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ORIGINAL ARTICLE

Hybrid Convergent Procedure for the Treatment of Persistent and Long-Standing Persistent Atrial Fibrillation

Results of CONVERGE Clinical Trial

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BACKGROUND: The limited effectiveness of endocardial catheter ablation (CA) for persistent and long-standing persistent atrial fibrillation (AF) treatment led to the development of a minimally invasive epicardial/endocardial ablation approach (Hybrid Convergent) to achieve a more comprehensive lesion set with durable transmural lesions. The multicenter randomized controlled CONVERGE trial (Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF) evaluated the safety of Hybrid Convergent and compared its effectiveness to CA for persistent and long-standing persistent AF treatment.

METHODS: One-hundred fifty-three patients were randomized 2:1 to Hybrid Convergent versus CA. Primary effectiveness was freedom from AF/atrial flutter/atrial tachycardia absent new/increased dosage of previously failed/intolerant class I/III antiarrhythmic drugs through 12 months. Primary safety was major adverse events through 30 days. CONVERGE permitted left atrium size up to 6 cm and imposed no limits on AF duration, making it the only ablation trial to substantially include long-standing persistent–AF, that is, 42% patients with long-standing persistent–AF.

RESULTS: Of 149 evaluable patients at 12 months, primary effectiveness was achieved in 67.7% (67/99) patients with Hybrid Convergent and 50.0% (25/50) with CA (P=0.036) on/off previously failed antiarrhythmic drugs and in 53.5% (53/99) versus 32.0% (16/50; P=0.0128) respectively off antiarrhythmic drugs. At 18 months using 7-day Holter, 74.0% (53/72) Hybrid Convergent and 55% (23/42) CA patients experienced ≥90% AF burden reduction. A total of 2.9% (3/102) patients had primary safety events within 7 days, and 4.9% (5/102) between 8 and 30 days postprocedure. No deaths, cardiac perforations, or atrioesophageal fistulas occurred. All but one primary safety event resolved.

CONCLUSIONS: The Hybrid Convergent procedure has superior effectiveness compared to the CA for the treatment of persistent and long-standing persistent atrial fibrillation.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT01984346.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: atrial fibrillation ■ catheter ablation ■ electrophysiology ■ pulmonary vein ■ tachycardia

Atrial fibrillation (AF) affects ≈6 million people in the United States and 33 million worldwide.[1,2] Approximately 70% of AF patients have nonparoxysmal AF,[3] that is, persistent AF, defined as continuous AF lasting >7 days, or long-standing persistent AF, lasting >12 months.[4] Although pulmonary vein isolation (PVI) has been shown to be effective in the treatment of patients with paroxysmal AF, the effectiveness of catheter ablation for treatment of

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WHAT IS KNOWN?

- There are limited effective treatment options for persistent and long-standing persistent atrial fibrillation (AF), with pulmonary vein isolation by endocardial ablation being insufficient and additive endocardial lesions yielding mixed results.
- A minimally invasive hybrid approach (Hybrid Convergent) was developed to leverage both epicardial and endocardial ablation to create durable, transmural lesions.

WHAT THE STUDY ADDS?

- Hybrid Convergent ablation had superior effectiveness compared to endocardial catheter ablation in persistent and long-standing persistent AF, with freedom from atrial arrhythmia absent new or increased dosage of previously failed class I/III antiarrhythmic drug of 67.7% versus 50.0%, respectively (risk ratio, 1.35, *P*=0.036), and off antiarrhythmic drugs success of 53.5% versus 32.0% respectively (risk ratio, 1.67, *P*=0.0128).
- At 18 months using 7-day Holter, 74% subjects in Hybrid Convergent arm achieved at least 90% AF burden reduction when compared to 55% with endocardial catheter ablation only (risk ratio, 1.34, *P*=0.0395).
- The randomized CONVERGE trial (Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF) is the only ablation trial to include a substantial proportion of patients with long-standing persistent AF (mean persistent AF duration of 4.4 months).
- The study supports a collaborative surgical-electrophysiological team approach to the management of persistent AF.

Nonstandard Abbreviations and Acronyms

AADs	antiarrhythmic drugs
AF	atrial fibrillation
AFL	atrial flutter
AT	atrial tachycardia
CONVERGE	Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF
MAE	major adverse event
PVI	pulmonary vein isolation

patients with the persistent forms of AF is limited[5–8] due to extensive electrical and structural atrial remodeling and increased left atrial size that occurs as AF progresses. Even with additional substrate ablation, it remains challenging to achieve transmural, durable, lesions with conventional catheter ablation while keeping the risk of esophageal injury low, as reflected in current AF treatment guidelines.[4] Surgical ablation can be performed to treat persistent and long-standing persistent AF but is usually performed concomitantly with cardiac surgery procedures[9] and has a class IIa recommendation as a standalone procedure only after failed catheter ablation.[4] Within the last decade, hybrid methods that combine minimally invasive surgical and electrophysiological approaches have been developed with the goal of leveraging the relative strengths of each ablation strategy to maximize efficacy and safety in treating persistent and long-standing persistent AF.[10,11] Several published reports, primarily single-center series, have described outcomes of a Hybrid Convergent procedure in which closed-chest, epicardial ablation is performed with a focus on the left atrial posterior wall and pulmonary vein ablation, followed by endocardial catheter ablation to complete PVI and address remaining gaps.[12–22] The current study is the first report of a multicenter, randomized controlled trial to compare the effectiveness of the combined hybrid epicardial and endocardial ablation (Hybrid Convergent) for the treatment of persistent and long-standing persistent AF with endocardial catheter ablation.

