

Hybrid procedures for persistent atrial fibrillation: necessity and timing of the catheter ablation stage

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In our recent paper (1) we tried to identify predictors of arrhythmia recurrence in patients undergoing a hybrid ablation procedure consisting of both an epicardial and endocardial radiofrequency (RF) ablation, performed in a delayed sequential manner, in patients with persistent atrial fibrillation (AF), with the majority presenting with long-standing persistent arrhythmia (87%). By design, our cohort of patients consisted of one of the “less curable” forms of arrhythmia, especially if treated using only conventional catheter ablation techniques. The majority of our patients might very well have been precluded from receiving invasive therapy if they had been assessed just for a catheter ablation, particularly in less experienced centers.

The epicardial ablation was carried under general anesthesia by a cardiac surgeon using AtriCure RF bipolar clamps [for pulmonary vein (PV) isolation] and a linear pen (for connecting linear lesions). The procedure was followed, 2–3 months later, by a transvenous endocardial catheter ablation, which was performed under conscious sedation using a CARTO 3D mapping system and ablation catheters equipped with contact-force technology. The setting of our trial was unequivocally conditioned on the cooperation between electrophysiologists and cardiac surgeons throughout the entire process from establishing the theoretical background (for instance setting up the

lesion set), indications, treatment, post-operative care, all the way through to long-term patient follow-up (AF Heart Team).

Our article inspired a response in the scientific community and recently, two renowned experts in the field commented on our group's results (2,3). Three extremely important questions were raised in the aforementioned Editorials and all of them deserve further clarification:

- (I) Should all patients undergo also the catheter-stage of AF treatment?
- (II) What is the optimal timing of the catheter stage of a hybrid procedure?
- (III) Are epicardial ablations accompanied by a significant number of complications?

Should all patients undergo the catheter-stage of AF treatment?

It is well known that PV reconnection is associated with arrhythmia recurrence after catheter ablation of AF (4). The truth is that these results refer mainly to the paroxysmal form of AF and data on completeness of linear lesions in relation to arrhythmia recurrence are scarce.

The main question is whether data from catheter ablation procedures are freely transferable to epicardial

surgical ablations. The few published studies on surgical ablations either used the (I) “cut and sew” approach during open heart surgery (5) instead of RF energy (mainly in the early days of surgical AF treatment), which inevitably facilitated occurrence of post-incisional atrial tachycardias, and/or (II) included an anecdotally low number of patients. Zeng *et al.*, for instance, included only eight patients that failed to retain normal sinus rhythm after surgical ablation (6). Three patients presented with typical right atrial flutter, the remaining patients had gaps in the line encircling the PVs. Before publication of our study, a systematic investigational approach, including all (not only arrhythmia-presenting) patients after epicardial ablation, was missing. In this respect, our study has significantly helped to fill this gap.

If we adopt the paradigm that durable PV isolation is the major factor precluding arrhythmia recurrence during long-term follow-up of patients after epicardial RF ablation, then based on our results, we should draw the conclusion that omitting endocardial catheter ablation after surgery would result in at least a 30% arrhythmia recurrence rate, which corresponds to the PV reconnection rate seen in our study (1). Extending this assumption to linear lesions (box lesion, trigone line) would lead to an arrhythmia recurrence rate of at least 70%. Moreover, 25% of our patients presented with sustained atrial arrhythmias shortly after surgery (typical right atrial flutters—7%, atrial tachycardias—11%, and AF—6%). If we simply restricted the ‘true hybrid procedure’ to only those presenting with sustained arrhythmias, we would have to admit that surgical ablation may successfully treat less than half of patients with persistent AF, a result which is just as achievable after a single endocardial catheter ablation, and with far fewer complications. Unfortunately, whether or not the incompleteness of epicardial ablation lines are directly linked with arrhythmia recurrence, remains to be fully investigated and needs to be confirmed by specifically designed randomized studies (7).

