AUGUSTA UNIVERSITY

December 17, 2018

Dr Fang-Fang Ji,

I appreciate the journal's prompt response regarding our manuscript entitled: Prevalence and Clinical Characteristics Associated with Left Atrial Thrombus Detection: Apixaban.

On behalf of all authors involved, I would like to thank the reviewers for the thoroughness of his or her work and the quality of feedback provided. Each reviewer's comments as well as the response from the authors is provided below.

Thank you for receiving the revised version of our manuscript and providing further consideration for publication. We thank you for your time and look forward to your response.

Hoyle L. Whiteside, MD
Resident Physician
Division of Internal Medicine
Medical College of Georgia at Augusta University

Reviewers' (03846820) comments:
Dear author, The paper represents results of the retrospective bedside study which is aiming to evaluate the prevalence of left atrial appendage (LAA) thrombus detection by transesophageal echocardiogram (TEE) in patients continuously anticoagulated with apixaban for ≥ 4 weeks and examine for any cardiac risk factors or echocardiographic characteristics which may serve as predictors of thrombus formation. The article is written with the good English-speaking adduction of the arguments. The article is sufficiently novel and very interesting to warrant publication. All the key elements are presented and described clearly. The most discussable options in the article are: 1) There in Discussion must be mentioned some clinical cases of the successful treatment of AF with apixaban sometimes after switching from another NOAC (doi: 10.2169/internalmedicine.8893-17, doi: 10.1002/ccr3.933,). 2) Methods: please, provide a reader with your sample size calculation and some info to estmate the statistcal power of the study. It must be clarified in your Limitations either. How the definitions of the clinical conditions were unified. Did you proceed with the expert analysis of your imaging data either? If not, this all must be mentioned and elaborated. 3) I would generally suggest to upgrade the paper with the plots.

Response from Authors:
This study was a retrospective analysis involving all patients undergoing TEE and compliant with apixaban during the study period. Therefore, analysis for statistical power and sample size estimations were not performed prior to data collection. We feel the methodology of the study is clearly outlined in the manuscript and limitations adequately transparent including the retrospective nature of the study. With regards to the expert analysis of the imaging data, all echocardiograms were reviewed by at least one of two Cardiologists as outlined in the methods. Strong agreement was observed between the two reviewers (Cohen's kappa: 0.89).

Reviewers' (03652653) Comments:
This study evaluated the prevalence and clinical course of patients with left atrial appendage thrombus treated with apixaban. The manuscript is well written, the results are clear, and the conclusions appear reasonable – and reflect clinical experience of many cardiologists. Strong items are the clinical relevant rationale, the comprehensive presentation of data, and the presentation of follow-up data. Limitations are the single center setting, the limited sample size/limited number of endpoints, and the analysis of only one NOAC. Actually, I do not have any major further comments since this manuscript reads very well. If the authors want to improve their manuscript, I would consider including one comparison of the study cohort and the cohort of patients receiving any other NOAC or patients receiving warfarin (key question: different incidence of thrombus formation and resolution over time) – only if these data are available.

Response from Authors:
We agree with the reviewer's assessment of the limitations including retrospective nature, single center setting, and limited sample size. With regards to comparison of an additional NOAC, this was strongly considered during the study design. However, the available sample size for two commonly utilized NOACs (dabigatran and rivaroxaban) would be smaller than other recently published cohorts with similar methodology. Data for patients anticoagulated with warfarin was extracted as part of the initial data collection and analysis. However, it was subsequently identified that patients within the warfarin cohort had a higher prevalence of known cardiac risk factors, limiting the ability to compare the two populations. For this reason, we elected to not report this data alongside the apixaban cohort as to 1) avoid misinterpretation of the efficacy of apixaban vs warfarin and 2) not detract from the clinical and echocardiographic risk factors identified within the apixaban cohort. It is our opinion that this information will make the greater contribution to the literature as a great deal of data exists for patients anticoagulated with warfarin.