# Outcome and predictors of treatment failure in early post-surgical prosthetic joint infections due to *Staphylococcus aureus* treated with debridement

**F. Vilchez[1], J. C. Martínez-Pastor[1], S. García-Ramiro[1], G. Bori[1], F. Maculé[1], J. Sierra[2], L. Font[1], J. Mensa[2] and A. Soriano[2]**

1) *Department of Orthopedics of Hospital Clínic of Barcelona and* 2) *Department of Infectious Diseases of Hospital Clínic of Barcelona, Hospital Clínic Universitari, IDIBAPS, Barcelona, Spain*

## Abstract

Experience with debridement and prosthesis retention in early prosthetic joint infections (PJI) due to *Staphylococcus aureus* is scarce. The present study aimed to evaluate the outcome and predictors of failure. Patients prospectively registered with an early PJI due to *S. aureus* and 2 years of follow-up were reviewed. Demographics, co-morbidity, type of implant, clinical manifestations, surgical treatment, antimicrobial therapy and outcome were recorded. Remission was defined when the patient had no symptoms of infection, the prosthesis was retained and C-reactive protein (CRP) was ≤1 mg/dL. Univariate and multivariate analysis were performed. Fifty-three patients with a mean ± SD age of 70 ± 10.8 years were reviewed. Thirty-five infections were on knee prosthesis and 18 were on hip prosthesis. The mean ± SD duration of intravenous and oral antibiotics was 10.6 ± 6.7 and 88 ± 45.9 days, respectively. After 2 years of follow-up, 40 (75.5%) patients were in remission. Variables independently associated with failure were the need for a second debridement (OR 20.4, 95% CI 2.3–166.6, p 0.006) and a CRP > 22 mg/dL (OR 9.8, 95% CI 1.5–62.5, p 0.01). The onset of the infection within the 25 days after joint arthroplasty was at the limit of significance (OR 8.3, 95% CI 0.8–85.6, p 0.07). Debridement followed by a short period of antibiotics is a reasonable treatment option in early PJI due to *S. aureus*. Predictors of failure were the need for a second debridement to control the infection a CRP > 22 mg/dL and the infection onset within the first 25 days after joint arthroplasty.

**Keywords:** Infection, joint, outcome, risk factors, *Staphylococcus aureus*

**Original Submission:** 17 January 2010; **Revised Submission:** 4 April 2010; **Accepted:** 6 April 2010
Editor: D. Raoult
**Article published online:** 20 April 2010
*Clin Microbiol Infect* 2011; **17:** 439–444
10.1111/j.1469-0691.2010.03244.x

**Corresponding author:** F. Vilchez, Department of Orthopedics of Hospital Clínic of Barcelona, C/Villarroel 170, Barcelona 08036, Spain
**E-mail: drvilchez@live.com.mx**

## Introduction

Debridement and prosthesis retention in early post-surgical prosthetic joint infections (PJI) is an accepted therapeutic approach when the duration of symptoms is <2–4 weeks and there are no radiological signs of loosening [1,2]. In the last 15 years, the combination of rifampin with other antibiotics (i.e. fluoroquinolones) has demonstrated a higher success rate [3–8]; however, the number of patients included in these studies with a PJI due to *S. aureus* was low.

The main predictor of failure when *S. aureus* PJI is treated mainly with $\beta$-lactams is the duration of symptoms before debridement [9]. Prosthesis that were debrided >2 days after onset of symptoms were associated with a higher probability of treatment failure. There are no specific studies directed to identify predictors of failure among patients with *S. aureus* PJI treated mainly with a combination of oral anti-staphylococcal antibiotics.

The present study aimed to evaluate: (i) the efficacy of debridement, retention of the implant, a short course of intravenous antibiotics and an oral antibiotic regimen combining two anti-staphylococcal agents and (ii) predictors of failure among a prospectively followed-up cohort of acute and early PJI due to *S. aureus*.

