

## **Author's response to reviews**

**Title:** Detrimental Effects of Specific Periodontopathic Bacterial Infection on Tachyarrhythmia Compared to Bradyarrhythmia

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### **Author's response to reviews:**

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Professor Marzia Cottini

Editor-in-Chief  
BMC Cardiovascular Disorders

Dear Dr. Cottini,

Thank you very much for your kind review of our paper. We enclose our revised manuscript entitled “Detrimental Effects of Specific Periodontopathic Bacterial Infection on Tachyarrhythmia Compared to Bradyarrhythmia” by Norio Aoyama et al. to be considered for publication in the BMC Cardiovascular Disorders.

We have modified the text according to the comments from the reviewers. We have carefully addressed all the items raised by the reviewers and our answers are listed on the separate sheets. We highlighted the changes in the document using red font text.

We hope that this manuscript is suitable for publication in the BMC Cardiovascular Disorders. We deeply appreciate your consideration.

Sincerely yours,

Norio Aoyama

Dear Reviewer 2,

Thank you very much for your kind review. Following is our reply to your comments.

Reviewer #2:

In the present manuscript (BCAR-D-17-00376) the authors demonstrate a study to analyze the impact of the presence of specific periodontopathic bacteria in older patients showing symptoms of tachyarrhythmia or bradyarrhythmia. From my point of view, the experiments were well performed. But prior publication several comments should be addressed as it is stated here:

Result section: Please describe much more precisely how many patients were positive for which bacteria. You may use an additional table and a boxplot diagram with whiskers or scatter blots for individual groups. Right now, the presentation of data is not very satisfactory.

Thank you very much for your advice. As you recommended, we calculated positive rate of each bacterium and showed the data. We added the information in the sections of Methods, Results and Table 4.

<P. 9>

Chi-square test was performed to compare sex, smoker rate, positive rates of DM, HT and DL and bacterial detection rates.

<P. 10>

We also showed positive rate of *P. intermedia* the bacteria (Table 4). The TA group had an increased detection rate of compared to the BA group in 71-80 year-old patients.

Discussion: Please provide some idea how the presence of periodontopathic bacteria may influence symptoms associated with tachyarrhythmia.

Thank you very much for your comment. In the present study, we diagnosed arrhythmia using echocardiographic examination, however, we did not assess the relationship of symptoms of arrhythmia and periodontal infection. There are symptomatic and asymptomatic arrhythmia. We added and modified discussion of the relationship between periodontal bacteria and symptoms associated with tachyarrhythmia. We also added information in Methods section.

<P. 7>

TA and BA were diagnosed by electrocardiogram.

<P. 12-13>

Hosomi et al. demonstrated a relationship between serum antibodies against periodontal pathogens and ischemic stroke. They evaluated patients with acute ischemic stroke and patients without previous stroke or stroke subtype. The results showed that the serum-antibody level of *P. intermedia* was significantly higher in athero-thrombotic stroke patients than in patients with no previous stroke. Serum antibody against *P. gingivalis* was also significantly associated with atrial fibrillation. They concluded that infection with specific periodontal bacteria was associated with stroke and atrial fibrillation 16. Pussinen et al. also showed serological evidence that a chronic infection caused by *P. gingivalis* and *A. actinomycetemcomitans* was associated with stroke incidence in prospective case-control studies 17,18, while the etiology of the stroke was not clarified. These previous studies suggested that periodontal pathogens such as *P. gingivalis* and *P. intermedia* may have some crucial effects on stroke and/or TA. The mechanisms connecting periodontal infection and TA are not clear, but long-term systemic exposure to periodontal pathogens may influence cardiac homeostasis.

And please, discuss your findings also in the context of older people positive for periodontopathic bacteria but without any symptoms of tachyarrhythmia or bradyarrhythmia.

Thank you very much for your valuable information. As you recommended, we added the information in the section of Discussion.

<P. 13>

Generally, the elderly cardiovascular patients including arrhythmia patients have a higher prevalence of asymptomatic disorders than young patients. And also the elderly patients often have other systemic diseases. These factors may reduce statistical sensitivity of symptomatic arrhythmia. This may be a reason why elderly people positive for periodontal bacteria had decreased symptoms of TA or BA.

We hope that this revised manuscript is suitable for publication in BMC Cardiovascular Disorders. We deeply appreciate your consideration.