METHODS

The CONVERGE trial (Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF) is a prospective, multicenter, randomized controlled trial, longitudinal study to compare the effectiveness of Hybrid Convergent procedure to endocardial catheter ablation and to demonstrate its safety for the treatment of symptomatic persistent and long-standing persistent AF (URL: https://www.clinicaltrials.gov; Unique identifier: NCT01984346). Institutional Review Boards or ethics committee approval and patient informed consent form was obtained. Data management was performed by a contract research organization. Holter monitors were read by a core laboratory, which was blinded to the study group. The Data Safety Monitoring Board, which included a cardiothoracic surgeon, electrophysiologist, and biostatistician, and Clinical Events Committee comprised of cardiothoracic surgeons and an electrophysiologist, provided oversight of the study. The data that support the findings of this study are available from the corresponding author upon reasonable request.

STUDY PARTICIPANTS

Twenty-seven sites (25 United States and 2 United Kingdom) participated in the trial. Eligible patients were between 18 and 80 years of age, with symptomatic persistent AF that was refractory or intolerant to at least one class I/III antiarrhythmic drug (AAD) and had a left atrium size of ≤6.0 cm. There was no limitation on duration of AF. Complete inclusion/exclusion criteria have been previously published.[23] Enrolled patients were randomly assigned 2:1 to Hybrid Convergent or endocardial catheter ablation.

INTERVENTIONS

Lesion Set

In the Hybrid Convergent group, epicardial ablation was performed with the vacuum-assisted, unipolar

radiofrequency device (EPi-Sense, AtriCure, OH). The pericardial access was gained through a transdiaphragmatic or subxiphoid approach, and the radiofrequency device was positioned inside a pericardioscopic cannula with an endoscope. Pericardial reflections were not dissected. Epicardial ablations were made around the right and left PV antrum and contiguous, parallel lesions were made across the posterior wall of the left atrium (Figure 1). Endocardial pacing of the posterior wall after epicardial ablation was not required; however, endocardial mapping was performed to identify the breakthrough locations, especially at the pericardial reflections to guide endocardial ablation. Following epicardial lesions, endocardial ablation was performed with an irrigated radiofrequency catheter via standard approach to complete isolation of the PVs, address breakthrough gaps based on electroanatomical mapping, and to create a cavotriscupid isthmus line. Standard entrance/exit block was performed to confirm PVI after endocardial ablation.

In the catheter ablation group, endocardial ablation was performed with an irrigated radiofrequency catheter to isolate the left and right PVs and connect them via atrial roofline. Standard entrance/exit block was confirmed. A cavotriscupid isthmus line was created, with confirmation of bidirectional block. Complex fractionated atrial electrogram ablation was left to physician discretion if the patient did not convert after the other mandatory lesions were created.

Endocardial Catheters

Of 153 endocardial catheters used in the study, the majority (87%) were contemporary contact sensing catheters such as Thermocool SMARTTOUCH (SF) (Biosense Webster, Irvine, CA) and Tacticath Quartz (Abbott, Plymouth, MN). The remaining 13% were noncontact sensing irrigated radiofrequency catheter. The use of contact sensing versus noncontact sensing catheters across both study groups was similar.

Follow-Up

In-person follow-up visits were performed at 7 days, 1, 3, 6, and 12 months and included an electrogram and review of medications and adverse events. The trial also includes an in-person longer-term follow-up visit at 18 months and phone follow-up at 2, 3, 4, and 5 years. Specific evaluation details at each follow-up have been described previously.[23] Twenty-four–hour Holter monitoring was performed at 6 and 12 months. A 7-day Holter at 18 months was performed for longer-term effectiveness and AF burden assessment.

Anticoagulation management has been previously described.[23] In June 2016, the protocol was amended to recommend administration of a prophylactic regimen of steroids (or nonsteroidal medications) to prevent Dressler syndrome, pericarditis, and other inflammatory mechanisms that have been shown to cause late