## Patients and Methods

From January 2000 to October 2007, all patients with a PJI (hip hemiarthroplasty, total hip and knee arthroplasty) were prospectively registered in a database and prospectively followed up. Relevant information about demographics, co-morbidity, type of implant (hip or knee prosthesis), clinical manifestations, leukocyte count and value of C-reactive protein (CRP) at the moment of admission for infection, surgical treatment, isolated microorganism, antimicrobial therapy and outcome were recorded. For the present study, only those cases with an early PJI due to *S. aureus* with at least 2 years of follow-up were included and retrospectively reviewed.

Early PJI due to *S. aureus* in the present study was defined by the presence of local inflammation of acute onset (<15 days of symptoms duration) during the first 2 months after joint arthroplasty, macroscopic evidence of extension of the infection through the capsule during debridement and isolation of *S. aureus* in deep samples.

In terms of debridement, pre-existing incisions were always used, necrotic tissue was excised and the joint was washed with 6–9 L of sterile water. The components were left *in situ* after confirming that no signs of loosening were found at the time of surgery. In knee arthroplasties, the polyethylene component was removed and replaced with a new component and, in total hip arthroplasties, modular components were substituted. When systemic or local signs of infection persisted after debridement, the patient was taken back to the operating room for repeating the irrigation and debridement. The need for a second debridement, within the first 10 days after the first one, was not considered as failure. Three or more deep samples of synovial fluid and periprosthetic tissue were submitted to the microbiology laboratory. In addition, blood cultures were performed to patients with fever at the moment of admission for infection. An antibiogram for all the isolates was performed by microdilution method.

After debridement, a broad-spectrum intravenous antimicrobial regimen including vancomycin (1 g/12 h) plus ceftazidime (2 g/8 h) was started and maintained until definitive microbiological results were obtained. When *S. aureus* was susceptible to methicillin, vancomycin was switched to intravenous cloxacillin (2 g/4 h). The definitive oral antibiotic treatment was levofloxacin (500 mg/24 h) plus rifampin (600 mg/24 h), except in those cases with resistant strains or polymicrobial infection, in which an alternative was selected according to the antibiogram. The protocol of our hospital recommends 10 days of intravenous antibiotics, although the duration of oral antibiotics was not standardized and it was decided by a member of the team (A.S.) in each case according to the clinical manifestations and the CRP value.

After being discharged, patients were followed-up monthly when they were receiving treatment and every 3–6 months after finishing the therapy. Outcome was evaluated according to: (i) remission, when the patient had no symptoms of infection, the prosthesis was retained and CRP was ≤1 mg/dL after 2 years of follow-up and (ii) failure, when inflammatory signs and high CRP remained during treatment or re-appeared after completing it (relapse or re-infection depending on the microorganism isolated) or when the patient developed an aseptic loosening that required the exchange of prosthesis, but deep samples taken during surgery were negative.

### Statistical analysis

Variables analyzed were age, sex, co-morbidity (having or not having one or more of the following entities: diabetes mellitus, liver cirrhosis, chronic renal failure, rheumatoid arthritis or chronic obstructive pulmonary disease), type of prosthesis (hip or knee), age of implant, duration of symptoms, presence of fever, leukocyte count, CRP value, positive blood cultures, the need for a second debridement, resistance to methicillin or fluoroquinolones and polymicrobial infection. For the statistical analysis, continuous variables were explored and categorized as: age (≤70 years or >70 years); time from arthroplasty to diagnosis of infection (age of implant) (≤25 days or >25 days); duration of symptoms (≤2 days or >2 days); leukocyte count (≤10 000 cells/mm$^3$ or >10 000 cells/mm$^3$); and CRP (≤22 mg/dL or >22 mg/dL), at the moment of admission for infection. Categorical variables were compared by the the chi-square test or Fisher's exact test when necessary and continuous variables were compared by Student's *t* test. Variables significantly associated with failure in the univariate analysis were included in a forward and backwards stepwise logistic regression model to identify the independent variables associated with failure. For the analysis, the dependent variable (failure) included relapse, reinfection and aseptic loosening. The Kaplan–Meier survival method was used to estimate the cumulative probability of treatment success of the whole cohort. Statistical significance was defined as a two-tailed $p < 0.05$. The analysis was performed using SPSS, version 12.0 (SPSS, Inc., Chicago, IL, USA).

