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Complications - Infection

# Continuous Antibiotic Therapy Can Reduce Recurrence of Prosthetic Joint Infection in Patients Undergoing 2-Stage Exchange

Tiziana Ascione, MD [a,*], Giovanni Balato, MD, PhD [b], Massimo Mariconda, MD [b], Renato Rotondo, MD [c], Andrea Baldini, MD [d], Pasquale Pagliano, MD [a]

[a] Department of Infectious Diseases, D. Cotugno Hospital, AORN Dei Colli, Naples, Italy
[b] Department of Public Health, Orthopedic Unit, "Federico II" University, Naples, Italy
[c] Department of Orthopedic Surgery, C.T.O. Hospital, AORN Dei Colli, Naples, Italy
[d] Orthopedic Unit, IFCA Institute, Florence, Italy

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ABSTRACT

*Background:* Reimplantation microbiology and serum C-reactive protein have low diagnostic accuracy in predicting recurrence in patients with prosthetic joint infection (PJI) undergoing 2-stage exchange. We aimed at identifying factors relating to failure and comparing effect of continuous antibiotic therapy versus a holiday antibiotic period pre-reimplantation.

*Methods:* This observational study included patients with PJI undergoing 2-stage exchange. Group A patients did not discontinue antibiotic treatment pre-reimplantation; in group B patients, antibiotic treatment was followed with 2 weeks of holiday antibiotic period pre-reimplantation. We defined cure as absence of recurrence for 96 weeks post-reimplantation. Statistical analyses were performed using Mann-Whitney *U* test, Fisher exact test, and multivariate analysis.

*Results:* We evaluated 196 patients with PJI (median age, 66 years [interquartile range, 59-72], 91 [46%] males). Comorbidity was reported in 77 (39%), and microbiologic evidence was obtained in 164 (84%). *Staphylococcus aureus* was isolated in 63 of 164 (38%) patients; coagulase-negative staphylococci were isolated in 71 of 164 (43%). Favorable outcome was achieved for 169 (86%) patients (91% and 79% in groups A and B, respectively). No immunocompromise (odds ratio [OR], 2.73; 95% confidence interval [CI], 1.3-7.3; $P = .04$), a positive culture (OR, 3.96; 95% CI, 1.55-10.19; $P = .02$), and no antibiotic discontinuation (OR, 3.32; 95% CI, 1.3-8.44; $P = .02$) predicted favorable outcome using multivariate analysis.

*Conclusion:* Treatment with continuous antibiotic therapy ameliorated success rate, permitting a better outcome in immunocompromised and reducing the time to reimplantation. Continuous antibiotic therapy can be considered a valid option for the treatment of patients with PJI undergoing 2-stage exchange.

*Level of evidence:* Therapeutic level II.



Infection is a threatening complication of prosthetic joint implant placement causing further disability and increasing the total procedure cost. The 2-stage exchange, which permits joint function restoration and infection resolution, is an option in the management of prosthetic joint infection (PJI) [1–6].

While the 2-stage procedure is commonly used, many aspects still require investigation. It is not clear how best to determine the duration of the antibiotic treatment nor the real predictive value of diagnostic and microbiologic investigations at the time of reimplantation [7]. In common practice, patients undergoing 2-stage exchange replacement have to observe a holiday antibiotic period before reimplantation to ensure eradication of infection, but no comparative study supports this treatment option [8–15]. In practice currently, serum inflammatory markers, synovial fluid cell count, and preoperative and intraoperative cultures at

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* Reprint requests: Ascione Tiziana, MD, Department of Infectious Diseases, D. Cotugno Hospital, AORN Dei Colli, Naples, Italy.

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reimplantation are used as tools to establish the definitive cure and to predict treatment success [7,8]. However, none of these diagnostic tools accurately predict the risk of PJI recurrence after 2-stage replacement [16–25].

The Infectious Diseases Society of America Clinical Practice Guidelines on PJI and the International Consensus Group on PJI have consistently underlined the difficulty in establishing the appropriate duration of antibiotic treatment and the appropriate reimplantation time when using these markers [1,2]. Moreover, on the basis of investigations highlighted by the International Consensus Group on PJI, no evidence fully supports a holiday antibiotic period before reimplantation to establish infection eradication (Web reference [1]).

