Effectiveness and Safety of Hybrid Epicardial and Endocardial Ablation Versus Endocardial Ablation in Patients With Persistent and Longstanding Persistent Atrial Fibrilation: Primary Results of the Cease-AF Trial

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Introduction

As atrial fibrillation (AF) progresses, a higher proportion of patients tend to have extra-pulmonary vein (PV) drivers. Advanced AF is characterized by a high degree endocardial-epicardial dissociation, as demonstrated by simultaneous endo-epi phase mapping in persistent AF. Due to complex 3D wave propagation, endocardial ablation alone may not be sufficient for advanced AF. The hypothesis of the CEASE-AF trial was that minimally invasive Hybrid Ablation that combines endocardial and epicardial ablation would achieve superior effectiveness when compared to endocardial Catheter Ablation alone in persistent AF with enlarged left atrium or longstanding persistent AF (LSPAF).

Methods

CEASE-AF (NCT02695277) is a prospective, multi-center, randomized controlled trial (RCT). It enrolled 170 patients at 9 sites in 5 European countries. Eligible patients were adults with persistent AF and left atrial diameter (LAD) > 4 cm or LSPAF ≤10 years, with AF classification defined by the 2012 HRS/EHRA/ECAS consensus statement. Patients with LAD >6 cm, previous ablation procedure, BMI >35 kg/m2, and left ventricular ejection fraction <30% were excluded. Patients were randomized 2:1 to Hybrid Ablation or Catheter Ablation.

The Hybrid Ablation arm procedure consisted of a first stage epicardial index procedure for PV isolation, posterior wall box, and left atrial appendage (LAA) exclusion. Between 91 and 180 days after the index procedure, the second stage endocardial procedure was performed, which included endocardial mapping and ablation to address gaps.

The Catheter Ablation arm procedure consisted of an endocardial index procedure for PV isolation. Between 91 and 180 days after the index procedure, a repeat endocardial ablation procedure could be performed if clinically indicated.

In both arms, additional ablation techniques/lesions were permitted per institutional practice for non-paroxysmal AF. Follow-up for primary effectiveness started at T0, which was 6-months after the index procedures. Primary effectiveness was freedom from AF/atrial flutter (AFL)/atrial tachycardia (AT) >30 seconds off anti-arrhythmic drugs (AADs) (except those not exceeding previously failed doses) through 12-months follow-up beginning at T0. Composite major complications were evaluated during the study.

Results

The intention-to-treat population (ITT) who received the index procedures included 102 patients in the Hybrid Arm and 52 patients in the Catheter Arm. Baseline characteristics such as age, sex, BMI, and AF duration were similar between arms. Twenty-one percent of patients in the Hybrid Ablation Arm and 17% of patients in the Catheter Ablation Arm had LSPAF. Mean left atrial size was 4.7 cm in both arms.

Total procedure time was higher in the Hybrid Arm. Endocardial ablation time and fluoroscopy time were shorter in the Hybrid Arm. Six patients in the Catheter Arm had a repeat ablation before T0.

Primary effectiveness results are shown in the Table for the modified ITT population who received the index procedure and had follow-up available for effectiveness. Staged Hybrid Ablation resulted in superior freedom from atrial arrhythmias compared to endocardial Catheter Ablation in the overall mITT population. For the persistent and LSPAF subtypes, p-values were not adjusted for multiplicity.

Table 1. CEASE-AF Primary Effectiveness Results

Group	Hybrid Arm	Catheter Arm	Absolute Benefit Increase	P-value	Relative Benefit Increase
Overall mITT population	71.6% (68/95)	39.2% (20/51)	32.4%	<0.001	82.7%
Persistent AF and enlarged LAD	72.7% (56/77)	41.9% (18/43)	31%	0.002	74%
LSPAF	66.7% (12/18)	25.0% (2/8)	42%	0.09	167%

From T0 through 12-months follow-up, repeat ablations (4.2% versus 35.3%) and cardioversions (11.6% vs. 25.5%) were significantly lower in the Hybrid Arm than in the Catheter Arm.

Major complication rates through 30-days post-index and post-second stage/repeat ablation procedures were 7.8% (8/102) in the Hybrid Arm and 5.8% (3/52) in the Catheter Arm (p=0.751). Through 12-months, one patient in the Hybrid Arm died, which was determined by the Clinical Events Committee to be unrelated to the devices/procedure and instead due to underlying conditions

Key Takeaways

- CEASE-AF is the largest prospective, multi-center RCT that demonstrated superior freedom from atrial arrhythmias for staged Hybrid Ablation compared to endocardial Catheter Ablation including repeat ablation in patients with advanced AF.
- Hybrid Ablation with LAA exclusion resulted in a 32.4% absolute and 82.7% relative benefit increase compared to Catheter Ablation through follow-up.
- Adverse safety rates were numerically higher in the Hybrid Arm, but not statistically different than the Catheter Arm.
- Success of an epicardial-endocardial approach emphasizes the role of a collaborative heart team approach in the treatment of non-paroxysmal AF.

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