## Results

During the study period, 53 patients met the inclusion criteria of the study. The mean ± SD age of the cohort was 70 ± 10.8 years; 25 were male and 28 were female, 35 infections were on knee prosthesis and 18 were on hip prosthesis, and all except two were primary arthroplasties. The mean ± SD duration of intravenous and oral antibiotics was 10.6 ± 6.7 and 88 ± 45.9 days, respectively. Patients with good outcome were followed-up for at least 2 years, except one case who died after 6 months as a result of unrelated cause and without evidence of failure. The cumulative probability of being in remission according to the Kaplan–Meier survival curve is shown in Fig. 1.

Six patients failed before starting oral antibiotics and underwent implant removal. The other 47 patients received an oral combination of two anti-staphylococcal agents. Rifampin (600 mg/24 h) was administered to 43 patients and it was associated with levofloxacin (500 mg/24 h) in 33 cases, clindamycin (300 mg/8 h) in four, linezolid (600 mg/12 h) in three, amoxicillin-clavulanate (875/125 mg/8 h) in two and cotrimoxazole (800 mg/12 h) in one. Among cases that did not received rifampin ($n$ = 4), two received levofloxacin plus cotrimoxazole and two received levofloxacin plus linezolid. The mean ± SD duration of rifampin combinations was 78 ± 45 days, whereas the mean ± SD duration of combinations without rifampin was 138 ± 51 days (p 0.01). Linezolid was administered for 90 days in all cases. After a mean ± SD follow-up of 879.3 ± 205 days, 40 patients (75.5%) were in remission. Thirteen patients (24.5%) failed as a result of reinfection in seven cases (five during treatment and two after finishing antibiotics), relapse in five (three during treatment and two after finishing antibiotics) and aseptic failure in one. In relapse cases, no resistant strains to rifampin or other antibiotics were isolated.

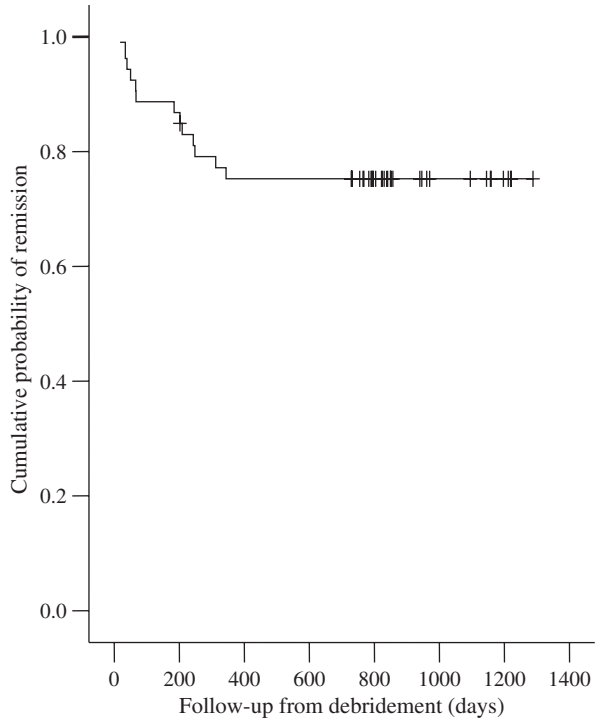


**FIG. 1.** Kaplan–Meier survival curve for the whole cohort. The *x*-axis represents days since debridement and the *y*-axis represents the proportion without treatment failure. Vertical bars indicate censored patients in remission.