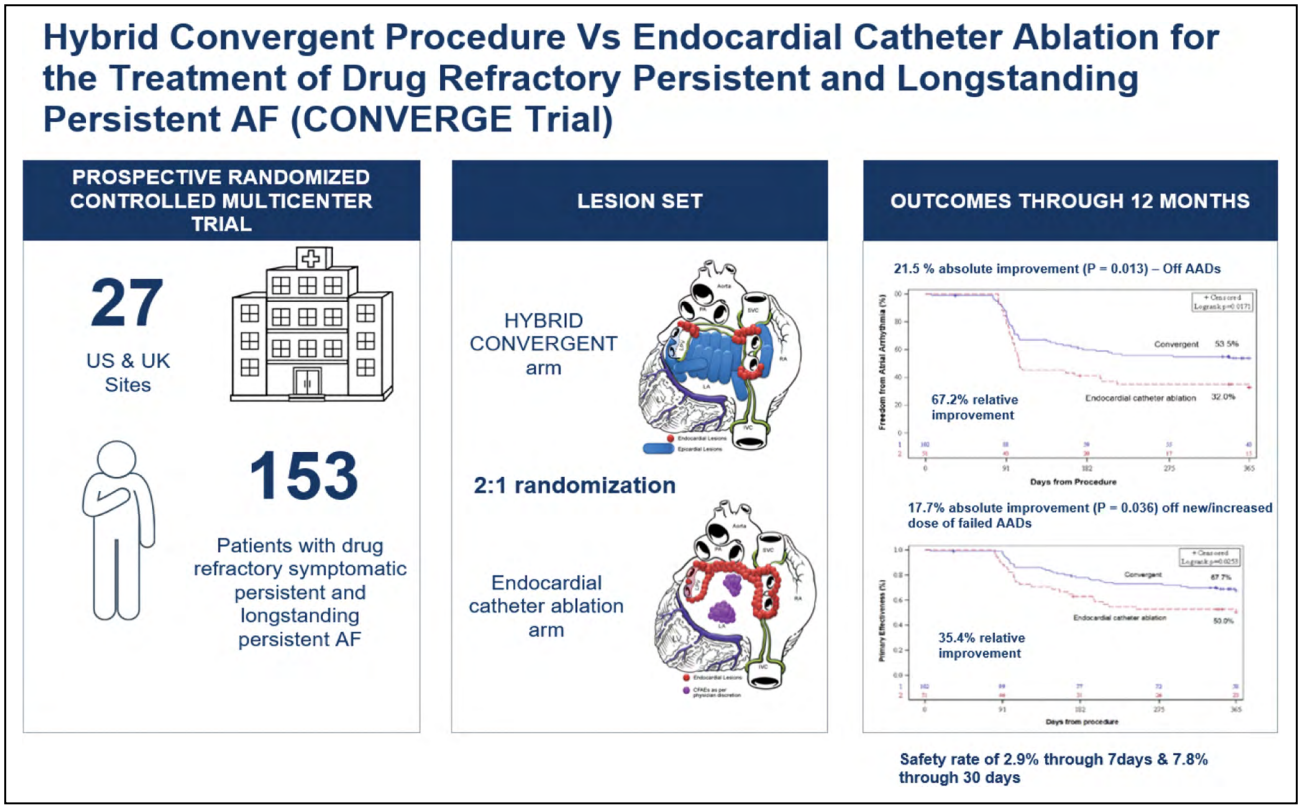

Figure 1. CONVERGE trial (Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF). AADs indicates antiarrhythmic drugs; and AF, atrial fibrillation.

pericardial effusions, provided the patient was able to tolerate such regimen.

Statistical Considerations

The statistical considerations have been previously published,[23] and are briefly described here. It is assumed that the primary effectiveness success rate for the catheter ablation is 40% and at least 65% for the Hybrid Convergent. The sample size results are based on a 2-sided α=0.05, 80% power, a 2:1 allocation of Hybrid Convergent: control and a 10% drop out rate are 102:51 or 153 subjects.

For primary effectiveness analysis, the binary primary end point of success or failure is compared between the 2 study arms using a χ^2 testing using a 2-sided alpha of 0.05. The hypothesis to test is

$$H_O{:}P_T = P_C \text{ vs } H_a{:}P_T \neq P_C$$

where P_T is the true failure rate for the Treatment arm and P_C for the Control arm. H_o is rejected in favor of H_a if the resulting $P<0.05$ and the estimated P_T exceeds P_C.

The secondary and exploratory end points are compared between the study arms using either a χ^2 test for binary end points or 2-sample Z test, for numerical end points. The safety criterion is defined as an acceptable level of major adverse events (MAEs). It is estimated that the true incidence rate for MAEs in this study population is no more than 12% with an upper bound of less than 20%. Kaplan-Meier analysis and log-rank tests are used for time-to-event-analyses.

Study End Points

Effectiveness

The hypothesis was to demonstrate the superiority of Hybrid Convergent procedure compared to endocardial catheter ablation in achieving the primary effectiveness. The primary effectiveness end point was freedom from AF/atrial flutter (AFL)/atrial tachycardia (AT) absent of class I/III AADs, except previously failed or intolerant AADs with no increase in dosage, following a 3-month blanking period through the 12 months postprocedure. Primary effectiveness failures were defined by any AF/AFL/AT episode of at least 30 seconds by Holter monitor or for full 10 seconds recording on a standard 12 lead electrogram; use of a new AAD or dosage increase of a previously failed class I/III AAD; direct current cardioversion for AF/AFL/AT; subsequent left-sided catheter ablation for AF/AFL/AT; or catheter ablation for right-sided typical atrial flutter. Catheter ablations for AF, left-sided atypical AFL, or AT at any time point after index procedure (even within the 3-month blanking period) were also considered primary effectiveness failures.

The key secondary effectiveness end points were (1) AF burden reduction, defined as the proportion of patients achieving at least 90% reduction in AF burden at 12 months when compared with baseline, absent an increased dose or new class I/III AADs, and (2) AF freedom, absent an increased dose or new class I/III AADs, through 12 months. AF burden from the Holter recording, as adjudicated by an independent core lab blinded to the study group, was used to compute the burden reduction from baseline.

