Reviewer's report

Title: Inflammatory parameters predict prognosis in infective endocarditis but do not allow for individual prediction of etiology

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Reviewer: Stanisław S Ostrowski

Reviewer's report:

Major Compulsory Revisions:

1. The manuscript title isn't properly defined as it's a conclusion and not the hypothesis of the issue raised in this work. What's more there is an incoherence between the title, which considers the 'inflammatory parameters' the abstract, which includes only PCT measurements in the Methods and main manuscript, in which all inflammatory parameters are included.

2. The clinical outcome in the endocarditis depends on multi factors, not only the age, size of vegetation and causative organism. That are important but only the inter alia factors. Patient’s characteristics, complications of infective endocarditis, the data obtained in the echocardiographic examination and etiology (without giving details) contribute equally in the final clinical prognosis.

3. The sentence: "Serial measurements showing elevated serum CRP levels one and two weeks after initiation of treatment have shown to predict poor outcome [8, 9, 10]" should include particular elevated values of CRP in the first or second week of treatment that indicate poor outcome.

4. The statement: "but initial serum levels of CRP at time of diagnosis failed to predict the clinical course" isn’t propped by appropriate evidences from the literature. According to my knowledge and experience, high initial values of CRP or others inflammatory markers can demand more careful and invasive management.


6. There should be information given about the antibiotic treatment applied to patients included in the study. The shortest time of in-hospital stay for the event-free survival is 3 days..I wonder if OPAT was administered in those patients?
7. I believe it’s a serious methodology mistake that only one, admissional measurement was performed and taken into consideration for all patients included in the study. For such parameters like PCT, not a single measurement but dynamics of its alterations is of a greater value. So it cannot be just skipped. Furthermore, it also applies to CRP, which is extremely sensitive but unspecific parameter of sudden and marked tendency of changes.

8. The part of the Results: During the study period 67 patients with the diagnosis of IE were treated at our hospital. In the retrospective analysis nine patients failed to match Duke endocarditis service’s criteria for IE. In patients fulfilling the Duke criteria, eight had no initial PCT measurement before start of antibiotic therapy and were therefore excluded from the study. In total, 50 patients qualified for further analysis.

The study population had a mean age of 57 ± 17 years (range 23 to 87 years), and 72 % were male (Table 1). All patients were hospitalised. In most cases the aortic (58 %) or mitral valve (28 %) were involved.” should be given in Methods paragraph because it is a description of the study population.

9. There are some limitations of the study listed. It could be mentioned why 14% of cultures are negative in the authors’ opinion.

10. Strong site of the study is statistical analysis, which includes all significant calculations, needed to objective evaluation of the study results.

11. I think there should also be referential values of PCT and CRP of Your laboratory given in the manuscript.

12. The part about that the S.aureus etiology was connected with more adverse events and worse prognosis than the other etiology could be also include in Results, not only mentioned in Discussion. Although PCT is a sensitive and specific marker for bacterial infection it has its diagnostic limitations. In healthy it doesn’t raise above 0.1ng/ml or in other authors even 0.5 ng/ml It can precede inflammatory process symptoms. Some other than sepsis or endocarditis states can result in its increase, for example surgery or trauma, and other conditions with SIRS development. The highest values are then observed on the 1st or 2nd day from an event. Especially the values 0.5-2.0 ng/ml are problematic for interpretation (*U. Zielińska-Borkowska, Naserdib, W. Tarnowski Prokalcytonina w diagnostyce i monitorowaniu zakażeń chirurgicznych.. Pol. Merk. Lek., 2009, XXVII, 162, 514,**J.Sikora, R. Kwiatkowska “Clinical usefulness of evaluation of C-reactive protein and procalcitonin concentrations in the diagnosis and the monitoring of systemic inflammatory response syndrome”Alergia Astma Immunologia 2005,10;2:63-68). The statement given in Discussion:” As a result PCT levels in IE are higher than in other infections like e.g. lower respiratory tract infections, where a lower PCT cut-off of 0.25 ng/mL is applied [19]” should be enlarged by more literature giving other cut-off levels for different clinical states. Our experience show that wide range of PCT values observed in patients with endocarditis also can be problematic.
Minor Essential Revisions—none
Discretionary Revisions—none

Main conclusion:
Despite all indicated advantages and disadvantages of this paper I believe that in a current form the manuscript isn’t innovative in the undertaken issue, the methodology of the work isn’t appropriately managed and I wouldn’t recommend it for publication in a well impacted journal. Although after the authors’ revision of the manuscript and appropriate explanations, the article could be given second reviewers’ evaluation and taken into consideration for potential submission.

**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.

**Declaration of competing interests:**

I declare that I have no competing interests