

Paroxysmal atrial fibrillation ablation: Achieving permanent pulmonary vein isolation by point-by-point radiofrequency lesions.

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We sincerely appreciate the thorough review of the manuscript by World Journal of Cardiology reviewers. We hope that this new version of the manuscript would be considered for publication. In this new version we have modified the manuscript according to reviewers' suggestions. Below, you will find a point-by-point response to reviewers' comments.

Reviewer 1

Thank you for writing this clear and in depth review article. My only comment would be that this review is on RF ablation, please add this to the title of the manuscript.

We find this comment very appropriate. According to reviewer's suggestion, the title has been modified as follows:

"Paroxysmal atrial fibrillation ablation: Achieving permanent pulmonary vein isolation by point-by-point radiofrequency lesions."

Reviewer 2

The Authors describe in this review how to achieve a persistent Pulmonary Vein Isolation in the treatment of Paroxysmal Atrial Fibrillation. Although the manuscript is well written, I have 2 main drawbacks greatly limiting the generalizability of the review:

- The use of irrigated catheters represents common clinical practice when ablating in the left atrium, so I suggest to trim that part focusing more on the use of contact force catheters and pacing maneuvers in order to prove electrical isolation and Adenosine testing to confirm it.

We appreciate this comment. The paragraph dealing with irrigated catheters has been shortened and the heading “Irrigated Catheters” has been deleted (page 6, paragraph 2):

“Techniques to improve lesion durability

The use of irrigated catheters for PVI was associated with a dramatic decrease in PV reconnection rate ¹¹. However, even when irrigated catheters are used, the recurrence rate after a single PVI procedure remains high (30-35%) ¹². Further strategies are required in order to improve long-term durability of the lesions obtained with this type of catheters.”

- Usually the purpose of a review is to cover the complete knowledge regarding the main subject, trying to achieve completeness when addressing an important issue, as it is the case. After STAR AF trial, PVI has achieved a more relevant position in the treatment of AF, also in the treatment of persistent AF. However, in the era of ‘one shot devices’ (i.e. balloon guided technology or single application RF devices), isolation persistency can be achieved not only with RF focal catheters. A review regarding this issue cannot be considered complete if it is not dealing with such technology.

We understand reviewer’s point. We agree that one-shot devices is an important subject that has not been addressed in the present review. However, the aim of this manuscript was to deal with the issue of PVI by point-by-point radiofrequency ablation. In order to clarify this, the title and abstract have been modified as follows (changes highlighted in yellow):

Title:

“Paroxysmal atrial fibrillation ablation: Achieving permanent pulmonary vein isolation by point-by-point radiofrequency lesions.”

Abstract:

“Pulmonary vein isolation by point-by-point radiofrequency catheter ablation constitutes the cornerstone of catheter ablation strategies for the treatment of atrial fibrillation. However, despite advances in PVI ablation strategies, long-term success rates after ablation remain suboptimal, which highlights the need to develop techniques to achieve more durable lesions. Strategies proposed to improve the durability of pulmonary vein isolation can be divided into two groups: those addressed to improving the quality of the lesion and those that optimize the detection of acute PV reconnection during the ablation procedure. This manuscript reviews the role and potential benefits of these techniques according to current clinical evidence.”

In addition, a word of caution has to be spent when talking about clinical arrhythmia recurrences after PVI. There is a certain amount of patients not experiencing AF recurrences after PVI although they present a PV reconnection, whereas paroxysmal patients may have clinical AF with all the PVs still isolated. The future has to be focused on the identification of each patient specific mechanism (drivers, rotors, focal activity, etc..) since some patient may show a non PV trigger and still experiencing paroxysms. In such cases, fortunately a minority, the sole PVI may not be enough. A final comment from the Author would be appropriate and well accepted for the readers of the Journal.

We find this comment particularly appropriate. According to reviewer’s suggestion a short paragraph dealing with the issue of non-PV sources of AF recurrence has been added (page 14):

“Non-PV sources of AF recurrence

It should be noted that a variable proportion of patients may have AF recurrence despite persistent PVI. This could be due to the existence of non-PV triggers⁵⁷. Typically, these non-PV triggers are located in specific regions such as the crista terminalis, the superior vena cava, the Eustachian ridge, the fossa ovalis, the left atrial appendage, the

inferior mitral annulus and the coronary sinus. Empirical ablation of these common origins of triggers is not recommended. However, once a trigger is identified, it should be eliminated in order to achieve better outcomes ⁵⁸.”

Furthermore, the following comment (highlighted in yellow) has been added to “conclusions” paragraph:

“Conclusions

PVI is the cornerstone of catheter-based therapies for AF. PV reconnection after PVI represents the main limitation of AF ablation techniques. Efforts should be made to develop strategies that achieve more durable lesions. Current techniques associated with better acute (and probably long-term) outcomes include antral PVI guided by circular mapping catheters, the use of CF catheters, lesion contiguity, and the assessment of dormant PV conduction by adenosine and/or pace and ablate. Finally, a subset of patients may still have AF recurrences despite persistent PVI, due to the presence of non-PV triggers. Efforts should be made in order to individualize the treatment according to each patient’s specific mechanism of recurrence (drivers, rotors, focal activity...).”

Reviewer 3

With small corrections this atrial fibrillation is good and I think worth publishing.

Thank you for your comment. The manuscript has been modified according to reviewers's suggestions.