Author’s response to reviews

Title: Value of dual Doppler echocardiography for prediction of atrial fibrillation recurrence after radiofrequency catheter ablation

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Version: 2 Date: 18 Sep 2019

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Response to Reviewers for Manuscript ID BCAR-D-19-00477R1

First of all, I would like to use my second email address jwtian2004@163.com as my means of communication, which is more formal.

Jun Ren (Reviewer 1): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format. Please overwrite this text when adding your comments to the authors.

We thank the Reviewer for the excellent suggestions. We have revised them according to your suggestion.
Stefan Simovic, M.D. (Reviewer 2): However, there is one concern regarding patients with previous acute coronary syndrome and ischaemic heart disease in the experimental group, were there any included? Authors mention including coronary heart disease patients in the control group.

Neither the patients in the AF group nor the control group had severe acute coronary syndrome, they were only admitted to the hospital for AF, primary hypertension, chronic coronary heart disease, or physical examination (Methods section, line 102, page 5).

Valentina O Puntmann, MD, PhD (Reviewer 3):

Major comments:

1) The evaluation of LV diastolic function, in patients with AF, according to ASE/EACVI recommendations for the evaluation of Left Ventricular diastolic function by echocardiography (J Am Soc Echocardiogr 2016; 29:277-314), is based on the following 5 measurements: Peak acceleration rate of mitral E velocity (≥ 1,900 cm/sec2), IVRT (≤65 msec), DT of pulmonary venous diastolic velocity (≤220 msec), E/Vp ratio (≥1.4) and Septal E/e' ratio (≥11). According to Authors, the parameters which were measured within identical cardiac cycles are: the TE-e', the Tei index, the ratio E/e'(S) and the ratio E/e' (L). As is evident, the Authors omitted to mention some of the classic parameters that help to classify patients with AF into those with and without LV diastolic dysfunction.

We thank the Reviewer for the constructive suggestions. Our team added relevant parameters of the AF group and control group through retrospective analysis: Peak acceleration rate of mitral E velocity; IVRT; DT of pulmonary venous diastolic velocity and E/Vp ratio(Methods section, line 122-127, page 6) (Methods section, line 140-141, page 7).

2) In Table 3, which demonstrates the characteristics of patients with and without AF recurrence after ablation, there is a difference in the incidence of preexisting Long Persistent AF, between those patients with AF recurrence (9,52%) and those with no AF recurrence (4,3%). In the text there is no clear comment of this difference or the statistical significance of it.

We thank the Reviewer for your detailed review. Although there was a difference in the incidence of preexisting Long Persistent AF between those patients with AF recurrence (9,52%) and those with no AF recurrence (4,3%), the difference was not statistically significant. We have commented it as “Demographics, duration/type of AF, renal function and clinical risk factors were similar between the two groups” (Results section, line 201-202, page 9).

3) According to the Authors, follow-up of patients included, detailed inquiries regarding arrhythmia-related symptoms (dizziness, chest distress or cardiopalmus), an echocardiography examination and a 24-hour Holter which was performed at 3, 6 and 12 months after the ablation
to confirm the presence or absence of AF recurrence. Even though 24-hour Holter is the standard method to detect AF, continuous Holter for up 72 hours or implantable loop recorder can improve the diagnostic accuracy and reveal some patients with rare episodes of paroxysmal AF. There is also no information, if there were patients with arrhythmia-related symptoms and no Holter confirmation of AF recurrence 1 year after ablation.

We thank the Reviewer for the valuable and excellent suggestion. I also think that continuous Holter for up 72 hours or implantable loop recorder can improve the diagnostic accuracy and reveal some patients with rare episodes of paroxysmal AF. This is where our study needs to be further improved, and its limitations have been noted in the study limitations section. We look forward to further research results with large samples and long follow-up in the future (Study limitations section, line301-304, page14).

There were 7 patients with arrhythmia-related symptoms but no Holter confirmation of AF recurrence 1 year after ablation, and we have added this sentence in manuscript (Results section, line198-200, page9).

Minor comments:

1) According to Authors, it was detected the late recurrence of AF (up to one year) after ablation without any information about the very-late recurrence which is the incidence of AF beyond one year after ablation and one of the major causes of re-ablation.

We thank the Reviewer for the constructive suggestions. Due to the time limit, we only conducted follow-up for a period of one year, and we will follow up for a longer time in the near future. We have expressed this limitation in manuscript (Study limitations section, line301-304, page14).

It is written in the text that all 67 patients with AF underwent successful pulmonary vein isolation or elimination by RFCA, but two patients in this study were subjected to repeated ablation. There is no information about the cause of why these two patients were subjected to repeat ablation and if this cause can act as a confounding variable.

In this study, we focused on the factors related to the AF recurrence after the first radiofrequency ablation. Patients undergoing secondary radiofrequency ablation were considered as the recurrence group, which was the end point of the event. I just want to express the operation status of these patients. The sample size of the secondary ablation is too small. In the future, I will continue to collect some cases of patients undergoing secondary ablation, study the reasons why patients undergoing secondary ablation(Results section, line194-195, page9).

2) In this study it was measured the LA diameter instead of LA maximum volume index which is suggested by ASE/EACVI recommendation and it is more reproducible parameter for statistical outcomes.
Thank the Reviewer for the excellent suggestions. We have measured the LA maximum volume index of the AF group and the control group, and added the parameter in Table 2 and Table 4 (Methods section, line116-119, page5-6).

Christoph Sinning, MD (Reviewer 4): The authors did provide interesting results regarding the use of echocardiography in terms of identifying patients with atrial fibrillation which are at a high risk of recurrence. Since all patients had to undergo the echocardiography anyway before ablation there were no additional procedures. Although the dual Doppler technique might be of interest in this setting, a close investigation with flow Doppler and tissue Doppler is as well possible if not done simultaneously.

We have added close investigation with flow Doppler and tissue Doppler such as E, e’ (S), e’ (L), peak acceleration(PkAcc) of the E velocity and DT of pulmonary venous diastolic velocity(Methods section, line119-127, page 6).

I have cited the current ESC guidelines with Paulus Kirchhof as first author(Background section, line70-72, page 4).

Agathi Rosa Vrettou, MD (Reviewer 6):

1. I would suggest to emphasize more on the value of TE-e' for patients with intermediate E/e' values as your work suggests. If any data on NT-pro BNP levels are available could be also added in your analysis

   Thank the Reviewer for this suggestion. We have added the values of Plasma NT-proBNP level in the manuscript and Table 4, it now reads “Plasma NT-proBNP level was measured in the AF group.” (Methods section, line109, page5)

2. Maybe a different abbreviation for E/e' for lateral and septal wall could be chosen instead of S, L as these might be somewhat confusing.

   Thank the Reviewer for the valuable suggestion. I also think a different abbreviation for E/e' for lateral and septal wall could be better. However, based on the literatures I have read, E/e’(L) and E/e’(S) appeared in most of the references.