Meanwhile the patient became an integral part of the decision process according to the current guidelines, therefore the final decision may be left to the discretion of the patient. The patient might accept the higher risk of developing future arrhythmias during follow-up, and simultaneously might accept the risks of continuation of antithrombotic therapy. Then, if arrhythmias do appear, the patient could be scheduled for a catheter ablation. In such cases, we should expect only mild symptoms

of subsequent arrhythmias (8) and long-term ECG monitoring should be used in such scenarios to draw definite conclusions about sinus rhythm stability. On the other hand, the patient might prefer the hybrid procedure, which includes a low-risk catheter ablation stage, since the hybrid procedure offers the benefits of very unlikely arrhythmia recurrences (i.e., <10%) during long-term follow-up as well as an opportunity to discontinue antithrombotic medications in low-risk patients. In our opinion, both approaches are justifiable; however, we have no data to prefer one over the other.

Timing of the staged catheter ablation in hybrid procedures

Our study (1) and others (9,10) have clearly showed that complete transmural lesions in the left atrium cannot be obtained, in the majority of (let alone all) patients, after an epicardial ablation alone (using bipolar RF energy). The worst outcomes are more associated with left atrial linear lesions compared to PV isolations. Indeed, endocardial touch-up ablations were necessary in 56% of cases according to a recent meta-analysis that included 195 patients. However, these data probably underestimate the real clinical values due to biased patient selection (11). There are multiple reasons for epicardial lesions failures, many of which have been discussed in detail elsewhere (12).

When it comes to the endocardial stage, we are strongly convinced that correct timing of the subsequent endocardial catheter ablation, during hybrid procedures, is crucial for preventing future arrhythmia recurrences. Correct timing is critical for excluding false negatives, i.e., transmural lesions that appear to be complete during acute assessment but, in reality, are not complete.

The full scope of the synergistic effects of epi- and endocardial ablation can only be realized when the endocardial stage is delayed long enough to insure that the epicardial lesions are mature and fully healed with fibrous tissue and that neither edema nor mechanical trauma is contributing to the electrical conduction block. Additional reasons, such as the necessity for hybrid operating theater equipment, less bleeding, fewer infection risks, and lower general anesthesia time also favor the staged, i.e., non-simultaneous, approach. Last but not least, from the standpoint of the electrophysiologist, when endocardial mapping is delayed for at least several

weeks, the maturation of epicardial “burns” allows easier identification of non-isolated substrate boundaries and of target points.

Once we conclude that the hybrid procedure should not be performed simultaneously, then the question arises—what is the best delay period. Choi *et al.* advocates for at least 3 months (2). One can imagine that complete tissue healing, after epicardial ablation, cannot occur over a period of a few days or even 2–3 weeks, therefore our personal opinion is that the reasonable time delay between the epicardial ablation procedure and the catheter ablation stage should be between 1 and 3 months. Shorter delays would probably catch immature epicardial lesions, while longer delays could expose patients to excessive risk of arrhythmia recurrence.

Rate of complications during thoracoscopic ablations

We absolutely agree with the position of Choi *et al.* in their Editorial (2), in which they state that the safety of hybrid procedures is of utmost importance and that there is a considerable learning curve, which most likely consists of 40–50 procedures. We have currently performed epicardial ablations on more than 100 patients and the last 60 were without complication, except for one insignificant PV stenosis (unpublished data). A recent meta-analysis of thoracoscopic epicardial ablations revealed that the overall incidence of major complications was $\approx 3\%$, with phrenic nerve paralysis occurring in only 0.7% of patients (13). However, the majority of papers included in this meta-analysis did not state explicitly, whether or not all patients were routinely screened for diaphragmatic motion using an X-ray examination. We are solidly convinced that phrenic nerve palsies are very likely under-reported in the surgical literature, mainly because severe symptoms only appear in a small percentage of patients and because symptoms may disappear once the phrenic nerve regains its functionality, even before the actual reason for ‘dyspnea on exertion’ is explained. We stress that all precautions must be taken to keep the incidence of this debilitating complication to a minimum.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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