

I would like to thank you and the reviewers for the time devoted to reviewing our manuscript entitled: **“Multimodality Imaging in the Diagnosis and Management of Prosthetic Valve Endocarditis: A Contemporary Review”**

We have made the changes to the manuscript that you and the reviewers requested, and have detailed below. It is our hope that the manuscript now meets sufficient quality for publication in your journal and we are happy to make any additional edits that the editorial staff and reviewers deem necessary.

Best regards,

Saberio Lo Presti, MD and Bo Xu, MD

**Reviewers' comments:**

**Reviewer #1:**

**In this review, the authors aimed to discuss diagnosis of PVE with a special emphasis on the emerging complementary use of multimodality imaging modalities. It is a well-written and highly scientific manuscript. The following points should be corrected:**

- 1) ‘morality’ should be corrected as ‘mortality’ in the following sentence: However, when both groups were matched, there was no significant difference in morality [13].

*Changes made.*

- 2) In the Introduction section, it was stated that in cases where TEE yields a negative result and clinical concern persists, guidelines recommend to either repeat the study in 5 days. On the other hand, in the Transthoracic and Transesophageal Echocardiography section, it was stated that in cases where the

clinical suspicion remains high despite an initial negative result, short-term interval follow-up is a strategy that can enhance imaging sensitivity at the expense of prolonging the time to diagnosis, this can usually be performed one week following the initial evaluation. Which one is correct? Five days or one week?

*Clarification made. Guidelines ranges from 3-7 days (ESC 5-7 days, AHA 3-5 days)*

3) 'detected on' should be added and comma should be deleted before 'CCT' in the following sentence: In a cohort of 155 patients with surgically proven IE, 112 (72.3%) corresponding to patients with previous valve replacement (metallic and bioprosthesis) or repair, the presence of pseudoaneurysm, abscess, and fistulas, CCT independently predicted mortality.

*Changes made*

4) Recent important studies for IE including especially Habib et al (The ESC-EORP EURO-ENDO (European Infective Endocarditis) registry. Eur Heart J Qual Care Clin Outcomes. 2019 Jul 1;5(3):202-207. doi: 10.1093/ehjqcco/qcz018) and Habib et al (Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study. Eur Heart J. 2019 Oct 14;40(39):3222-3232. doi: 10.1093/eurheartj/ehz620) should be mentioned.

*The following modification was made*

*"Although contemporary data reported equipment availability in 70.3% of European centers and 56.3% non- ESC centers, the availability, cost and expertise needed with this imaging modality impose additional limitations on its employment in routine clinical practice [4, 68].*

*Real world data from the ESC-EORP EURO-ENDO (European infective endocarditis) registry in 3116 adults with IE from around the globe (2470 from Europe, 646 from non-ESC countries), identified 939 (30.1%) cases of PVE and 308 (9.9%) with device related infection. 18F-FDG PET/CT was implemented in 518 cases (16.6%) and leucocyte scintigraphy in 38 (1.2%). Around 25% of the 18F-FDG PET/CT were obtained in patients with PVE and 26% in patients with device infections, which was significantly higher when compared with NVE (9.5%) ( $P < 0.0001$ ). The test performance was superior in patients with PVE with a reported sensitivity of*

66.8% (versus 28% for NVE and 16.3% for device infections). Extracardiac foci were observed in close to 40% of patients (34.5% in PVE, 42.3% in NVE, and 43.8% in device infections), most frequently seen in the lungs (27.1%) [4] "

5) References should be re-written according to the Journal's style.

*References modified.*

**Reviewer #2: Dear author thanking you for the effort. I have some suggestions to improve this submission as follows**

**1. Mention whether the review is brief/narrative /systematic and accordingly revised the submission as instructed to the author in preparing a review submission.**

*Modifications made.*

**2. References need to be updated till date: in 2021 only there 4 interesting journal articles those the author has missed**

*The authors agree with this statement. References have been updated.*

**3. If the author is planning to focus the role of imaging modalities to manage infective endocarditis, this submission needs significant improving to achieve the objective.**

*The authors agree with this statement. The purpose of this manuscript is to focus on the use of multimodality imaging in the diagnosis and management of prosthetic valve endocarditis. This section aims to present a brief discussion of general principles for management. Clarification statement added.*

**4. Your take home message is in Table-1 but the provided information is significantly inadequate**

*To improve the quality of Table please elaborate further.*

*Reviewer # 3: Science editor*

- 1. The “Author Contributions” section is missing. Please provide the author contributions**

*Statement added*

- 2. The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and (3) If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.**

*Figures will be re-submitted in power point document.*