# *Pseudomonas aeruginosa* implant-associated Bone and Joint Infections : Experience in a Regional Reference Center in France

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## INTRODUCTION

Implant-associated bone and joint infection (BJI) is an uncommon, but dreadful complication of arthroplasties and orthopedic trauma. *P. aeruginosa* is a particular GNB (Gram-negative bacteria) commonly considered as non-fermenting bacterium, that causes 5 to 20% of the GNB infections and is considered as one of the most difficult-to-treat GNB,.

The aim of this study is to analyze the impact of optimal surgical treatment, effective antimicrobial IV therapy and ciprofloxacin use on the prognosis of implant-associated *P. aeruginosa* BJI.

## POPULATION - METHODS

We included all patients, with *P. aeruginosa* implant-associated infection managed in our institution between January 2011 and June 2018. Definitions were:

- Implant-associated infection was diagnosed according to the definition of organ/space surgical site infection proposed by the CDC .
- Implant-associated infections in this study were defined as “early” (within 1 month from the date of implantation), “delayed” (between 1 and 3 months from the date of implantation )and “chronic” if the onset of symptoms was >3 months from the date of implantation.
- Treatment failure was defined as any type of relapse of implant-associated infection including persistence (new surgery with *P. aeruginosa* in culture), superinfection or any other cause of relapse such as the need for a subsequent surgery.
- Optimal surgical treatment was evaluated according to the type of surgery and the timing of the infection.
- Effective initial antibiotic treatment was defined by the use of an active IV beta-lactam drug, based on drug-susceptibility on the antibiogram.

**Table 1**

| Characteristics | Whole population (n=90) | Failure (n=23) | Remission (n=67) | p[a] |
|---|---|---|---|---|
| Age in years (median, IQR) | 60 (47-72) | 61 (43-74) | 59 (47-72) | 0.90 |
| Male sex (n, %) | 56 (62) | 17 (74) | 39 (58) | 0.18 |
| BMI ≥30 (n, %) | 24 (28) | 6 (29) | 18 (29) | 1 |
| Active smoking (n, %) | 29 (35) | 10 (44) | 19 (32) | 0.34 |
| Score ASA > 2 (n, %) | 30 (34) | 8 (35) | 22 (33) | 0.90 |
| Score Charlson > 4 (n, %) | 24 (27) | 7 (30) | 17 (25) | 0.64 |
| Previous infection at the same site (n, %) | 19 (21) | 6 (26) | 13 (19) | 0.50 |
| Prosthesis (n, %) | 30 (33) | 7 (30) | 23 (34) | 0.73 |
| Age of implant in days (median, IQR) | 47 (21.7-247.5) | 40 (21-222) | 63 (26-798) | 0.29 |
| Acute infection (n, %) | 56 (62) | 14 (61) | 42 (63) | 0.98 |
| Sub-acute infection (n, %) | 8 (9) | 2 (9) | 6 (9) | |
| Chronic infection (n, %) | 26 (29) | 7 (30) | 19 (28) | |
| Polymicrobial infection (n, %) | 66 (73) | 18 (78) | 48 (71) | 0.54 |
| BJI due to *P. aeruginosa* ciprofloxacin-resistant (n, %) | 11 (12) | 9 (39) | 2 (3) | <0.001 |
| Optimal surgical treatment (n, %) | 54 (64) | 9 (39) | 45 (72) | 0.004 |
| Effective initial IV treatment (n, %) | 64 (71) | 12 (52) | 52 (77) | 0.020 |
| Treatment with ciprofloxacin (n, %) | 79 (88) | 13 (57) | 66 (99) | <0.001 |

## RESULTS

Among the 1638 implant-associated BJI occurring over the 7-year study period, 90 patients (5,49%) were infected by *Pseudomonas aeruginosa* and were included (Table 1).

Twenty-five patients experienced 28 adverse events under antibiotics active against *P. aeruginosa* (13 SAE).

Fifty-six (62%) patients were considered to have optimal surgical treatment, including 21 DAIR for an acute infection, 2 had incomplete implant removal, 31 complete implant removal for a chronic infection, one complete ablation followed by amputation and one DAIR followed by amputation. During a prolonged follow-up (median follow-up of 20 months [IQR, 9-37]; 40 patients were lost to follow-up during the first two-years; 24 patients without failure were followed at least 2 years, 23 patients experienced a treatment failure: 7 patients experience a persistence of *P. aeruginosa* after treatment, while 16 had a superinfection. Optimal surgical treatment was significantly associated with a higher success rate in the univariate analysis (p=0.003) and in the Kaplan-Meyer survival curve (log-rank test, p=0.009) (panel A).

As long as it concerns the antimicrobial treatment, sixty-four (71%) patients received effective initial treatment against *P. aeruginosa* administered by IV, while 26 (29%) did not. Not receiving an effective initial IV drug exposed the patient to an early failure (panel B) and when we considered an IV treatment of at least 3 weeks, which was undertaken by 90 (81%) patients, it correlates with a higher success rate both in the univariate analysis (p=0.020) and according to the Kaplan-Meyer curve (log-rank test, p=0.009) (panel B).

Eleven (12%) patients had an infection due to a *P. aeruginosa* resistant to ciprofloxacin and this impacted as well (p<0.001). Seventy-nine (88%) patients received a course of therapy with ciprofloxacin and this was significantly associated with a higher success rate in the univariate analysis (p<0.001) (panel C). Moreover, we observed a higher risk of failure if patients received less than 3 months of ciprofloxacin (log-rank test, p=0.007) (panel D).

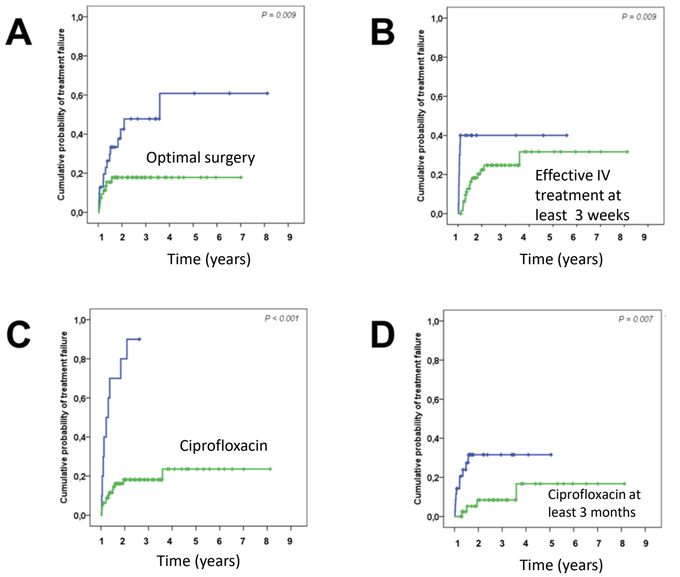


**Figure 1** : Kaplan-Meier curves showing the probability of treatment failure depending on the surgical and medical treatments

## CONCLUSIONS

Our data show that these infections are mostly acute and often polymicrobial. After a long-term follow-up, the remission rate of patients with a *P. aeruginosa* implant-associated BJI was 74% . Surgical treatment is the cornerstone of Implant-associated infections and choosing the correct operation for the case among the number of option should follow as possible the current guidelines. It must be a multidisciplinary, meticulous process, and it must take into account the patient status and integrate its functional prognosis in case of implant removal. *P. aeruginosa* implant-associated BJI is one of the most difficult-to-treat BJIs, with a strong impact on the prognosis of the surgical strategy. An effective initial IV antibiotic treatment for at least 3 weeks seems to be required, followed by oral ciprofloxacin for a total duration of 3 months.