Safety

The hypothesis was to demonstrate that the risk of adding epicardial posterior wall lesions to the endocardial catheter ablation, to achieve superior effectiveness, was acceptable. It was estimated that the incidence of primary safety events as a result of additive epicardial lesions would be no more than 12%. The primary safety end point was the incidence of the following MAEs in the Hybrid Convergent group from procedure through 30 days postprocedure, irrespective of device or procedure relatedness: (1) cardiac tamponade resulting in hemodynamic compromise, pericardiocentesis, and 1 cm or more of pericardial effusion; (2) severe PV stenosis; (3) excessive bleeding; (4) myocardial infarction; (5) stroke; (6) transient ischemic attack; (7) atrioesophageal fistula (AEF); (8) phrenic nerve injury; (9) death.

RESULTS

Patients

One-hundred fifty-three patients (102: 51) were randomized and treated from December 2013 to August 2018. The baseline characteristics were comparable between the groups (Table 1). A total of 58% (88/153) had persistent and 42% (65/153) had long-standing persistent AF at the time of enrollment. Baseline medications are shown in Table 2.

Procedural Parameters

The procedure parameters are summarized in Table 3. An example of the post epicardial/pre-endocardial and postendocardial /postepicardial procedure left atrial voltage maps are shown in Figure 2.

Pulmonary vein lesions were created in all patients in both study arms. A total of 96% patients in each arm (98/102 in convergent arm and 49/51 in catheter ablation arm) received cavo-tricuspid isthmus ablation. Linear lesions connecting superior PVs were created in 100% (51) patients, complex fractionated atrial electrograms in 26% (13/51) patients, and septal lesions in 4% (2/51) patients in the catheter ablation arm. In the Hybrid Convergent arm, endocardial PV touch-ups or ablation of common PV were performed in 38% (39/102) patients, mitral isthmus line was created in 2% (2/102) patients, and additional linear/ focal touch up to address gaps around PV reflections were created in 12.7% (13/102) patients.

Table 1. Baseline Characteristics

Characteristic	Hybrid Convergent procedure (N=102)	Endocardial catheter ablation (N=51)	*P* value
Age, y, mean±SD	63.7±9.6	65.1±6.7	NS
Male, n (%)	80 (78%)	27 (53%)	0.0016*
BMI, kg/m^2, mean±SD	32.9±5.9	35.1±7.1	NS
Left atrial diameter, mean±SD	4.4±0.6	4.3±0.6	NS
Left ventricular ejection fraction, mean±SD	55.3±7.8	55.7±6.1	NS
Number of failed AADs, mean±SD	1.3±0.57	1.4±0.85	NS
Years since AF diagnosis, mean±SD (Min, Max)	4.4±4.8 (0.5, 26.0)	4.5±4.7 (0.6, 26.0)	NS
Cardioversions within the last 12 mo	2.0±1.1	3.0±2.3	NS
Hypertension, n (%)	79 (77.5%)	38 (74.5%)	NS

AADs indicates antiarrhythmic drugs; AF, atrial fibrillation; BMI, body mass index; max, maximum; min, minimum; and NS, not significant.
*The presence of more males in the Hybrid Convergent group did not impact the overall study results. The subgroup analysis by gender shows a similar treatment effect for both males and females.

Follow-Up Visits

A total of 96% patients in the Hybrid Convergent group and 98% in the catheter ablation group completed the 12-month visit. Six- and 12-month Holter data were available for 97.1% and 96.1% patients in the Hybrid Convergent group, and 100% and 98% patients in the catheter ablation group.

Effectiveness End Points

Primary Effectiveness

The primary effectiveness end point was achieved in 67.7% (67/99) patients in Hybrid Convergent compared to 50% (25/50) in the catheter ablation group, without imputation for missing data as failures. The absolute success rate difference is 17.7% (risk ratio [RR], 1.35, χ^2 *P*=0.036) in favor of the Hybrid Convergent (Figure 3).

Primary Effectiveness by AAD usage

To determine the impact of AAD on effectiveness, a subanalysis stratified by AAD use was performed. The effectiveness absent class I/III AAD was 53.5% (53/99) in the Hybrid Convergent compared to 32.0% (16/50) in the catheter ablation group. The absolute success rate difference is 21.5% (RR, 1.67, χ^2 *P*=0.013) in favor of the Hybrid Convergent group (Figure 4).

The effectiveness irrespective of AAD use was 76.8% (76/99) in the Hybrid Convergent group compared with 60.0% (30/50) in the catheter ablation group. The absolute success rate difference is 16.8% (RR, 1.28, χ^2 *P*=0.033) in favor of the Hybrid Convergent group (Table 4).

The effectiveness of amiodarone was 62.8% (60/99) in the Hybrid Convergent group compared to 48.0% (24/50) with catheter ablation. Although the absolute success rate difference of 14.8 % (RR, 1.31, χ^2 *P*=0.088) did not reach statistical significance, this is an important observation considering the side effects of amiodarone.

AF Burden Reduction

A total of 80% (60/75) subjects in the Hybrid Convergent group achieved at least 90% AF burden reduction at 12 months (24-hour Holter), compared with 56.8% (25/44) in the catheter ablation group. The absolute success rate difference is 23.2% (RR, 1.41, χ^2 *P*=0.007) in favor of the Hybrid Convergent.

