principles of evacuating infected hematoma or purulent tissue, debriding infected, inflamed and necrotic tissue, and removal of tissue films that may line a prosthetic surface and prevent interaction of the organism with antibiotics, must be strongly emphasized. In this regard, we have pursued systematic debridement including wound excision from superficial to deep, and mechanized pulsatile lavage with copious amounts of physiological saline (10–12 L) interspersed with iodine-based and chlorhexidine irrigation. This was repeated on 2–3 occasions, separated by 2–3 days each time, and wound closure was performed after each arthrotomy. From a clinical point of view, we

have observed that the tissues appeared far healthier after such serial debridement and irrigation, and we speculate that this and the serial dilution of residual organisms must have contributed to the efficacy of our antibiotic regime.

Despite having been able to eradicate or suppress infection in our series, relapse of prosthetic infections treated by conservative means remains possible. Although relapse is more often observed within 6 months following cessation of antibiotic therapy (Schoifet and Morrey 1990, Tsukayama et al. 1991, Brandt et al. 1997), late relapse has also been reported (Tsukayama et al. 1996, Brandt et al. 1997, Zimmerli et al. 1998). In this regard, continued vigilance should always be exercised with serial clinical, hematological, and radiographic examinations after discontinuation of antibiotic treatment.

Although this report examines the outcome of a specific treatment regime, the retrospective nature of the analysis, the variability in follow-up time, and the heterogeneity of our study group are important limitations. The results, while favorable, should be considered with caution until far larger randomized, controlled trials of antibiotic treatment have been instituted and their results known. Future studies should concentrate on the criteria for diagnosis and cure, and there should be greater consensus on the antimicrobial regimes employed and the clinical situations in which they are used.

In conclusion, aggressive debridement, antibiotic therapy, and prosthetic retention can be successful in suppressing acute prosthetic infection. The resultant preservation of long-term function of the joint prosthesis and good tolerance of oral antibiotics make this a viable alternative to major excisional and subsequent re-implantation joint surgery.

Contributions of authors

PFMC: author, supervisor, patient follow-up. MMD: author, patient follow-up. DC: patient follow-up. JD and PS: authors with respect to infectious disease treatment.

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