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Letters to the Editors

Letter to the Editor on “Continuous Antibiotic Therapy Can Reduce Recurrence of Prosthetic Joint Infection in Patients Undergoing 2-Stage Exchange”
**To the Editor:**

We had the opportunity to read the article by Dr Ascione et al and we did it with great interest, as the authors address a relevant question regarding the treatment of periprosthetic joint infection, which has not been answered yet. We congratulate the authors for this initiative to determine which protocol of antibiotic treatment before reimplantation during 2-stage exchange leads to higher success rates [1]. However, the results and conclusions drawn from the study could be misleading, as there are some major methodological shortcomings that might jeopardize the validity of the results.

First, the authors find a statistically significant difference in the results of cure rate after reimplantation among groups: 91% in group A and 79% in group B ($P = .029$) [1]. Remarkably, the success rate reported for group B is considerably lower than most results previously reported for 2-stage exchange for both hip and knee [2–5]. As long as the aforementioned difference is the result of a comparison between 2 hospitals rather than 2 protocols, there are several factors other than the reimplantation regimes which might be affecting the success rates of the study groups. Although we acknowledge the outstanding effort of the authors describing the demographic characteristics of the study groups, which actually are comparable, there are other variables that influence the results of 2-stage revision that are difficult to control in this study design (ie, surgical technique).

A second comment is regarding the title and conclusion of the study, which could be misleading as well. To our understanding, both groups received antibiotic therapy during 8 weeks without interruption, as recommended by local clinical practice guidelines, and the only difference lies on the span between the end of the antibiotic and the reimplantation surgery. As both study groups receive the same antibiotic regime, even in the hypothetical scenario of valid results, the study intervention should have been defined as the reimplantation timing rather than the continuity of the antibiotic therapy protocol.

In summary, this is a relevant question, but the design of the current study is not able to isolate the effect of reimplantation timing in relation to the end of antibiotic therapy. Therefore, this interesting question is yet to be answered.

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Reply to the Letter to the Editor on “Continuous Antibiotic Therapy Can Reduce Recurrence of Prosthetic Joint Infection in Patients Undergoing 2-Stage Exchange” by Castaño et al



In Reply:

Castaño et al raise some questions on the methodology of our recent paper investigating the usefulness of an antibiotic-free period prior to reimplantation in patients with prosthetic joint infection (PJI) undergoing 2-stage procedure. Main questions are that the response rate obtained for patients undergoing definitive reimplantation after an antibiotic holiday period was lower than reported in their literature analysis and that the difference reported was not attributable to the effect of continuous therapy, but to the surgical procedure [1].

We thank Dr Castaño for the interest in our work, but we think that the analysis does not permit to draw the present conclusions. In fact, Castaño et al refer to 2 recent studies to justify the affirmation that the success rate obtained in patients observing a holiday period of antibiotic therapy prior to reimplantation was lower than generally reported in PJI undergoing 2-stage procedure [2,3]. However, when we examined the studies cited by Castaño et al, we did not find any data on the antibiotic protocol adopted for the patients included in the study by Svensson et al and found that the patients evaluated in the study by Akgün et al did not stop antibiotic therapy prior to reimplantation reporting a success rate comparable to that observed in our patients belonging to continuous therapy group. Consequently, these studies cannot be used to sustain that the success rate for the patients who discontinued antibiotic therapy (group B) was lower than reported in the literature analysis.

Furthermore, the review papers cited by Castaño et al report a wide variability in terms of success rate (between 70% and 100%) and do not support the affirmation that the success rate in the patients enrolled in our study and treated with an antibiotic holiday period prior to definitive reimplantation was lower than generally reported in studies reporting the success rate of PJI undergoing 2-stage exchange.

Cure rate after 2-stage procedure can be affected by a number of factors and composition of the study population can influence the percentage of the cases receiving a successful treatment [4]. For these reasons, any comparison through studies can be highly misleading. When we stratified the patients in respect to the different variables influencing the cure rate, we found that the groups were absolutely

comparable for all the variables considered and demonstrated the effect of “continuous therapy” by the multivariate analysis that accurately predict the independent risk related to each factor.

Indeed, Castaño et al refer to surgical techniques that can affect the success rate. As we know that factors related to surgery can affect the outcome, we choose to compare the patients treated in these centers because all participant surgeons had proven experience and expertise in 2-stage revision surgery (senior surgeons), shared their experience during all the study period, adopted the same procedures (as highlighted in the Materials and Methods section), and received infectious diseases consultation by the same infectious diseases group. In this way, we virtually reduced to zero the risk of any surgical bias.

Also, the affirmation that title and conclusion (I think the final paragraph of the conclusion section) are misleading, as the “study intervention should have been defined as the re-implantation timing rather than the continuity of the antibiotic therapy protocol,” is questionable. In fact, when we referred to “continuous therapy” we aimed to underline that the high success rate of the 2-stage procedure was obtained without any antibiotic discontinuation prior to definitive reimplantation. In this scenario, the “continuous antibiotic therapy” was proposed to treat the periprosthetic osteomyelitis until to reimplantation avoiding any growth of bacteria eventually embedded within biofilm, which can occur when antibiotic treatment was “discontinued” prior to reimplantation to perform frequently unnecessary examinations (eg, intraoperative cultures or synovial fluid aspirate cultures).

In summary, we believe that our study addresses an important issue for patients undergoing 2-stage exchange who received no sufficient attention before our analysis, and highlights a new option for the management of PJI undergoing 2-stage exchange with proven efficacy in reducing recurrence rate.

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