

Catheter Ablation Versus Standard Conventional Treatment in Patients with Left Ventricular Dysfunction and Atrial Fibrillation (CASTLE-AF Trial)

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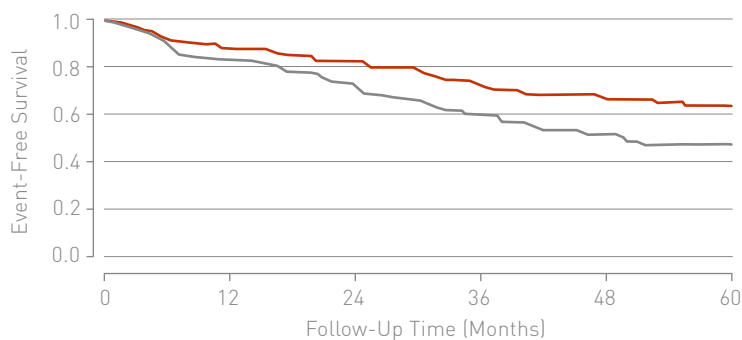
Study Design

- Prospective, randomized, multicenter, international
- Evaluated the effectiveness of catheter ablation of atrial fibrillation in patients with heart failure on mortality and morbidity when compared to medical treatment
- 398 patients at 33 sites in Europe, USA, and Australia

Main Result

Catheter ablation of atrial fibrillation in patients with heart failure is associated with a significant reduction in mortality and morbidity.

Death or Hospitalization for Worsening Heart Failure



38%

Reduction of Relative Risk for **All-Cause Death or Hospitalization** for Heart Failure

HR, 0.62 (95% CI, 0.43–0.87); P=0.007
Log-rank test: P=0.006

No. at risk

Ablation	179	141	114	76	58	22
Medical Therapy	184	145	111	70	48	12

Clinical Relevance

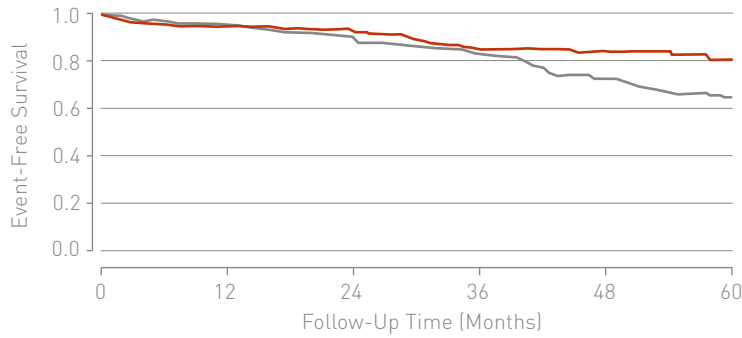
CASTLE-AF is the first large, randomized study providing clinical evidence that ablation of atrial fibrillation improves hard outcome parameters in heart failure patients.

Catheter ablation for patients with heart failure and concomitant AF can be suggested as a first-line therapy, as early as possible during the course of heart failure.

The results strongly indicate that catheter ablation of atrial fibrillation is a crucial element in managing advanced heart failure, next to CRT and continuous remote monitoring.

Rhythm Control Through Ablation is Associated with Improved Survival and Reduced Hospitalization Rates

Death from Any Cause



47%

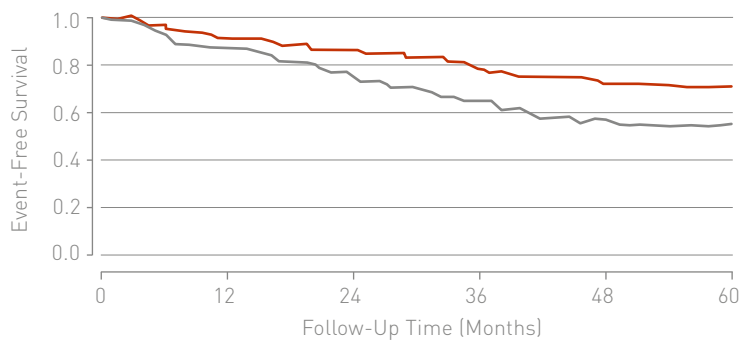
Reduction of Relative Risk for **All-Cause Death**

