Author's response to reviews

Title: Long-term outcome of infective endocarditis: a study on patients surviving over one year after the initial episode treated in a Finnish teaching hospital during 25 years

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Author's response to reviews: see over
Dear Editor,

Thank you for your positive letter regarding our manuscript: MS: 5666109001596981 entitled “Long-term outcome of infective endocarditis: a study on patients surviving over one year after the initial episode treated in a Finnish teaching hospital during 25 years” by Maija Heiro, Hans Helenius, Saija Hurme, Timo Savunen, Kaj Metsärinne, Erik Engblom, Jukka Nikoskelainen and myself.

We were pleased to hear that two of the Reviewers already recommended acceptance of this manuscript and have addressed the comments of the third Reviewer (Ana Revilla, Reviewer 2) in our accompanying letter. Moreover, the manuscript has now been revised according to her/his suggestions. The changes made have been indicated in our accompanying letter.

We hope that after these revisions and clarifications, you will find this paper satisfactory and suitable to be published in your Journal. Finally, we would like to thank you and the Reviewers for your time, consideration and valuable criticism.

Yours sincerely,

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Comments on the criticism presented by the Reviewers and a list of the changes made according to their suggestions.

**Reviewer 1 (Maurizio Cotrufo)**

We thank the Reviewer for his positive attitude towards our work and for his time, consideration and valuable criticism during the Reviewing process.

**Reviewer 2 (Ana Revilla)**

**Discretionary Revisions**

**Comment 1.**

The Reviewer asks us to address in our Discussion section the finding that patients with recurrent episodes of IE had significantly lower mortality rates than those with no recurrences. The Reviewer also notes that patients with recurrent episodes of IE required cardiac surgery less frequently, perhaps for the same reason.

**Response:**

We have added the following discussion on page 13, lines 13-15:

“At least a partial explanation for this could be that IVDU was a risk factor for the recurrences of IE. The patients with IVDU had a significantly lower mortality than those with no drug use, evidently due to the fact that they commonly had tricuspid valve IE with low mortality.”

Regarding the less frequent requirement for cardiac surgery in the patients with recurrences, we note on page 13, lines 19-20:

“Also this could be partly explained by the positive association between the development of recurrences and IVDU.”

**Comment 2.**

Regarding the 27 patients who died of sequelae of IE, the Reviewer asks which these sequelae were.

**Response:**

Of the 27 patients who died of sequelae of IE, the cause of death was established to be heart failure in 18 patients and sudden death due to arrhythmia in 9 patients. This information has been added on page 6, lines 21-22.
Comment 3.

The Reviewer comments on that the tables of the manuscript are extensive and suggests that either we include only the significant data in the tables or exclude the enumeration of the non-significant findings from the text.

Response:

We have chosen the second alternative and omitted from the Results section the data regarding the patient characteristics that were non-significant regarding the long-term overall outcome (on page 7, lines 18-21, original manuscript) and the long-term cardiac mortality (page 8, lines 18-23, original manuscript).

Comment 4.

The Reviewer points out that the heterogeneity of the population included in this study makes it difficult to take conclusion applicable to the daily clinical practice and recommends that this limitation should be mentioned at the end of the text when applying the results for the clinical practice. Moreover, she/he recommends that in the future, an analysis of long-term prognostic factors in more specific subpopulations of our patients should be performed.

Response:

We have added the following discussion at the end of the Conclusions section, page 14, lines 7-10. “It must be admitted that the heterogeneity of the patient population included in this study may be one limitation when applying our results in the daily clinical practice. An analysis of long-term prognostic factors in some defined subgroups of our whole study population may provide further valuable information in the future.”

Reviewer 3 (Raul Moreno)

We thank the Reviewer for his positive attitude towards our work and for his time, consideration and valuable criticism during the Reviewing process.