The main characteristics of the patients according to their outcome are summarized in Table 1. Variables significantly associated with failure were onset of infection ≤25 days after joint arthroplasty (p 0.01), a C-reactive protein at admission >22 mg/dL (p 0.01), documented bacteraemia (p 0.02) and the need for a second debridement (p 0.002). Failure was more frequent in patients older than 70 years, with co-morbidity, fever or leukocyte count >10 000 cells/mm$^3$, and when the infection affected a knee prosthesis or it was polymicrobial; however, these variables did not achieve statistical significance. In the multivariate analysis, variables independently associated with failure were the need for a second debridement (OR 20.4, 95% CI 2.3–166.6, p 0.006) and a CRP > 22 mg/dL (OR 9.8, 95% CI 1.5–62.5, p 0.01).

## Discussion

The success rate in our cohort of patients with a PJI due to *S. aureus* treated with debridement and retention of the implant after at least 2 years of follow-up was 75.5% (40 out of 53), considering relapse, reinfection and aseptic loosening as failure, and 90.5% (48 out of 53) when only relapse was considered as failure. Clinical experience focus on infections due to this microorganism using a conservative surgical approach is scarce. Brandt *et al.* [9] analyzed 33 patients by administering an intravenous $\beta$-lactam for 4–6 weeks and showed a cumulative probability of failure (2 years after debridement) of 70%. The results obtained in the present study and those from other studies [6–8,10] support the usefulness of rifampin in staphylococcal infections (including *S. aureus* and coagulase-negative staphylococci); however, we cannot rule out the possibility that the differences observed between Brandt's study and others could be the result of factors such as the higher percentage of patients with bactaeremia (36%) or prosthesis loosening (39%).

**TABLE 1. Characteristics of patients according to outcome**

| Characteristics | Failure ($n$ = 13)[a] | Remission ($n$ = 40) | p |
|---|---|---|---|
| Mean ± SD age (years) | 67 ± 11.9 | 71 ± 10.4 | 0.25 |
| Age > 70 years (%) | 4 (30.8) | 23 (57.5) | 0.11 |
| Sex (female) (%) | 6 (46.2) | 22 (55) | 0.75 |
| Comorbidity[b](%) | 6 (46.2) | 10 (25) | 0.17 |
| Primary arthroplasty (%) | 13 (100) | 38 (95) | 1 |
| Type of prosthesis (%) | | | |
| Hip | 2 (15.4) | 16 (40) | |
| Knee | 11 (84.6) | 24 (60) | 0.17 |
| Mean ± SD age of prosthesis (days) | 16.3 ± 7.2 | 26 ± 17.9 | 0.06 |
| Age of prosthesis, days (%) | | | |
| ≤25 | 12 (92.3) | 21 (52.5) | |
| >25 | 1 (7.7) | 19 (47.5) | 0.01 |
| Mean ± SD duration of symptoms (days) | 5.1 ± 4.2 | 5.7 ± 4.5 | 0.66 |
| Duration of symptoms (days) | | | |
| ≤2 | 4 (30.8) | 14 (35) | |
| >2 | 9 (69.2) | 26 (65) | 1 |
| Fever | 5 (38.5) | 7 (17.5) | 0.14 |
| Mean ± SD leukocyte count (cells/mm$^3$) | 10149.2 ± 3838.9 | 8697.1 ± 3097.3 | 0.17 |
| Leukocyte count > 10 000 cells/mm$^3$ | 6 (46.2) | 9 (24.3) | 0.13 |
| Mean ± SD C-reactive protein (mg/dL) | 14.5 ± 12.2 | 7.8 ± 10.5 | 0.06 |
| C-reactive protein > 22 mg/dL | 6 (46.2) | 5 (12.8) | 0.01 |
| Methicillin-resistant *Staphylococcus aureus* | 0 | 4 (10) | 0.56 |
| Fluoroquinolone-resistant *S. aureus* | 2 (15.4) | 6 (12.8) | 1 |
| Bacteremia | 4 (30.8) | 2 (5) | 0.02 |
| Polymicrobial infection | 6 (46.2) | 9 (22.5) | 0.15 |
| Need for second debridement | 6 (46.2) | 2 (5) | 0.002 |
| Duration of oral antibiotic[c] | | | |
| >90 days | 3 (49.2) | 12 (30) | |
| ≤90 days | 4 (57.1) | 28 (70) | 0.66 |
| Oral antibiotic[c] | | | |
| Rifampin | 6 (85.7) | 37 (92.5) | 0.48 |
| Levofloxacin | 5 (71.4) | 32 (80) | 0.63 |
| Clindamycin | 1 (14.3) | 3 (7.5) | 0.48 |
| Cotrimoxazole | 1 (14.3) | 2 (5) | 0.28 |
| Linezolid | 0 | 5 (12.5) | 1 |
| Amoxicillin-clavulanate | 1 (14.3) | 1 (2.5) | 0.27 |
| Mean ± SD days of follow-up from debridement | 155 ± 114.1 | 879.3 ± 205.2 | – |

