Author's response to reviews

Title: Which method of left atrium size quantification is the most accurate to recognize thromboembolic risk in patients with non-valvular atrial fibrillation?

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Point-by-Point Answer to the Reviewers' Comments

Reviewer 1: Dr Lorenza Pratali

Major Revisions

1. One of the principles problems of the study is due to the well-known problem variability in the echocardiogram measurements. Should be useful to assess the inter and intra individual agreement in the TTE LA measurements and in the recognition of TEE surrogate markers of stroke (i.e. LLA thrombus, SEC) in a sample of patients

#This is an extremely pertinent comment that we have addressed in the revised version of the article. Inter- and intra-observer variability was evaluated using the Bland-Altman Analysis (for LA quantification methods) and correlations (for LAA thrombus and dense SEC). These results are presented in Table 7.

Minor revisions

1. Should be valuable for the CU readers to add echo images or movies of the different LA measurements used in the study.

#We agree with the Reviewer’s view that this article can be more didactic indeed. Therefore, a Figure (number 1) has been added, exemplifying the different methods for assessing LA size in our investigation.

2. The authors showed many tables. Maybe some of these data can be showed as figures.
We have now organized more correctly our data, and the content of Tables regarding data from c-statistics (ROC curves) was merged with the respective Figures.

Reviewer 2: Dr Leopoldo Perez de Isla

Major compulsory revision:

1. The work by Faustino et al is a very nice and well written paper. Nevertheless there is an important point the authors should manage. The presence of spontaneous contrast is not related with the presence /absence of anticoagulant therapy. Thus, the authors should avoid using this variable in the subgroup of patients under anticoagulant therapy. I suggest to carry out an specific analysis for this subgroup, including all the echocardiographic variables for embolism prediction except spontaneous contrast.

We thank the Reviewer from remind us of this important point. Following his suggestions, a sub-analysis of the discriminatory ability of LA measurements for predicting LA thrombus, LAA low flow velocities or at least one of these two parameters, was carried out for patients previously under oral anticoagulation. The results are now presented in Figure 3 and discussed.

“Taking into account the possible influence of oral anticoagulation on dense SEC, a sub-analysis of the discriminatory ability of LA measurements for predicting the other surrogate markers of stroke (LA thrombus, LAA low flow velocities or at least one of these two parameters), was carried out for patients previously under oral anticoagulation (Figure 3). In this subset of 165 patients, LAA thrombus was found in 21 patients, LAA low flow velocities in 23 patients and at least one of these parameters in 40 patients. There was a good discriminatory ability of the LA measurements for identifying LAA low flow velocities in this sample, though the results were not as consistent for identifying LAA thrombus (Figure 3).”

Minor comments:

1. The introduction is very long. I suggest to reduce it

#The introduction has been reducing following this suggestion.

2. Method section: The authors should describe which type of AF suffered the enrolled patients (persistent, paroxysmal,...) and show the frequencies

#This relevant information was missing in the previous version of the manuscript and has now been added.

“The duration of the current atrial fibrillation episode was estimated to be longer than one year in 26.8% of patients (Table 1). AF was persistent in 73.2% of patients (n=366) and long-standing persistent in 26.8% of patients (n=134).”

3. Echocardiographic data acquisition: I suggest to reduce a little bit the extent
According to this recommendation, we have reduced that aforementioned section.