Author's response to reviews

Title: Profile of infective endocarditis observed over a 7-year period in a single centre in Italy

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Author's response to reviews: see over
Reply to Reviewers

Ms. No. 3529721989597980
Title: Profile of infective endocarditis observed from 2003 – 2010 in a single center in Italy

Reviewer n. Dr Katsuomi Iwakura

1) We agree with the reviewer comment. We have reported in a better way the data regarding the incidence trend and we also specified that it is not statistically significant (Figure 1 legend and result section, page 6, line 10). We also clearly stated the bias represented by our single-center study in reflecting IE incidence in the general population (discussion section, page 10, line 3 and following).

2) In 92% of the patients studied, ecocardiography was performed in our Hospital, whereas in 8% of the casistic (15 cases) it was performed in other institutes and the detailed results were not available in patient's charts. We clarify this point in the text (page 8, line 18-20), according to reviewer's remark. We also better reported the incidence of dehiscence/paravalvular leakage in PVE, as requested (page 7, line 18 and last line).

3) According to reviewer's comment we added to the paragraph on “relapse/reinfection” (page 7, line 8,9) the number of subjects that presented a relapse or a reinfection.

4) We evaluated the annual incidence of the main microorganisms isolated during the study period and we did not find a significant trend for any of them. This point has been added (page 8, from line 9).

5) Actually, 29% of patients diagnosed to have IE in our cohort had been admitted after a long history of fever (>21 days). We could not define them as “fever of unknown origin” as they do not fulfilled the FUO criteria (data not available for all the patients in the study). We clarified this point in the results (page 6, from line 20) and in the Discussion section (page 10, from line 6).

6) According to the reviewer's suggestion the percentage of patients admitted for a long-lasting fever among IE has been moved to the Results section (page 6, from line 20).

7) According to the reviewer's suggestion, we split the Table 1 in 2 parts and we showed the results of Table 2 in a pie chart.

8) The format has been reviewed throughout the text in accordance with journal instructions. English language has been reviewed by an professional medical writer.
Reviewer n. Dr Chris Duncan

Major revisions:
We agree with the comments of the reviewer. Due to the retrospective nature of our analysis and to the complexity of antimicrobial associations used, it was very hard to classify and analyze the medical treatment regimens. We tried to group the regimens under the “leading” compound, but we are aware that it only partially represents the huge complexity of the associations retrieved and of the weak power of the analysis, as reported. The lack of antimicrobial therapy data in the majority of retrospective cohorts probably mirrors this difficulty. For the same reason, although a high rate of rifampin use was found in native valve IE, we could not fully retrieve the reason of most of these choices, though intolerance, hypersensitivity to other compounds or drug interactions may be argued. We therefore decided to delete from table 4 the data of antibiotic drugs used.
We also agree with the reviewer's observation that the analysis on HIV patients is highly influenced by their IDVU status. We intended to show the characteristics of IE in this subpopulation, that was highly represented in our cohort, but since 85% of HIV-positive patients were IVDU vs 10% of HIV-negative, the high rate of right-sided IE and MSSA is to referred to the IVDU status, as previously reported. We deleted table 3 and reported the results in the text, undelying this issue.
Finally, we reported the results of the Cochran-Armitage test in the figure legend (Figure 1) and clearly specified in the results section that there is no significant increase in the incidence trend.

Minor revisions:
1) Incidence of IE was calculated on all hospitalized patients in our Hospital during the study period. It has been better clarified in the text (page 5, line 15).
2) We added to the paragraph on “relapse/reinfection” (page 7, line 7,8) the number of subjects that presented a relapse or a reinfection. We agree that a second IE episode caused by the same microorganism within the 6 months period after the initial episode it might still represent a reinfection in the IDU population. We actually observed 12 recurrences in 7 IVDU patients, 3 of which were classified as relapses and 9 as reinfections. Only one relapse was caused by S. aureus, being the other to due to Str. Viridans and P. aeruginosa. We better addressed this point in the text (page 11, from line 17).
3) Results. In 92% of the patients studied, echocardiography was performed in our Hospital, whereas in 8% of the casistic (15 cases) it was performed in other institutes and the detailed results were not available in patient's charts. We clarify this point in the text (page 8, line 18-20).
4) We clarified this point in the text according to reviewer's remark (page 9, line 14).

Discretionary revisions:
A large number of patients evaluated were admitted to our Hospital for fever and then transferred to Cardiology, Cardiosurgery, Infectious Diseases. Sometimes different Units were involved in the diagnostic and therapeutic course of a patient. The impact of the specialistic management is therefore not evaluable in our retrospective analysis.
Minor essential revisions:

1) the spelling of centre has been changed to center throughout the text.
2) We changed the type error in the Abstract as remarked.
3) We reported the main invasive procedures associated with health-care associated IE in the background section (page 3, line 8,9) and in the legend of table 2.
4) We modified the references citation according to the journal guidelines.
5) We changed the text accordingly, using “S. bovis”.
6) We modified the text accordingly and use MRSA where requested.

Discretionary revisions:

1) We modified the title following the reviewer's suggestion.
2) Due to the retrospective nature of our analysis and to the complexity of antimicrobial associations used, it was very hard to classify and analyse the medical treatment regimens. In fact, although a high rate of rifampin use was found in native valve IE, we could not fully retrieve the reason of most of these choices, though intolerance, hypersensitivity to other compounds or drug interactions may be argued. We therefore decided to delate from table 4 the data of antibiotic therapy that might be confounding.
3) Actually the rate of MRSA among the S. aureus isolates in our population was 16% (in line with the hospital's MRSA infection rate that is 20-23%). This result is consistent with the current prevalence of MRSA in most of European countries (20-25%) (Navarro MB et al. Curr Opin Infect Dis. 2008;21(4): 372–379; Pearson A, et al J Antimicrob Chemother. 2009;64(suppl 1):i11–i17).