In the past decade, catheter ablation of atrial fibrillation (AF) has evolved as one of the most frequently performed procedures in tertiary arrhythmia centers worldwide. With the observation of the actively firing trigger originating from within the pulmonary veins (PVs), ablation strategies have focused at least in paroxysmal AF patients on complete isolation of the PVs.1,2 Several different ablation devices (cryogenic energy, ultrasound, laser, etc) have been investigated to achieve more durable isolating lines around the PVs, with most of these novel ablation catheters allowing for a single-shot approach. Multielectrode phased radiofrequency ablation probes (PVAC; Medtronic, Minneapolis, MN) have been proposed using the standard radiofrequency energy through smaller but multiple electrodes.3,4 The aim of all these ablation devices is not only to improve outcome but also to allow an easier ablation procedure eventually being performed by non-electrophysiologists to be able to respond to the growing demand for AF ablation.

The results of the prospective, randomized Multielectrode Pulmonary Vein Isolation Versus Single Tip Wide Area Catheter Ablation (MYSTIC) trial are reported in this edition,5 which compared standard, irrigated tip radiofrequency ablation with multielectrode-phased radiofrequency ablation (PVAC). As per the reports from 4 experienced centers in the Netherlands and Belgium, rates of single-procedure acute success rates were identical and without any serious adverse events in the first 30 days. Only secondary study end points, such as procedure duration, fluoroscopy exposure and radiofrequency delivery time, showed significant reductions, while the clinical outcome was the same (76.3% versus 81% at 12 months).

These results are much in line with previous comparative trials reporting on other single-shot devices. Dukkipati et al6 reported on the laser ablation balloon randomized trial (also a noninferiority trial design), which achieved identical primary outcomes (61.1% in the visually guided laser balloon group versus 61.7% in controls). More trials are underway to report on similar comparisons of cryo versus radiofrequency or even among single-shot devices.7-9 Most of these are designed to demonstrate noninferiority to the control group with regard to the most important end point of freedom from arrhythmia.

Although outcome is the obvious and most important outcome of any ablation procedure, additional parameters such as procedure duration and fluoroscopy exposure are important. The shorter the overall duration to deliver an effective ablation, the lower the exposure to periprocedural risk (eg, stroke). With shorter procedure duration, more patients could potentially be treated by the same team, which could lower the burden on the waiting time for paroxysmal AF ablation. And finally, even untrained nonelectrophysiologists could carry out single-shot ablation procedures.

**Lesser Need for Training and Experience?**

Interestingly, the investigators in MYSTIC required operators to have an experience of at least 50 cases with each ablation technique to allow them to perform study procedures. This is probably why the procedure times are shorter in comparison with previous trials using PVAC.7,10

In comparison, the control-irrigated radiofrequency group received more fluoroscopy exposure, which is somewhat surprising, given the fact that after the transseptal puncture an experienced operator essentially does not need to use fluoroscopy at all.11,12 This author’s own experience used to range around 15 minutes average fluoroscopy time (when still performing PV angiography) and is now <10 minutes total exposure since using 3-dimensional image integration in nearly all cases. A detailed analysis of the mapping time in the standard, irrigated tip radiofrequency ablation group versus the time to position the PVAC catheter and the need for fluoroscopy and angiography would allow a better understanding of when the need for fluoroscopy occurred. Also using double (standard, irrigated tip radiofrequency ablation) or single transseptal access (PVAC) could have made potentially a difference because the PVAC can be also used to assess completeness of the PV isolation. If the standard, irrigated tip radiofrequency ablation group also only had a single transseptal access, then the need to exchange the mapping catheter for a circular mapping catheter would have been added to both procedure and fluoroscopy exposure.

**A Fair Comparison? The Downside of Randomized Trials With Slow Recruitment**

MYSTIC also demonstrates that innovation is constant and that findings (eg, on thrombogenicity) newly available during...
the course of a trial may change recruitment numbers.13,14 By now, both ablation tools used in the study seem outdated and one wonders what a head-to-head comparison with the new tools (contact force radiofrequency versus GOLD-PVAC) would show in a similar study design?

The Most Important Question: Is PV Isolation Really Enough in Paroxysmal AF?

Overall, the study outcome is somewhat sobering, although the noninferiority end point of the trial was well demonstrated. What are the reasons for the success rates of ≈61% in both groups? Is it that both PV isolation techniques have about the same amount of PV reconnection rate? Or is the end point of PV isolation not the only important end point? Maybe non-PV targets such as autonomic innervation, rotors, and non-PV triggers are more important for the maintenance of sinus rhythm even in this most simple group of paroxysmal atrial fibrillation patients with normal atrial size? Unfortunately, we do not learn much about lesion completeness in this trial. And even from the 2 patients requiring reablation within the 3 months blanking period, we have no knowledge of line completeness or in fact which randomization arm they belonged to in the first place.

As long as we still do not achieve durable PV isolation, we still cannot solve the question if this end point is in fact enough. The recently published GAP-AF trial demonstrated that the acute end point of complete PV isolation is definitely better in predicting SR in follow-up; however, the amount of reconnection assessed in a mandatory invasive reprocedure at 3 months was high.15 Again, one can only speculate how the same trial would fair if more durable ablation lesions could be achieved.

Recently, the importance of non-PV targets and the new light shed on the innervation of the atria as modulators for the maintenance and also for the initiation of AF by adjunct ganglionated plexus ablation16–17 or renal denervation18 leads to a new understanding of the underlying pathophysiology. This leads to the concept that achieving PV isolation alone will not solve the entire AF riddle. It is high time for improved understanding on who will benefit from PV isolation alone will not solve the entire AF riddle. It is high time for improved understanding on who will benefit from PV isolation alone and who requires additional strategies! However, this can only be achieved once we can rely on the applied ablation lesions to be truly permanent.

Conclusions

Single-shot devices for PV isolation in paroxysmal AF patients have been tested in the past 10 years and are by now routine ablation tools in many electrophysiology laboratories in the world. With the growing experience of the operators, outcomes and procedural complication rates have reached equality to the standard radiofrequency ablation techniques. Operator skills still are the most important feature defining the only discernible difference in secondary outcomes (procedure duration and fluoroscopy exposure), which demonstrates in return that this is not (yet) an ablation for the general interventionalist. Finally, PV isolation alone, irrespective of the tool that it was achieved with, might not be the final solution, and alternative ablation strategies need to be further investigated.

Disclosures

Dr Ernst is a consultant to Biosense Webster and Stereotaxis.

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