At 18 months using 7-day Holter, 74% (53/72) subjects in the Hybrid Convergent group achieved this end point compared with 55% (23/42) of subjects in the catheter ablation group. The absolute success rate difference of 19 % (RR, 1.34, χ^2 *P*=0.0395) is statistically significant in favor of Hybrid Convergent group.

Freedom From AF

A total of 71% (72/102) patients in the Hybrid Convergent group achieved AF freedom through 12 months, absent of an increased dose or new class I/III AADs, compared with 51.0% (26/51) patients in the catheter ablation group (RR, 1.39, χ^2 *P*=0.0172). At 18 months using 7-day Holter, a total of 63% (64/102) of subjects in the Hybrid Convergent group achieved this end point compared with 43% (22/51) in the catheter ablation group. The absolute success rate difference of 20% (RR, 1.47, χ^2 *P*=0.0212) is statistically significant in favor of Hybrid Convergent group.

Overall, the superiority of the Hybrid Convergent over the catheter ablation in achieving freedom from AF was demonstrated.

Cardioversion

Cardioversion for AF/AFL/AT was allowed during the 3-month blanking period but considered effectiveness failure post blanking period. A total of 14.7% (15/102) Hybrid Convergent and 31.4% (16/51) catheter ablation patients received cardioversion during blanking period and 9.1% (9/99) versus 26.0% (13/50) respectively postblanking (Table 5).

Table 2. Baseline Antiarrhythmic Drugs and Oral Anticoagulation Status

Baseline medication	Hybrid Convergent (N=102)	Catheter ablation (N=51)	*P* value
Oral anticoagulant	100% (102/102)	96% (49/51)	0.1096*
Class I or III AAD	84% (86/102)	80% (41/51)	0.5426
Amiodarone	25% (25/102)	27% (14/51)	
Quinidine (biquin durules)	0% (0/102)	0% (0/51)	
Bretylium	0% (0/102)	0% (0/51)	
Disopyramide phosphate	0% (0/102)	0% (0/51)	
Dofetilide	9% (9/102)	2% (1/51)	
Dronedarone	10% (10/102)	12% (6/51)	
Flecainide	19% (19/102)	27% (14/51)	
Ibutilide	0% (0/102)	0% (0/51)	
Mexiletine	0% (0/102)	0% (0/51)	
Procainamide	0% (0/102)	0% (0/51)	
Propafenone	14% (14/102)	16% (8/51)	
Sotalol	25% (25/102)	29% (15/51)	
Beta blocker	68% (69/102)	69% (35/51)	0.9025
Calcium channel blocker	33% (34/102)	43% (22/51)	0.2353
Digitalis	0% (0/102)	0% (0/51)	NA
Subjects with failed AADs	100% (102/102)	100% (51/51)	1.000
Amiodarone	32.35% (33/102)	33.33% (17/51)	
Disopyramide	0.00% (0/102)	1.96% (1/51)	
Dofetilide	10.78% (11/102)	1.96% (1/51)	
Dronedarone	14.71% (15/102)	17.65% (9/51)	
Flecainide	25.49% (26/102)	31.37% (16/51)	
Propafenone	19.61% (20/102)	13.73% (7/51)	
Quinidine	0.98% (1/102)	0.00% (0/51)	
Sotalol	28.43% (29/102)	43.14% (22/51)	

AAD indicates antiarrhythmic drug; and NA, not applicable.
*P value based on χ^2 test or Fisher exact test.

Safety Analysis

Primary Safety Events

There were no cardiac perforations, AEFs, or deaths. A total of 2.9% (3/102) subjects reported MAE within 7 days postprocedure; one stroke, one excessive bleeding, and one excessive bleeding with late pericardial effusion. After day 7 and through 30 days, an additional 5 (5/102; 4.9%) subjects reported MAEs; 3 pericardial effusions, one phrenic nerve injury, and one transient ischemic attack. These prespecified MAEs were not reported in the catheter ablation arm (0% versus 7.8%, Fisher exact P=0.0525).

The pericardial effusions reported in the trial were not cardiac perforations. These were delayed inflammatory response to pericardiotomy and ablation and were reported 1-3 weeks postprocedure as a result of symptoms (eg, cough, fatigue, shortness of breath). The subjects did not have significant hypotension and underwent a planned intervention for pericardial fluid drainage. The events resolved without sequelae.

DISCUSSION

CONVERGE is the first multicenter, randomized controlled trial to compare the effectiveness of combined epicardial and endocardial ablation to endocardial catheter ablation for the treatment of persistent AF patients. CONVERGE imposed no limits on the duration of AF and allowed patients with substantial left atrial dilation. This study is unique for several reasons including the fact that it is the only ablation trial thus far to include a large portion of patients with long-standing persistent AF, such that the mean duration of persistent AF was 4.40±4.71 years.