Therefore, to assess the usefulness of the holiday antibiotic period and the accuracy of diagnostic markers in a 2-stage exchange procedure, we evaluated all patients with PJI undergoing 2-stage exchange referred for an infectious diseases consultation to our Department of Infectious Diseases over an 8-year period, from 2009 to 2016. Patients were referred by 2 orthopedic centers that had adopted 2 different antibiotic treatment protocols: (1) continuous antibiotic therapy and (2) antibiotic treatment followed by a holiday antibiotic period pre-reimplantation. The main end point of the study was to compare the effect of continuous antibiotic therapy versus a holiday antibiotic period pre-reimplantation on PJI recurrence after 2-stage exchange. Moreover, we analyzed factors related to poor outcome after 2-stage exchange in PJI patients undergoing reimplantation with stable normalization of serum inflammatory markers and local symptoms disappearance.

## Materials and Methods

This observational cohort study comprised consecutive patients with PJI who had been treated in 2 different orthopedic centers adopting 2 different schedules of antibiotic treatment, both considering antibiotic administration for 8 weeks before reimplantation on the basis of their pre-established internal protocol. Duration of antibiotic treatment between stage 1 and 2 was established according to Italian guidelines on PJI and was standardized within each group [26]. In group A, patients did not discontinue antibiotic treatment pre-reimplantation, and in group B, antibiotic treatment was followed by 2 weeks of holiday antibiotic period pre-reimplantation (Fig. 1). The research was conducted in accordance with the Declaration of Helsinki and national and institutional standards, and patients gave their informed consent before being included in this observational study.

Case definition was based on Musculoskeletal Infection Society criteria as we previously described elsewhere [3,13]. The inclusion criteria were (1) a diagnosis of PJI as established above, (2) age > 18 years, and (3) delayed infection. The exclusion criteria were (1) post-therapy follow-up of less than 96 weeks, (2) HIV infection, and (3) infection persistence after spacer placement and adequate antibiotic therapy, as defined by clinical symptoms persistence, and persistently high erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

### *Preliminary Data Collection*

We recorded demographic data using a standardized case report form, before surgery, as well as the Charlson comorbidity index adjusted for age, detailed information concerning previous or underlying diseases, presenting signs and symptoms (sinus tract local inflammation and joint effusion), findings of the synovial fluid examinations (cell count, including neutrophil count percentage), and results of laboratory investigations. Patients were considered immunocompromised if they reported any condition associated with an impaired immune response such as diabetes, liver cirrhosis, autoimmune diseases (ie, rheumatoid arthritis), or were receiving immunosuppressive treatments (ie, steroids, tumor necrosis factor alpha inhibitors).

### *Microbiologic Studies*

Cultures for aerobic and anaerobic organisms were attempted for all patients. Synovial fluid aspirate was collected as part of the preoperative workup for cell count and microbiologic cultures before surgical stage 1 and pre-reimplantation, when feasible. At least 5 intraoperative specimens from tissues surrounding the prosthetic implant were collected for microbiologic examination either at the time of explantation or when reimplantation was performed. Fluid from implant sonication was cultured, when available, as previously described [27,28].

### *Treatment*

The adopted 2-stage exchange procedure has been extensively described elsewhere [13]. According to Italian guidelines on PJI,

