

Reviewer #1:

**Query 1:** This is a novel study looking at ACE/ARB efficacy in the paroxysmal Afib post CBA population. Your hypotheses do confirm that ACE/ARB use is not effective in reducing events post CBA in this population. Your conclusions so far agree with accepted understanding of the condition and pathogenesis.

Thank you for your review. We are very grateful for your positive feedback on our manuscript.

Query 2:

I would like to see some additions to the discussion section mainly the fact that your ACE/ARB population was very different from the non-users in terms of HTN and CAD.

Thank you for your insightful comment. We have incorporated modifications as suggested by you to the discussion as shown below (Manuscript page 8, paragraph 1, line 4)

“It is important to note, that the ACEi/ARB group of patients that underwent CBA for paroxysmal atrial fibrillation had significantly higher prevalence of HTN and CAD that are known to contribute to myocardial fibrosis. Additionally, both hypertension and CAD contributed to increased left ventricular compliance and left atrial (LA) filling pressure. Subsequent LA enlargement further promotes AA. These comorbidities, however, were adjusted for in multivariate analysis in Model 2 shown above.”

Query 3: You do not know if this CAD was previously treated or untreated or ischemic or not.

Thank you for your comment. We agree with you. We did not include data on whether coronary artery disease was optimally treated or required a revascularization procedure. We have added the same to our limitations as shown below. (Manuscript page 11, paragraph 2, line 7)

“Lastly, our patient population within the ACEi/ARB group had a higher rate of HTN and CAD. Although these factors were accounted for in the multivariate analysis, we did not collect the data on whether CAD was optimally treated or required a revascularization procedure.”

Query 4: Also HTN being a primary driver for all Afib and leading to subsequent LA enlargement should be explained in the discussion section due to this significant finding.

Thank you for your comment. We agree and have added to the discussion as below (Page 8, paragraph 1, line 6):

“Additionally, both hypertension and CAD contributed to increased left ventricular compliance and left atrial (LA) filling pressure. Subsequent LA enlargement further promotes AA.”

Query 5: Your study does not comment on future directions of research which could include a study with a much larger population or a study done at multiple locations in the US. The findings you present are significant and also another area of focus in future could be the systolic HF population and the use of drugs such as Entresto. A well done study.

We appreciate your valuable feedback. In the originally submitted manuscript, we had alluded to this fact in our conclusion: “Larger controlled studies, particularly in patients with persistent AF and those at risk for significant myocardial fibrosis such as cardiomyopathy or

valvular disease are necessary to fully evaluate the effect of ACEi and ARB in patients undergoing CBA for AF.”

We have modified the conclusion according to your suggestions as below (page 12, paragraph 1, line 2):

“Larger, **multicenter**, controlled studies, particularly in patients with persistent AF and those at risk for significant myocardial fibrosis such as cardiomyopathy, **HF** or valvular disease are necessary to fully evaluate the effect of ACEi, ARB or **angiotensin receptor neprilysin inhibitor (ARNI) such as sacubitril/valsartan** in patients undergoing CBA for AF.”

Reviewer #2:

**Query 1:** Greetings I read the article with interest. The authors have evaluated the role of ACEi and ARB in prevention of atrial arrhythmia in patients who underwent cryoballoon ablation for paroxysmal Atrial fibrillation. Overall the study is well conducted and written. The results represents the study objective and the conclusion is supported by the data. Although retrospective data and relatively smaller sample is the limitation, in my opinion, there is no major drawback of flaws in the study and can be considered for possible publication. The title, abstract, justification is fine. There are minor aspects which can be improved

**Authors Response:** Thank you for your feedback. We appreciate your positive comments.

1. The figure 1 is not required, rather the inclusion and exclusion criteria can be elaborated in the text.

Thank you for your comment. We have now removed Figure 1 and replaced it with a STROBE diagram as elaborated below. The inclusion and exclusion criteria are listed on page 4, paragraph 2, line 1 of the manuscript. The reference to old Figure 1 was removed from the page 4, paragraph 2, line 4 of the manuscript.

“All patients with a diagnosis of persistent or permanent AF were excluded from the study. **(Figure 1).**”

2. It is better to follow STROBE. A participant selection and data management flow chart can be added.

Thank you for your comment. We have attached STROBE diagram to the manuscript. The reference to STROBE diagram (new Figure 1) is listed in the manuscript page 7, paragraph 2, line 1.

3. Unit of Age in the abstract, although understood, can be included.

Thank you. We will include “years” as unit of age as shown below (page 2, paragraph 2, line 1):

**Methods:** We followed 103 patients (Age  $60.6 \pm 9.1$  years, 29% women) with paroxysmal AF undergoing CBA for one-year post procedure.

4. If ample size calculation was done, it can be included. If not done prior to research, post-hoc power analysis can be done and mentioned in the limitation section. Best of luck

Thank you. As this was a small sample retrospective study we did not perform a power analysis. We have added this to our limitations as shown below (Manuscript page 11, paragraph 2, line 6):

“Furthermore, since this was a small sample retrospective study, we could not perform a power analysis.”