Effectiveness

The recently published US Food and Drug Administration regulated PRECEPT IDE trial reported a success rate of mid-50s (61.7% with 5.7% repeat ablation rate within blanking period) on or off previously failed AADs in patients with persistent AF (mean persistent AF duration

Table 3. Procedural Parameters

Characteristic	Hybrid Convergent procedure (N=102)	Endocardial catheter ablation (N=51)	*P* value
Procedure time for the epicardial ablation, minutes, mean±SD*	42.9±13.7	Not applicable	Not applicable
Procedure time for the endocardial ablation, minutes, mean±SD	135.8±49.9	171.4±59.7	<0.001
Fluoroscopy time, minutes, mean±SD	17.6±16.5	17.0±13.4	0.862
Acute procedural success†	99% (101)	98% (50)	1.000
Epicardial access approach			
Transdiaphragmatic, % (n)	65.7% (67)	Not applicable	Not applicable
Subxiphoid, % (n)	34.3% (35)		Not applicable

PV indicates pulmonary vein.

*The total procedure time for the Hybrid Convergent procedure including case turnover was 293.9±80.4 min.

†Acute procedural success was assessed as completion of study defined lesion set and demonstration of conduction block for PVs and linear lesions. One subject in the Hybrid Convergent arm did not have conduction block tested due to access issues. One subject in the Endocardial Catheter ablation arm had conduction block confirmed at all locations except right inferior and superior pulmonary veins and hence is listed as failure.

of 15.9 months).[24] The catheter ablation arm of CONVERGE, which included similar endocardial lesion set as in PRECEPT trial, reported similar effectiveness at 50%. Notably, patients in the CONVERGE trial had comparatively more advanced AF (mean persistent AF duration of 4.4 years). Another recently published US Food and Drug Administration regulated IDE trial, STOP Persistent AF, reported 52% effectiveness with PVI alone in patients with early stages of persistent AF (mean persistent AF duration of 0.6 years).[25]

The addition of epicardial posterior wall lesions to the endocardial lesion set resulted in improved effectiveness irrespective of AAD use. This difference in effectiveness was sustained at 18 months and with more rigorous monitoring (7-day Holter). Additionally, a total of 74% patients in the Hybrid Convergent arm achieved ≥90% reduction in AF burden at 18 months using 7-day Holter, when compared with 55% in the catheter ablation group. The substantial reduction in AF burden observed in the Hybrid Convergent arm corroborates recent retrospective evidence reported in a single-center cohort of 92 patients with continuous monitoring in which 94% of patients had <5% AF burden at one-year post-Hybrid Convergent procedure.[22]

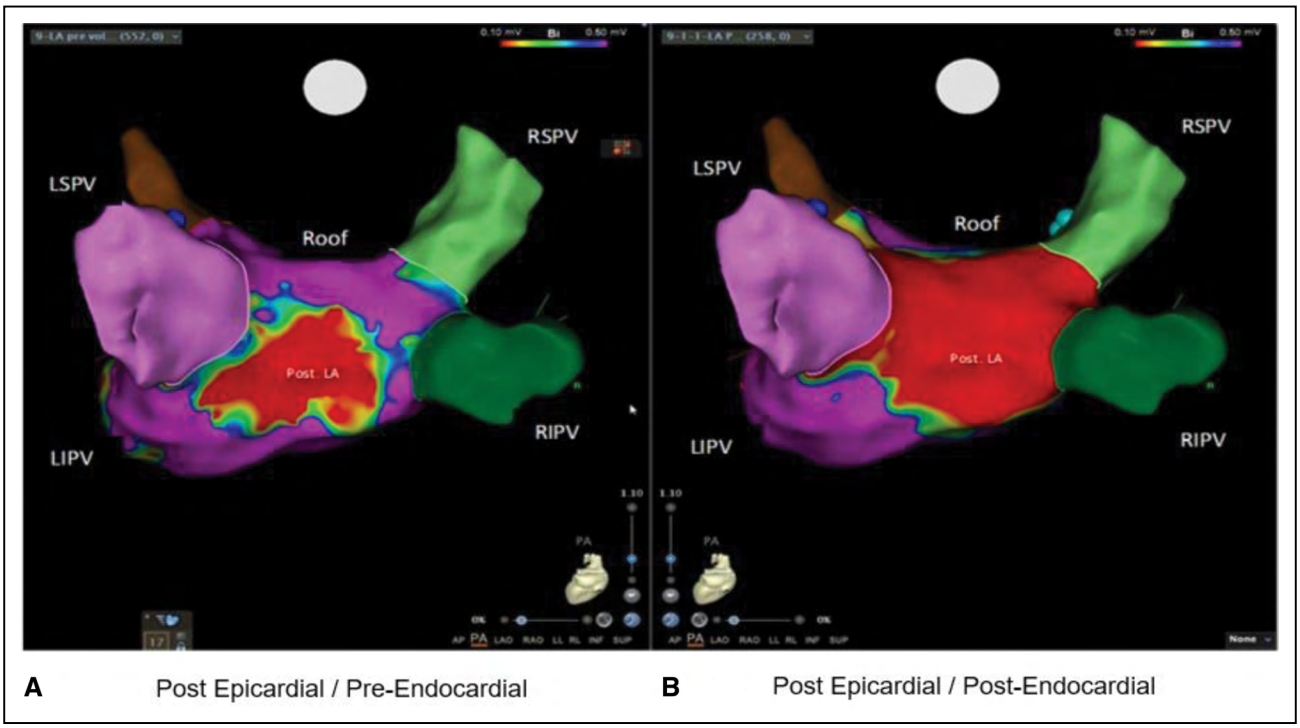

Figure 2. Left atrial voltage map on a study subject (715-118) in Hybrid Convergent group.
Left, Left atrial voltage map after epicardial ablation and before endocardial ablation. **Right**, Left atrial voltage map after epicardial ablation and endocardial ablation. LIPV indicates left inferior pulmonary vein; LSPV, left superior pulmonary vein; Post. LA, posterior left atrium; RIPV, right inferior pulmonary vein; and RSPV, right superior pulmonary vein.