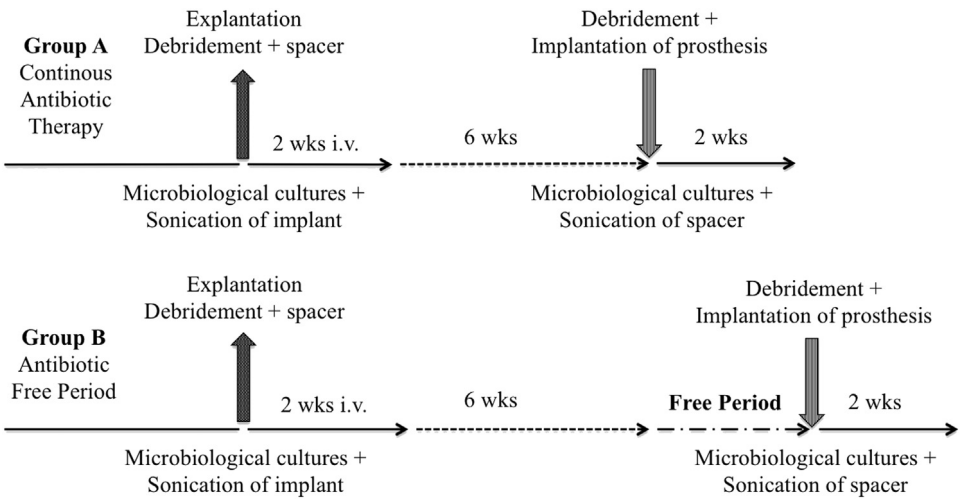


**Fig. 1.** Treatment plan in the centers adopting continuous therapy or not. i.v., intravenous.

antibiotic treatment protocol considered 2 consecutive phases consisting of a 2-week period of intravenous therapy followed by a 6-week period of oral targeted therapy (when feasible on the basis of microbiologic findings) [26]. Antibiotic therapy was started for each patient after implant removal with parenteral antibiotics for 2 weeks. Drug choice was based on the evidence obtained through synovial fluid culture before infected implant explantation, when available, or on empiric choices considering drugs active against Gram-positive methicillin-resistant bacteria, until the microbiologic culture of periprosthetic tissues or implant sonication results became available. The following 6 weeks of antibiotic therapy were based mainly on oral drugs (if possible) selected on the basis of microbiologic investigation. When culture results were negative, combination regimens containing a drug active against methicillin-resistant staphylococci such as cotrimoxazole or minocycline were considered as the first-line therapy after the period of parenteral antibiotic therapy. After completing the antibiotic therapy course, group A patients underwent reimplantation without discontinuation, whereas patients in group B stopped antibiotic therapy for 2 weeks before reimplantation. Reimplantation was scheduled in patients with persistent CRP and ESR normalization coupled with the absence of any local symptoms at the evaluation scheduled before reimplantation (Fig. 2).

### *Planned Examinations*

ESR, CRP, and a complete blood count were assessed before the infected implant removal and every 7 days during the 2 weeks following spacer placement. Thereafter, routine laboratory data were assessed after 4 weeks and before reimplantation. Synovial fluid aspiration investigation was attempted before reimplantation and synovial cell count and cultures were obtained, when available. After prosthetic implant replacement, CRP levels and ESR were assessed during a 96-week period. Cure was defined as the disappearance of all clinical and radiological evidence of PJI coupled with CRP normalization during a 96-week follow-up period after the discontinuation of antibiotic treatment.

### *Statistical Analysis*

Quantitative data were expressed as median (interquartile range [IQR]) and compared using the Mann-Whitney *U* test. Fisher exact test and the chi-squared test were used to compare qualitative variables. *P* values less than .05 were considered significant. Variables achieving statistical significance at a 95% level in the univariate analysis were simultaneously considered using multivariate logistic regression analysis to determine independent factors of adverse outcome.

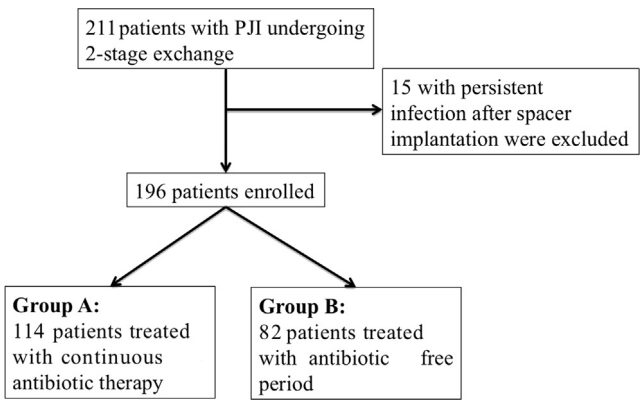


**Fig. 2.** Flowchart of the patients considered and included in the study. PJI, prosthetic joint infection.

## Results

We initially included 211 patients with PJI undergoing 2-stage exchange in this study. Fifteen patients did not undergo reimplantation procedure because of an ongoing infection after spacer implantation, defined as a persistently elevated ESR, and CRP coupled with local symptoms despite antibiotic treatment. For this reason, these patients were excluded by the final analysis.

