Reviewer's report

**Title:** Prevalence of systemic immunoreactivity to Aggregatibacter actinomycetemcomitans leukotoxin in relation to the incidence of myocardial infarction

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**Reviewer:** Peter Eickholz

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Prevalence of systemic immunoreactivity to Aggregatibacter actinomycetemcomitans leukotoxin in relation to the incidence of myocardial infarction

Aggregatibacter actinomycetemcomitans (AA) leukotoxin has been shown to cause abundant release of interleukin-1# from macrophages and thereby increased levels of systemic inflammation predisposing for cardiovascular disease (CVD). Thus, immunoreactivity against AA leukotoxin may be protective against (CVD). 532 myocardial infarction (MI) cases and 1,000 age and sex matched controls from Northern Sweden were compared regarding systemic (plasma) leukotoxin neutralizing capacity (reduction of leukocyte damage and subsequent lactate dehydrogenase leakage upon exposure to purified leukotoxin). Leukotoxin neutralizing capacity was found in 53% of all plasma samples. The study failed to show less leukotoxin neutralizing capacity in the MI group.

The authors report a well designed case control study on the highly relevant issue of putative periodontal systemic connections. However, there are some issues that the authors may wish to address.

**Comments:**

**MAJOR ISSUE**

**METHODS**

Study population

Page 5, lines 7-17: Cases (MI) and controls are matched for age and sex. However, there is a long list of further systemic factors influencing the risk for MI (e.g. smoking, diabetes mellitus, BMI, waist-to-hip ratio etc.). Further, some oral parameters may have influence: number of teeth (the less teeth, the smaller the oral systemic interface), periodontal health (the more severe periodontal disease, the larger the putative effect of leukotoxin). Keeping in mind that CVD and MI are diseases with multifactorial etiology, these factors may obscure the effect of leukotoxin neutralizing capacity. The present study fails to consider these factors. A multivariate logistic regression analysis adjusting at least for some of these factors (smoking in particular) may solve this issue.
MINOR ISSUES

BACKGROUND
Page 3, line 12: …humans [8]. Recent pyrosequenzing…

METHODS
Study population
Page 4, lines 14-15: Referencing does not comply with journal style. It seems that the authors forgot to erase the names of referenced authors.

Statistical analysis:
Refer to MAJOR ISSUE.

DISCUSSION
Page 8, line 22: …previously shown that…

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.