[a]Including, relapse ($n$ = 5), reinfection ($n$ = 7) and aseptic loosening ($n$ = 1).
[b]Diabetes mellitus, liver cirrhosis, chronic renal failure, rheumatoid arthritis or chronic obstructive pulmonary disease.
[c]Refers to those patients who received oral antibiotics ($n$ = 47). In this group, 40 patients were in remission.

In general, previous experience used 450 mg/12 h of rifampin, whereas the present study and our own previous experience [8] suggests that 600 mg/24 h of rifampin is equally effective. Rifampin is a concentration-dependent antibiotic and the best pharmacodynamic parameter related to its activity is $C_{max}$/MIC [11]. Rifampin administration in a 600 mg monodose is not only easier to administer and well tolerated (mild nausea in two cases), but also could result in a higher $C_{max}$/MIC than the 450 mg/12 h dosage. In addition, rifampin is added for killing biofilms and the doubling time of biofilm bacteria is significantly longer than planktonic [12]; therefore, the administration of rifampin once daily as for *Mycobacterium tuberculosis* infections, appears reasonable.

The available literature concerning factors associated with outcome in PJI treated with debridement is scarce and, to allow the analysis of larger series, different aetiological microorganisms and different surgical approaches were pooled. A common factor associated with failure in the precedent studies is the isolation of *S. aureus*. Predictors of failure in our cohort were the need for a second debridement to control the infection, CRP > 22.5 mg/dL and the onset of infection within the first 25 days after implantation. These factors suggest a higher bacterial inoculum, infection due to more pathogenic *S. aureus* strains or infection in inmunocompromised patients that favours the bacterial growth. The last option is unlikely because age and co-morbidity were not significantly different between patients in remission and those who failed. The main predictor of treatment failure in PJI due to *S. aureus* treated with $\beta$-lactams is the duration of symptoms [9]. Interestingly, this variable was not associated with treatment failure in our cohort. A possible explanation for this discrepancy could be that $\beta$-lactams are less effective *in vitro* than rifampin for eradicating bacterial biofilms [13] and, for $\beta$-lactams, it is critical to start therapy as soon as possible.

The current recommendation for the duration of antibiotic treatment in acute PJI treated without removing the implant is 2–4 weeks of intravenous therapy followed by oral regimen for 3 months in hip infections and 6 months in knee infections [2]. However, this recommendation is based on few observational studies [14]. Recently, Byren *et al.* [15] analyzed 112 patients treated with debridement and 6 weeks