A total of 196 patients with PJI were finally included. The median age was 66 years (IQR, 59-72) and 46% were males. Previous surgery comprised 84 (43%) hip arthroplasties and 112 (57%) knee arthroplasties. According to the pre-established internal protocol of the referring centers, 114 (58%) patients did not discontinue antibiotic therapy pre-reimplantation (group A) and 82 (42%) discontinued antibiotic therapy before reimplantation (group B) (Fig. 2). Median follow-up post-reimplantation placement was 96 weeks (from 96 weeks to 264 weeks). Known comorbidities relating to an increased risk of infection were reported in 77 (39%) patients, and patients with diabetes mellitus (n = 28), chronic hepatitis (n = 12), rheumatic disease (n = 10), and end-stage renal failure (n = 7) were those identified with the highest frequency. There were 15 (8%) patients with a body mass index (BMI) > 30 kg/m$^2$.

Microbiologic investigations were positive in 164 (84%) patients (polymicrobic infection, n = 8). Coagulase-negative staphylococci were isolated in 71 (43%) patients (21 were methicillin resistant). *Staphylococcus aureus* was isolated in 63 (38%) patients (22 were methicillin resistant). Gram-negative bacteria were isolated in 22 (13%) patients, and the most common Gram-negative bacteria cultured was *Pseudomonas aeruginosa.*

Table 1 shows the main baseline clinical and laboratory findings in the 2 study groups. No significant difference was noted in respect to all variables evaluated. Finally, 156 patients reported monomicrobic PJI, 8 polymicrobic PJI, and 32 culture-negative PJI.

The median antibiotic treatment duration was 8 weeks (IQR, 8-8) in both groups. All patients completed the prescribed course of antibiotic therapy. No patient had to discontinue antibiotic treatment due to major side effects. Group B patients discontinued antibiotic therapy for a median duration of 15 days (IQR, 14-17) before definitive reimplantation. As established through the internal protocols of the referring centers, patients reported no clinical signs suggestive of an active infection, and both ERS and CRP levels were below the upper normal value before reimplantation.

Specimens obtained at reimplantation revealed bacterial growth in 17 cases (group A, n = 8; group B, n = 9). No patient with positive microbiologic findings at reimplantation reported microbiologic concordance of bacterial isolation at explantation of the prosthesis and at reimplantation. No patient reported 2 or more positive cultures with an identical organism from specimens obtained at reimplantation. Table 2 shows the results of investigations obtained at the time of reimplantation. Synovial fluid examination findings (leukocyte and neutrophil percentage) did not differ between the 2 groups. No change in the antibiotic treatment and surgical plan was done for 3 patients with synovial fluid culture–positive findings before reimplantation which were discordant in respect to the findings at explantation.

A favorable outcome after reimplantation was achieved in 169 (86%) patients, of whom 104 (cure rate 91%) patients were in group A and 65 (cure rate 79%) were in group B (104/114 vs 65/82; $X^2$ = 4.78, $P$ = .029), as assessed following 96 weeks of follow-up (Table 3). There was no reported association according to sex, Charlson comorbidity index, age, and patient outcome. The cure