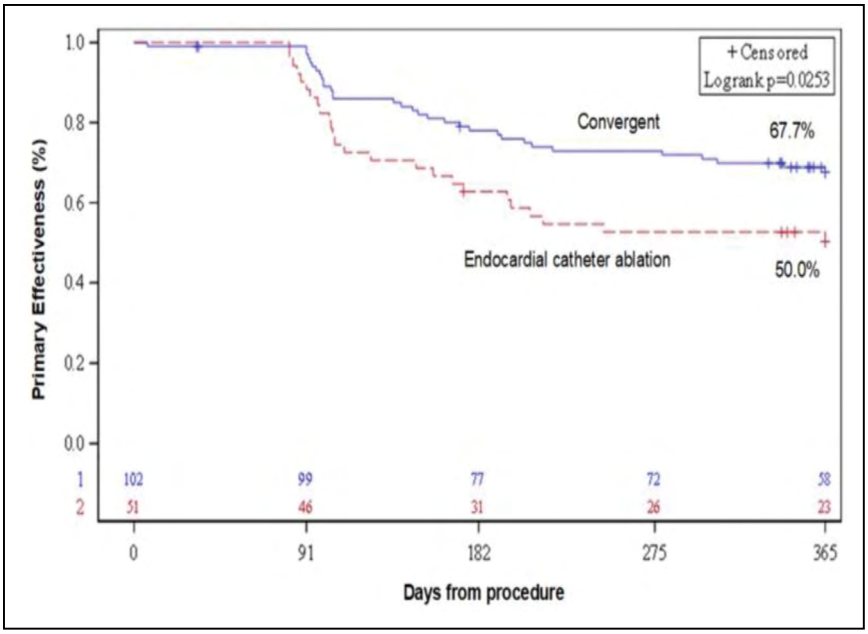

Figure 3. Primary effectiveness comparison between Hybrid Convergent and endocardial catheter ablation groups on or off previously failed class I/III antiarrhythmic drug.

This is an important clinical consideration given high preablation burden in persistent and long-standing persistent AF patients.

Posterior Wall Ablation

A limitation of this study is that while the Hybrid Convergent arm received epicardial posterior wall silencing, a comprehensive posterior wall silencing was not performed endocardially in the catheter ablation arm. Although linear lesions (roofline) and complex fractionated atrial electrograms (per investigator's discretion) were performed in the catheter ablation arm, empirical endocardial linear lesions throughout posterior wall were not performed primarily because this technique can be challenging with no compelling evidence to support that it is more effective. Whereas some studies have published improved outcomes,[26,27] others have reported no improvement with endocardial posterior wall ablation.[28] The BELIEF trial reported 28% efficacy with extensive ablation including endocardial posterior wall ablation in patients with long-standing persistent AF.[29] Similar results were reported by the STAR AF II study when endocardial linear lesions were added.[5] Several randomized controlled studies comparing PVI to PVI+ endocardial posterior wall ablation indicated no significant difference in the freedom from AF patients with this addition.[30–32] The reason for lack of benefit could be that more extensive ablation may cause new, iatrogenic areas of arrhythmogenesis where tissue is incompletely ablated, or linear block is not achieved. Although the benefits of endocardial posterior wall ablation are unclear, there is consensus on increased risk of

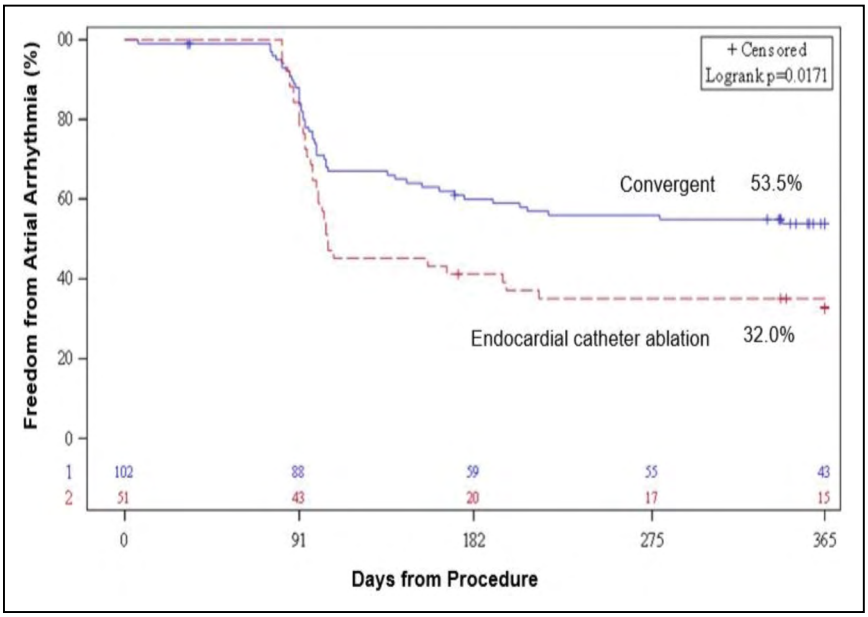

Figure 4. Primary effectiveness comparison between Hybrid Convergent and endocardial catheter ablation groups off class I/III antiarrhythmic drug.