of intravenous $\beta$-lactams or glycopeptides followed by oral regimen including rifampin for a minimum of 12 months. Despite the prolonged treatment, in *S. aureus* infections, the failure rate was 27.6% (13 out of 47), which was similar to that in the present study (24.5%) with a mean ± SD duration of intravenous and oral antibiotics of 10.6 ± 6.7 and 88 ± 45.9 days, respectively. The results of the present study support those previously presented by Berdal *et al.* [16] in 29 patients with acute post-surgical infections (18 due to *S. aureus*) treated with 3–7 days of intravenous antibiotics and 3 months of oral rifampin regimen. The rationale for this protocol is that, in acute foreign-body related infections, two bacterial populations could be found: free-floating (planktonic) bacteria that are responsible for acute symptoms and sessile (biofilm) bacteria that colonize the implant surface and are responsible for relapse after stopping antibiotic. One of the main differences between these two bacterial populations is that sessile bacteria double their population every 30 h, whereas planktonic do so in 1.6 h [12], explaining the tolerance to cell-wall active antibiotics shown by biofilm bacteria [13,17]. Planktonic bacteria could be eradicated through debridement and effective antibiotics against growing bacteria (e.g. $\beta$-lactams) for no longer than 7–10 days, similar to other wound infections without foreign material. To eradicate biofilm bacteria, it is necessary to use antibiotics with a better performance against stationary phase bacteria such as rifampin [18].

Early PJI frequently were polymicrobial (28.3%) and, although this might appear to be a high rate, in a recent article by Moran *et al.* [19], the rate of polymicrobial infections in acute PJI was found to be even higher than in the present study (47%). The high prevalence shown by Moran *et al.* [19], together with the high reinfection (seven out of 13 failures; 53.8%) rate observed in the present study, leads to the hypothesis that co-pathogens were not always identified in the microbiology laboratory and that directing the antibiotic therapy exclusively to *S. aureus* resulted in patient failure. In the future, to improve the outcome of these patients, it would be necessary to improve microbiological techniques aiming to identify all the possible aetiological agents and to standardize a broad-spectrum antibiotic until definitive results are obtained. An alternative explanation for reinfections may be contamination during open debridement or wound superinfection during the post-operative period. Therefore, we recommend a broad-spectrum prophylaxis during debridement as well as the need to take care of the wound, including plastic surgery in those cases where the soft tissue is damaged, or to avoid skin tension and further necrosis (especially in knee prosthesis).

A recent retrospective study comparing infections due to methicillin-susceptible ($n$ = 33) and -resistant ($n$ = 12) *S. aureus* showed that resistance to methicillin was an independent factor associated with treatment failure. However, only three cases with MRSA infection were managed with debridement and retention of the implant [20]. Five patients with MRSA infection were included in our series and all of them were in remission. Three patients received rifampin plus linezolid (for 90 days in two cases and 100 days in one) and two received rifampin plus clindamycin (for 60 days in both cases). Indeed, previous studies have documented the efficacy of linezolid in PJI [21,22].

In conclusion, debridement with retention of the implant followed by a short period of intravenous antibiotics and an oral combination of rifampin plus other antistaphylococcal agent is a reasonable treatment option in early PJI due to *S. aureus*. Predictors of failure were the need for a second debridement to control the infection, a CRP > 22 mg/dL and infection onset within the first 25 days after joint arthroplasty. In these cases, it is necessary to further evaluate the efficacy of other surgical strategies and new antibiotics.

## Transparency Declaration

None of the authors have any conflicts to declare. No specific funding was received for the present study.

## References

1. Tsukayama DT, Goldberg VM, Kyle R. Diagnosis and management of infection after total knee arthroplasty. *J Bone Joint Surg Am* 2003; 85-A (suppl 1):S75–S80.
2. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med* 2004; 351: 1645–1654.
3. Drancourt M, Stein A, Argenson JN, Zannier A, Curvale G, Raoult D. Oral rifampin plus ofloxacin for treatment of *Staphylococcus*-infected orthopedic implants. *Antimicrob Agents Chemother* 1993; 37: 1214–1218.
4. Javaloyas DM, Monreal PM. Oral antibiotic therapy in the adult bacterial osteomyelitis: results after two years of follow-up. *Med Clin (Barc)* 1999; 113: 488–489.
5. Widmer AF, Gaechter A, Ochsner PE, Zimmerli W. Antimicrobial treatment of orthopedic implant-related infections with rifampin combinations. *Clin Infect Dis* 1992; 14: 1251–1253.
6. Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. *JAMA* 1998; 279: 1537–1541.
7. Barberan J, Aguilar L, Carroquino G *et al.* Conservative treatment of staphylococcal prosthetic joint infections in elderly patients. *Am J Med* 2006; 119: 993–10.
8. Soriano A, Garcia S, Bori G *et al.* Treatment of acute post-surgical infection of joint arthroplasty. *Clin Microbiol Infect* 2006; 12: 930–933.