**Table 1**
Baseline Characteristics of the Study Patients.

| N° | All Study Patients | Group A | Group B |
|---|---|---|---|
| | N = 196 | N = 114 | N = 82 |
| Sex (no. of patients) | | | |
| Male | 91 (46%) | 52 (46%) | 39 (47%) |
| Female | 105 | 62 | 43 |
| Mean age (IQR) (y) | 66 (59-72) | 67 (58-74) | 66 (57-75) |
| Involved joint (no. of patients) | | | |
| Knee | 112 | 63 | 47 |
| Hip | 84 | 51 | 35 |
| Risk factors for an increased risk of infection (no. of patients [%]) | 77 (39%) | 45 (39%) | 32 (39%) |
| Mean ESR; mm/h (range) | 71 (31-108) | 65 (45-81) | 59.1 (31-108) |
| Mean CRP; mg/L (range) | 25 (8.1-50) | 22 (8.1-50) | 24 (9.3-45) |
| SF mean leukocyte count (cells/mL) | 7892 (3210-28,420) | 6106 (3250-28,420) | 7881 (3210-27,800) |
| SF mean neutrophil percentage | 84 (72-92) | 82 (72-92) | 85 (81-90) |
| Culture-positive rate (no. [%]) | 164 (84%) | 94 (82%) | 70 (85%) |
| *Staphylococcus aureus*[a] | 63 (38%) | 37 (39%) | 26 (37%) |
| (% MRSA) | 22 | 12 | 10 |
| CN staphylococci[a] | 71 (43%) | 41 (36%) | 30 (42%) |
| *Enterococcus spp*[a] | 8 (5%) | 5 (5%) | 3 (4%) |
| Gram-negative bacteria[a] | 22 (13%) | 12 (13%) | 10 (14%) |
| Other bacteria[a] | 8 (5%) | 4 (4%) | 4 (6%) |
| Polymicrobic[a] | 8 (5%) | 4 (4%) | 4 (6%) |

CRP, C-reactive protein; CN, coagulase-negative; ESR, erythrocyte sedimentation rate; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; SF, synovial fluid.

[a] Percentage is calculated in respect to the total of 164 patients with positive microbial findings in the second column, in respect to 94 group A patients with positive microbial findings in the third column, and in respect to 70 group B patients with positive microbial findings in the fourth column.

rate was higher in those without a comorbidity causing an impaired immune response (108/119 vs 61/77; $X^2 = 4.3$, $P = .038$). After all baseline clinical findings had been considered, neither the CRP concentration nor the blood analysis findings obtained at baseline predicted the outcome. Patients with a BMI < 30 reported a better response rate compared to obese patients (158/181 vs 11/15; $X^2 = 2.27$, $P = .13$), but this finding was not significant. There was no significant difference in infection cure rates based on hip or knee infection (73/84 vs 96/112; $X^2 = 0.06$, $P = .8$). When microbiologic findings were considered, we found that bacterial growth from operative specimens better predicted the outcome compared to negative culture (146/164 vs 23/32; $X^2 = 5.26$, $P = .02$). Moreover, Gram-positive growth was associated with a higher response rate than Gram-negative growth (133/143 vs 13/21; $X^2 = 15.1$, $P = .0001$). Following the 2-week period of intravenous therapy, 114 patients received oral antibiotic therapy. These patients demonstrated a favorable outcome more frequently than 74 patients receiving intravenous therapy during the entire treatment period (110/122 vs 59/74; $X^2 = 4.22$, $P = .04$). Moreover, the cure rate in those with positive microbiologic investigations at reimplantation was not different than for those with negative microbiologic investigations (15/17 vs 154/179; $X^2 = 0.06$, $P = .8$). After multivariate analysis was applied, we found that bacterial growth obtained from cultures (odds ratio [OR], 3.96; 95% confidence interval [CI], 1.55-10.19; $P = .02$), absence of comorbidity related to an increased risk of infection (OR, 2.73; 95% CI, 1.1-7.3; $P = .04$), and a surgical procedure without discontinuation of antibiotic therapy before reimplantation (OR, 3.32; 95% CI, 1.3-8.44; $P = .02$) predicted a favorable outcome.

After the cure rate was analyzed in patients who were immunocompromised, we found that cure rate was higher in 46 immunocompromised patients receiving continuous therapy than in 31 immunocompromised patients observing a holiday antibiotic period pre-reimplantation (41/46 vs 20/31; $X^2 = 5.4$, $P = .02$). Therefore, the cure rate in respect to continuous therapy was not different in immunocompetent patients (63/68 vs 44/51; $X^2 = 1.3$, $P = .2$).

**Table 2**
Findings of Biochemical and Microbiologic Investigations Before Reimplantation.

| Findings | Group A | Group B | *P* Value |
|---|---|---|---|
| Mean ESR; mm/h (range) | 23.0 (12.2-24.7) | 25.6 (4-35) | NS |
| Mean CRP; mg/L (range) | 3.7 (1.1-3.7) | 3.3 (1.2-3.5) | NS |
| SF mean leukocyte count (cells/mL) | 1122 (980-1439) | 1485 (1089-1730) | NS |
| SF mean neutrophil percentage | 47 (31.2-62) | 45 (32-61) | NS |
| Culture-positive rate (no. [%]) | 8 (7%) | 9 (11%) | NS |

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NS, not significant; SF, synovial fluid.