Table 4. Freedom From Atrial Arrhythmia (AF/AFL/AT) From 3 mo Through 12 mo Stratified by AAD Usage

Parameter	Hybrid Convergent ablation arm	Endocardial catheter ablation arm	Absolute difference (risk ratio)	*P* value
Absent class I/III AADs, % (n)*	53.5% (53/99)	32.0% (16/50)	21.5% (RR=1.67)	0.0128†
Absent class I/III AADs or Absent new or increased dosage of previously failed AADs, % (n)‡	67.7% (67/99)	50.0% (25/50)	17.7% (RR=1.35)	0.0360†
With or without AADs, % (n)	76.8% (76/99)	60.0% (30/50)	16.8% (RR=1.28)	0.0329†

All analyses are performed without imputing missing data as failure. AADs indicates antiarrhythmic drugs; AF, atrial fibrillation; AFL, atrial flutter; AT, atrial tachycardia; and RR, risk ratio.

*As per the definition of One-Year Success stated in 2017 HRS Expert Consensus on Catheter and Surgical Ablation of Atrial Fibrillation.

†*P* value based on χ^2 test; statistically significant.

‡As per prespecified definition of success in the CONVERGE IDE study protocol (https://www.clinicaltrials.gov; Unique identifier: NCT01984346).

esophageal injury with these lesions (class I). Kim et al[33] reported 0.5 % (2/398) AEF rate in a case series of persistent AF patients who received endocardial posterior wall ablation. Similarly, STAR AF II reported 0.4% (1/254) AEF rate with the addition of complex fractionated atrial electrogram ablation on the posterior wall.[5] Higuchi et al[34] reported 0.5% (1/217) vagal esophageal disorder in patients who underwent box isolation for the treatment of nonparoxysmal AF, and McLellan[35] reported 0.6% (1/161) esophageal tear with endocardial posterior wall isolation. Esophageal temperature rises were most commonly cited as the factor preventing successful posterior wall isolation, and the threshold for withholding ablation with such temperature rises varied considerably between operators. Posterior wall reconnections were common in such situations. Markman et al[36] recently reported a 40% rate of posterior wall reconnections after previously failed endocardial ablation of the posterior wall and hypothesized that risk of perforation, posterior wall overheating, and roof thickness contribute to the lack of durable posterior wall lesions with endocardial ablation. For these reasons, endocardial posterior wall ablation continues to be a class IIb, level C-LD recommendation, based on limited data and mixed results.[4]

A unique advantage of the Hybrid Convergent procedure is that transmural posterior wall ablation can be achieved with reduced risk for injury to the esophagus due to the application of radiofrequency energy towards the heart and away from the pericardium.[37,38] The CONVERGE trial provides a high-quality evidence from a randomized clinical trial that supports transmural posterior wall ablation, in addition to pulmonary vein isolation as an effective strategy in treating patients with advanced AF.

Safety

No deaths, cardiac perforations, or AEF were reported in the trial. The safety rate was primarily driven by inflammatory pericardial effusions that were reported between 1 and 3 weeks postprocedure, as a result of patient symptoms (eg, cough, fatigue, shortness of breath etc). These events did not result in significant hypotension and were managed by planned (nonemergent) intervention. Although the demonstrated safety profile of Hybrid Convergent procedure is acceptable, best practices for management of pericardial effusions such as adequate drain management, anti-inflammatory prophylaxis, and improved patient monitoring and should be implemented.

Lastly, this study reemphasizes the value of collaboration between the electrophysiologists and cardiac surgeons to achieve better outcomes for patients with advanced AF.

Limitations

The absence of empirical endocardial posterior wall ablation in the catheter ablation group is a limitation. As discussed above, due to challenges with obtaining transmural posterior wall ablation while maintaining safety, it is difficult to state if the outcomes would have been better in the catheter ablation arm posterior wall silencing was allowed.

The study allowed only irrigated radiofrequency catheters for endocardial ablation in both groups, primarily to maintain consistency. Cryoablation was not included. Additionally, electrical isolation or exclusion of LAA was not performed. Future trials with endocardial cryoablation and to assess incremental benefits of concomitant LAA exclusion and electrical isolation should be conducted.

Conclusions

The CONVERGE trial met its primary safety and effectiveness end points, demonstrating improved outcomes with a hybrid epicardial/endocardial ablation approach

Table 5. Freedom From Cardioversions Postprocedure

Freedom from cardioversion	Hybrid Convergent procedure	Endocardial catheter ablation	*P* values
From discharge through 3 mo blanking period	85.3% (87/102)	68.6% (35/51)	0.0156
From 3 mo to 12 mo post procedure	90.9% (90/99)	74.0% (37/50)	0.0060

compared with an endocardial-only ablation strategy. The trial is distinguished from other contemporary ablation trials because of the inclusion of subjects irrespective of nonparoxysmal AF duration, and therefore, the results reported here may have clinical implications for patients for whom AF has progressed.

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