9. Brandt CM, Sistrunk WW, Duffy MC *et al. Staphylococcus aureus* prosthetic joint infection treated with debridement and prosthesis retention. *Clin Infect Dis* 1997; 24: 914–919.
10. Laffer RR, Graber P, Ochsner PE, Zimmerli W. Outcome of prosthetic knee-associated infection: evaluation of 40 consecutive episodes at a single centre. *Clin Microbiol Infect* 2006; 12: 433–439.
11. Morris AB, Kanyok TP, Scott J, Peloquin Ch, Berning SE. Rifamycins. In: Yu VL, Merigan TC, Barriere SL, eds, *Antimicrobial therapy and vaccines*. Pennsylvania: Williams & Wilkins, 1999; 901–962.
12. Anderl JN, Zahller J, Roe F, Stewart PS. Role of nutrient limitation and stationary-phase existence in *Klebsiella pneumoniae* biofilm resistance to ampicillin and ciprofloxacin. *Antimicrob Agents Chemother* 2003; 47: 1251–1256.
13. Monzon M, Oteiza C, Leiva J, Lamata M, Amorena B. Biofilm testing of *Staphylococcus epidermidis* clinical isolates: low performance of vancomycin in relation to other antibiotics. *Diagn Microbiol Infect Dis* 2002; 44: 319–324.
14. Betsch BY, Eggli S, Siebenrock KA, Tauber MG, Muhlemann K. Treatment of joint prosthesis infection in accordance with current recommendations improves outcome. *Clin Infect Dis* 2008; 46: 1221–1226.
15. Byren I, Bejon P, Atkins BL *et al.* One hundred and twelve infected arthroplasties treated with 'DAIR' (debridement, antibiotics and implant retention): antibiotic duration and outcome. *J Antimicrob Chemother* 2009; 63: 1264–1271.
16. Berdal JE, Skramm I, Mowinckel P, Gulbrandsen P, Bjornholt JV. Use of rifampicin and ciprofloxacin combination therapy after surgical debridement in the treatment of early manifestation prosthetic joint infections. *Clin Microbiol Infect* 2005; 11: 843–845.
17. Ceri H, Olson ME, Stremick C, Read RR, Morck D, Buret A. The Calgary Biofilm Device: new technology for rapid determination of antibiotic susceptibilities of bacterial biofilms. *J Clin Microbiol* 1999; 37: 1771–1776.
18. Zimmerli W, Frei R, Widmer AF, Rajacic Z. Microbiological tests to predict treatment outcome in experimental device-related infections due to *Staphylococcus aureus*. *J Antimicrob Chemother* 1994; 33: 959–967.
19. Moran E, Masters S, Berendt AR, McLardy-Smith P, Byren I, Atkins BL. Guiding empirical antibiotic therapy in orthopaedics: the microbiology of prosthetic joint infection managed by debridement, irrigation and prosthesis retention. *J Infect* 2007; 55: 1–7.
20. Salgado CD, Dash S, Cantey JR, Marculescu CE. Higher risk of failure of methicillin-resistant *Staphylococcus aureus* prosthetic joint infections. *Clin Orthop Relat Res* 2007; 461: 48–53.
21. Soriano A, Gomez J, Gomez L *et al.* Efficacy and tolerability of prolonged linezolid therapy in the treatment of orthopedic implant infections. *Eur J Clin Microbiol Infect Dis* 2007; 26: 353–356.
22. Bassetti M, Vitale F, Melica G *et al.* Linezolid in the treatment of Gram-positive prosthetic joint infections. *J Antimicrob Chemother* 2005; 55: 387–390.