

Dear Editor

Thank you and thanks to all reviewers. The answers for reviewers are highlighted in red below and in the revised manuscript. We will be very happy to answer any further questions.

Ibrahim Marai MD

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Reviewed by 00214291 (major revision):

This is an interesting article analysing the influence of novel technologies (image integration and contact force evaluation) on the outcome of catheter ablation of atrial fibrillation. However, the number of patients enrolled in the study is rather low. The authors should present data about the adjunctive antiarrhythmic medication. Furthermore, they should provide the number of patients with recurrences of atrial fibrillation and atrial tachycardia / or atrial flutter in detail.

Answer : of note all patients who had recurrence of atrial tachyarrhythmia had atrial fibrillation except 1 patient from CT group and 2 patients from EAM group who had atypical atrial flutter (see results).

AADs? All patients with PAF were treated with IC AADs, and all patients with persistent AF were treated with amiodarone.(see methods and materials)

Reviewed by 00503536 (rejection):

The manuscript written by Marai et al. describes the useful therapeutic option for atrial tachyarrhythmia using the combination of CT imaging and contact force technology with electroanatomical mapping. The data show that the combination technology significantly reduce the recurrence of atrial tachyarrhythmia. The data are interesting but the study is not a randomized one with small numbers of patients. There are some more concerns that need to be addressed. Major points 1. The mechanism why the novel combination therapy is more useful for reducing the recurrence of atrial tachyarrhythmia is not clear. 2. Adverse events or important technological points for the novel therapy should be mentioned. Minor points 1. Selection criteria and their backgrounds need to be described in more detail in the Materials and Methods section. 2. Discussion should be more focused. 3. There are many grammatical errors.

Answer:

Major points:

1. We do not know the exact mechanism why combination therapy is more useful. We think these results emphasized the fact the AF is a complex arrhythmia. The AF ablation is also a complex procedure with

relatively high rate of recurrence due to PV reconnection. Recently, many technologies were introduced to overcome this issue. However, there is no specific technology that is significantly more useful than others. So, we think that combination of technologies may be more useful and it is important to investigate the combination used in our study and another technologies in a randomized studies in order to improve the results of AF ablation. (see discussion)

2. Major adverse events did not occur in both groups (Major complications (pericardial effusion/ tamponade , cerebrovascular accident/transient ischemic attack, vascular access injury requiring intervention) did not occurred in both groups). We will be happy to answer any specific question regarding this issue. See results

Minor points:

1. Selection criteria: *All patients had symptomatic recurrent paroxysmal AF or persistent AF (less than 3 months duration) who was treated with at least 1 anti arrhythmic medication or intolerant to medication. See material and methods*

4. Discussion should be more focused: See discussion

Reviewed by 00227355 (minor revision):

This is an interesting paper for the clinical practice. Ibrahim Marai et al. reported that CT integration and contact force technology may reduce the recurrence of atrial tachyarrhythmia after catheter ablation for AF. Overall the paper appears to be carefully examined and data adequately discussed. I suggest that this paper has the priority to be published in WJC. I have a few comments to make.

- 1) Do you have a group including some patients who underwent AF ablation with contact force technology in the EAM group? No (see figure 2)
- 2) How about the mean AF duration in the EAM group and CT group?
The AF duration in both groups was 1-3 years (see results).

Reviewed by 00225356 (major revision):

The paper by dr. Marai et al. reports the results of a small non-randomized study which evaluates the impact of the combination of two new technologies (imaging integration and contact force sensing) on catheter ablation of atrial fibrillation, by comparing its clinical outcome with the one of the same procedure performed without these two technologies. The limitations are obvious, but well acknowledged. The perspective of the study are interesting, although the small sample size limits the importance of the results. There are several parts of the manuscript which require revision and clarification.

1. The design of the study is not very clear (a part of the patients in the CT group still received ablation without contact force sensing). A figure with a flowchart reporting the different patient groups and the results will help in understanding better at first sight the study and its results. (done: See figure 2)

2. It is not clear how many operators were involved in the study and if they were equally distributed in the different groups. This is crucial in this type of ablation, since the results are very much operator-dependent. All the procedures in both groups were performed by 2 experienced operators (see materials and methods)

3. The authors state that they delivered RF energy only when the contact force was > 10 g, but they did not give the range of the values that they considered optimal for ablation (10-40 g?). Moreover, in the results, no numeric data are given for contact force, such as mean/median/range of contact force values and stability of contact force (for how much time the contact force was stably within the predetermined range?). The last parameter proved quite important in the Smart-AF trial, since this is not a “plug-and-play” technology that by definition improves the results; the outcome, on the other hand, improves when some criteria are fulfilled. The Smart Touch group in this study is too small for sub-analysis, but the difference between the two groups in terms of outcome might become significant when these parameters are considered.

Optimal range for ablation was considered as 10-40 g. We tried to deliver RF energy when the contact force is > 10 g and is stable for at least 20 seconds (see materials and methods)

4. The authors should speculate on the role of imaging integration to improve the clinical outcome. Was the procedure outcome better because the lesion set was more proximal and/or precise?

We think that image integration could improve clinical outcome because it helps to understand better the 3D complex anatomy of LA/PV and appreciate the variant anatomy of PV including common trunks or more than 4 veins. In addition, it could help to make the lesion set more precise (see discussion).

5. Figure 1 should have a second panel showing the lesion set of the procedure in the EAM group.

Done- See figure 1

6. It is not clear how many patients completed the 24 month follow-up in each group: in the Kaplan-Meier estimate both curves become very flat after 12 months, which suggests that there are no events (less likely) or no data (more likely).

All patients completed the 24 months follow-up (see results). Indeed, the curves become flat after 12 months. In our experience most of AF recurrence occurs during the first year. Because of that, we extensively follow our patients during the first year. It is possible that some events of AF were missed in both groups during the second year because of less extensive follow up compared to first year.

7. In table 1, the meaning of the line AADs is not clear.

Anti arrhythmic drugs (AADs) was deleted from table 1. See materials and methods

8. There are several typographic errors throughout the manuscript. For example: medazolam instead of midazolam, gram instead of g, 43 C instead of 43° C. Done