## Discussion

Patients undergoing a 2-stage exchange procedure receive antibiotic treatment to treat periprosthetic infection [4]. In daily practice, antibiotic treatment can be withdrawn before definitive reimplantation to monitor clinical symptoms and inflammatory markers, and to ensure the highest accuracy of microbiologic investigations in regard to synovial aspirate and intraoperative specimens when assessing microbiologic cure [10,11,18–20]. On the basis of recent data and meta-analysis, time to reimplantation has to be considered a “team choice” [7,8,26,29]. In our study, despite including only patients with normalized inflammatory markers and no clinical signs of infection, we reported a 14% rate of PJI recurrence in the entire study population. Other investigators have reported similar data regarding the difficulty in assessing a definitive cure using an inflammatory index dosage and through the disappearance of clinical symptoms. Ghanem et al [19] analyzed a large series of PJI patients having undergone a 2-stage exchange procedure and reported that CRP and ESR levels at reimplantation in patients undergoing a holiday antibiotic period were similar to those experiencing infection recurrence and to those having had a successful procedure. Moreover, receiver operator characteristic curve and area under curve analyses reported by Muhlhofer et al [20] demonstrated that CRP measured after a 14-day antibiotic-free interval could not be used to exclude persistent infection and that no cutoff value could be determined due to low area under curve values. We can conclude that clinical signs and inflammatory markers play a key role in diagnosing PJI, but their role in predicting a successful procedure is very low [2,3,22–24].

**Table 3**
Main Factors Associated With a Favorable Outcome.

| Findings | Favorable Outcome | Unfavorable Outcome | Odds Ratio (95% CI) by Univariate Analysis | *P* | Odds Ratio (95% CI) by Multivariate Analysis | *P* |
|---|---|---|---|---|---|---|
| Continuous therapy | 104 | 10 | 2.72 (1.17-6.30) | .02 | 3.32 (1.31-8.44) | .01 |
| Holiday period | 65 | 17 | | | | |
| Bacterial growth | 146 | 18 | 3.17 (1.26-7.90) | .02 | 3.96 (1.55-10.19) | .01 |
| No bacterial growth | 23 | 9 | | | | |
| Gram-positive growth | 133 | 10 | 8.18 (2.75-24.3) | <.001 | — | NS |
| Gram-negative growth | 13 | 8 | | | | |
| Oral therapy | 110 | 12 | 2.33 (1.02-5.30) | .03 | — | NS |
| Intravenous therapy | 59 | 15 | | | | |
| Absence of immunocompromisation | 108 | 11 | 2.58 (1.12-5.90) | .03 | 2.73 (1.1-7.3) | .04 |
| Presence of immunocompromisation | 61 | 16 | | | | |

CI, confidence interval; NS, not significant.

As expected, we reported a low rate of positive cultures at reimplantation in both treatment groups. No correlation was observed between positive cultures at reimplantation and recurrence of infection during follow-up either in those treated using continuous antibiotic therapy or in those observing a holiday antibiotic period pre-reimplantation. Furthermore, the microbiologic findings obtained at reimplantation did not match with those retrieved at explantation. Bejon et al [12] and Puhto et al [11] reported positive microbiologic findings in 5% and 14%, respectively, of patients undergoing the second step of the 2-stage procedure in 2 large case series involving patients observing an antibiotic holiday period. In these studies, microbiologic findings at reimplantation matched those at explantation in only a few patients, and positive microbiologic findings were not predictive of an unsuccessful procedure. Tan et al reports [24] report similar data and highlight that bacteria cultured at reimplantation are responsible for 2-stage failure in the minority of the cases. Therefore, the need for culture at reimplantation cannot justify observing an antibiotic holiday period, as data deriving from this practice are ineffective in predicting procedure success and in guiding the surgical plan.

