

# Lessons to be Learned from the CEASE-AF Trial Comparing Hybrid Epi and Endocardial Ablation to Endocardial Catheter Ablation Alone in Advanced Atrial Fibrillation

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### INTRODUCTION

As the largest prospective, multi-center, randomized controlled trial, CEASE-AF revealed an 83% relative benefit increase in terms of rhythm outcome in patients with advanced Atrial Fibrillation (AF) when thoracoscopic epicardial ablation is added to endocardial catheter ablation in a hybrid fashion as compared to endocardial ablation alone. Moreover, a comparable safety profile was maintained [1].

## DESCRIPTION

### The myth of "oranges and apples"

The trial was not designed to compare specific lesion sets, but to evaluate the outcome of two fundamentally different treatment approaches for patients with advanced AF, meaning either persistent AF and enlarged left atrium or long standing persistent AF. Those patients are currently deemed to be rejected for rhythm control interventions or have high failure rates with any treatment strategy and therefore stay exposed to symptoms, the risk of stroke, the risk of heart failure development and even death [2].

While device specific limitations in effectively ablating the left atrial posterior wall leaves pulmonary vein isolation as the only proven corner stone in endocardial ablation, the approach of hybrid ablation allows to overcome those limitations and to target epi/endocardial dissociation in this area more efficaciously which should result in superior rhythm outcome. This hypothesis was confirmed by the trial [3].

Since only a minimal lesion set was defined but additional lesions according to the center's clinical practice were allowed, it is important to understand that differences in lesion sets between the two arms reflect what is currently considered standard of care and is the nature of each of the two treatment approaches rather than a potentially unfair comparison of oranges and apples. Saying this, endocardial catheter ablation differs fundamentally from antiarrhythmic medication but evolved to a commonly applied treatment strategy because of its superior rhythm outcome. The same should be applied when comparing hybrid ablation with catheter ablation [4].

Even more, although the trial protocol suggested the ablation strategy currently recommended by guidelines and applied by most centers and therefore allowed for inhomogeneity in terms of lesion sets, the recent HARTCAP trial reported a similar significant benefit increase for hybrid ablation while requiring the identical, standardized lesion set in terms of a box lesion isolating the pulmonary veins and the left atrial posterior wall in both arms [5].

#### Reproducibility

At first glance, success rates of the endocardial catheter ablation arm appear to be strikingly low. However, if we look at recent trials of catheter ablation, results were in line with what has been reported for this difficult to treat subgroup of patients with advanced AF. Moreover, all participating centers have a wellestablished catheter ablation program and the same electrophysiologist who performed the endocardial ablation in the catheter arm also performed the endocardial part in the hybrid arm. Thus, the general performance should have reflected equally on the results of both arms and still confirms the gap in success between the two approaches [6].

#### Safety and beyond

Per definition hybrid ablation must be considered as one treatment, consisting of two parts endo and epicardial ablation. This can be done in a single approach or in a staged fashion as in CEASE-AF. While in any case this means an extension compared to endocardial catheter ablation alone, we also expected an increase in complications. However, the safety profile was comparable for both arms. Moreover, the epicardial part facilitated endocardial ablation by significantly shortening fluoroscopy and endocardial procedural time necessary to achieve superior rhythm outcome compared to a pure endocardial approach.

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## CONCLUSION

Overall, three randomized controlled trials revealed a significant benefit increase for hybrid ablation in terms of rhythm outcome in patients with non-paroxysmal AF and this independently from a specific lesion set, the staging of epi and endocardial ablation or the used platform. This suggests that epicardial ablation is a driver for efficaciously targeting the left atrial posterior wall and potential endo/epicardial dissociation. It is our responsibility as physicians to put this evolving evidence into perspective. Complication-rates of any intervention for AF are not zero. This needs to be taken into account and balanced against expected success in sinus rhythm restoration and avoiding the potential harmful impact which AF might have in a considerable number of patients. However, if complication rates are not affected, this responsibility should not be mistaken by subjectively judging what level of invasiveness is generally reasonable, acceptable or tolerable for an entire patient population. While experience and knowledge of evidence is always the base of our recommendation to the patient, an interdisciplinary team approach should warrant thorough information, so patient are put into a position to make a reasonable decision together with the treating physicians.

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