Data derived from synovial aspirate at reimplantation did not predict reinfection. In fact, the synovial leukocyte count before the second step of the procedure did not correlate with infection persistence, regardless of when antibiotic therapy was discontinued, and bacterial growth on synovial fluid aspirate was reported in only 3 patients. In the study by Muhlhofer et al [20], a high synovial fluid leukocyte count before the second step of the procedure was not able to predict infection recurrence. Moreover, synovial fluid culture was able to predict procedure failure only in the cases investigated after an antibiotic holiday period of 4 weeks in a small series of PJI undergoing 2-stage surgery [30].

In this study, we obtained a cure rate of 86% by the administration of antibiotic treatment for 8 weeks before definitive reimplantation and no patient had to discontinue the treatment due to major side effects. Our schedule of antibiotic treatment is atypical for standard of care in many Western countries, but no comparative study suggests the ideal duration of antibiotic treatment. When we planned the study, we followed the indications highlighted by the Italian guidelines on PJI that considered 2 to 3 weeks of intravenous therapy followed by 5 to 6 weeks of oral therapy [26].

Administration of a sequential intravenous to oral therapy was associated with better outcome only by univariate analysis, but not by multivariate analysis. Most of the cases receiving an intravenous therapy had infection sustained by multidrug-resistant Gram-negative bacteria or had a culture-negative infection, justifying the lack of significance, when we applied multivariate analysis. Our study was not tailored to establish the efficacy of oral or intravenous therapy in patients with PJI undergoing 2-stage exchange but demonstrates that switching to an oral therapy has to be considered as safe and effective as continuing intravenous therapy during the complete antibiotic treatment period [13].

Cure rates after hip or knee 2-stage exchange were similar. No comparative data demonstrate a difference in terms of outcome for those with hip or knee infection undergoing 2-stage exchange, as extensively reviewed by Tande and Patel [31].

Current investigations demonstrate that a high BMI is associated with an increase in the risk of infection after arthroplasty [30]. In our study, only 8% of patients were overweight (BMI > 30) and the association retrieved between BMI and outcome was not significant probably due to the small size of the sample of overweight patients. The percentage of obese in our study is lower than that reported in other Western countries, but it is representative of the incidence of obesity in Italy (Web reference [2]).

In our case series, we analyzed data derived from patients undergoing definitive reimplantation with or without a holiday antibiotic period and found that the highest rate of cure was reported in those observing continuous antibiotic therapy. This beneficial outcome was higher among the immunocompromised patients. An association between the presence of comorbidity and immunosuppression and poor outcome has previously been reported [6,13]. Bacteria present in sanctuaries such as bone sequestration or on the spacer surface before the second stage of the procedure can actively replicate because of compromised immunity against capsulate agents, as reported in aging patients, in those with chronic inflammatory diseases receiving immunosuppressive drugs, or in those with diabetes mellitus or chronic hepatitis [15,25,27,32–36]. It could be assumed that persistent inhibition of bacterial growth due to continuous antibiotic therapy reduces low-grade bacterial replication in the sanctuaries. This explains the high success rate obtained by continuous antibiotic therapy in immunocompromised patients, with no detrimental effect due to the theoretical loss of accuracy of microbiologic investigations performed at the time of reimplantation.

Moreover, it is important to note the practical usefulness of continuous therapy in shortening the overall time needed for the 2-stage procedure (Fig. 1). On theoretical basis, avoiding a holiday antibiotic period could ameliorate the definitive outcome in terms of joint function, as no more than 8 weeks pass between infected implant removal and definitive prosthetic implant reimplantation. It is notable that a definitive reimplantation performed at >11 weeks was associated with a higher frequency of poor outcomes and, as recently reported by Tan et al, the duration of spacer implantation was significantly associated with reinfection [8,37].

In conclusion, our study demonstrates that reimplantation remains a challenge in clinical practice due to a lack of preoperative procedures that can assess a definitive microbiologic cure. No single examination finding can guarantee infection cure before

reimplantation using either biochemical examinations or microbiologic investigations. In our study, treatment with continuous antibiotic therapy ameliorated success rate, permitting a better outcome particularly in immunocompromised and reducing the time to reimplantation, so continuous antibiotic therapy can be considered a valid option for the treatment of patients with PJI undergoing 2-stage exchange.

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