HR, 0.53 (95% CI, 0.32–0.86); P=0.011
Log-rank test: P=0.009

No. at risk

Ablation	179	154	130	94	71	27
Medical Therapy	184	168	138	97	63	19

Hospitalization for Worsening Heart Failure



44%

Reduction of Relative Risk for **Hospitalization for Heart Failure**

HR, 0.56 (95% CI, 0.37–0.83); P=0.004
Log-rank test: P=0.004

No. at risk

Ablation	179	141	114	76	58	22
Medical Therapy	184	145	111	70	48	12

Subgroup Analysis of the Primary Endpoint

Subgroup	Ablation no. of events/no. of patients	Medical Therapy	HR [95% CI]	P Value for Interaction
Type of atrial fibrillation				0.90
Paroxysmal	17/54	34/64	0.60 [0.34–1.08]	
Persistent	34/125	48/120	0.64 [0.41–0.99]	
CRT-D implanted				0.60
No	37/131	57/132	0.65 [0.43–0.98]	
Yes	14/48	25/52	0.54 [0.28–1.04]	
ICD indication				0.20
Primary	43/160	72/163	0.57 [0.39–0.83]	
Secondary	8/19	10/21	1.03 [0.41–2.62]	
Gender				0.36
Female	9/23	12/29	0.93 [0.39–2.21]	
Male	42/156	70/155	0.58 [0.39–0.84]	
Age				0.17
< 65 years	18/96	34/99	0.48 [0.27–0.85]	
≥ 65 years	33/83	48/85	0.79 [0.50–1.23]	
NYHA functional class				0.06
II	20/101	46/109	0.42 [0.25–0.72]	
III	22/50	26/49	0.89 [0.51–1.58]	
LVEF				0.01
< 25%	20/34	15/27	1.36 [0.69–2.65]	
≥ 25%	29/130	61/145	0.48 [0.31–0.74]	
Cause of heart failure				0.56
Nonischemic	26/107	29/88	0.74 [0.43–1.25]	
Ischemic	25/72	53/96	0.60 [0.37–0.97]	
Diabetes				0.06
No	32/136	48/117	0.52 [0.33–0.81]	
Yes	19/43	34/67	1.01 [0.58–1.78]	
Hypertension				0.88
No	12/50	19/48	0.59 [0.28–1.21]	
Yes	39/129	63/136	0.63 [0.42–0.93]	
Amiodarone use				0.66
No	37/122	61/133	0.65 [0.43–0.97]	
Yes	13/55	18/46	0.55 [0.27–1.13]	
Digitalis use				0.68
No	41/146	52/124	0.65 [0.43–0.98]	
Yes	9/31	27/56	0.56 [0.26–1.19]	
Beta-blocker use				0.47
No	4/12	4/9	1.01 [0.25–4.05]	
Yes	46/165	75/171	0.60 [0.42–0.87]	

CASTLE-AF. First Large, Randomized Clinical Study on Atrial Fibrillation Ablation in Patients with Heart Failure

1° Endpoint	All-cause mortality or worsening of heart failure requiring unplanned hospitalization, whichever came first		
2° Endpoints	<ul style="list-style-type: none"> All-cause mortality Worsening of heart failure admissions Cerebrovascular accidents Cardiovascular mortality Unplanned hospitalization due to cardiovascular reasons All-cause hospitalization Quality of Life: Minnesota Living with Heart Failure and EuroQoL EQ-5D 	<ul style="list-style-type: none"> Exercise tolerance (6 minutes walk test) Number of delivered ICD shocks, and ATPs (appropriate/inappropriate) LVEF Time to first ICD shock, and time to first ATP Number of device-detected VT/VF episodes AF burden: cumulative duration of AF episodes AF free interval: time to first AF recurrence after 3 months blanking period post ablation 	
Main Inclusion Criteria	<ul style="list-style-type: none"> Symptomatic paroxysmal or persistent AF Failure or intolerance to ≥ 1 or unwillingness to take antiarrhythmic drug LVEF $\leq 35\%$ 	<ul style="list-style-type: none"> NYHA class \geq II ICD/CRT-D with BIOTRONIK Home Monitoring capabilities already implanted due to primary or secondary prevention 	
Main Exclusion Criteria	<ul style="list-style-type: none"> Documented left atrial diameter > 6 cm Contraindication for chronic anticoagulation therapy or heparin Previous left heart ablation procedure for atrial fibrillation 	<ul style="list-style-type: none"> Acute coronary syndrome, cardiac surgery, angioplasty or stroke within 2 months prior to enrollment Untreated hypothyroidism or hyperthyroidism Cardiac assist device implanted Uncontrolled hypertension 	
Study Flowchart	<pre> graph LR A[Enrollment & Randomization (1:1) 398 patients] -- Run-in 5 weeks --> B[Baseline] B --> C[Ablation] B --> D[Medical Therapy] C --> E[Follow-up after 3, 6, 12, 24, 36, 48, 60 months] D --> E </pre>		<ul style="list-style-type: none"> ICD/CRT-D check Adverse event documentation Echocardiography 6-minute walk test Optimization of medication for HF Home Monitoring programming NYHA, weight, blood pressure, QoL Patients' diary
Reference no.	NCT00643188 (ClinicalTrials.gov)		

Marrouche, Nassir F.; Brachmann, Johannes; Andresen, Dietrich; Siebels, Jürgen; Boersma, Lucas; Jordaens, Luc; Merkely, Béla; Pokushalov, Evgeny; Sanders, Prashanthan; Proff, Jochen; Schunkert, Heribert; Christ, Hildegard; Vogt, Jürgen; Bänsch, Dietmar; Catheter Ablation for Atrial Fibrillation with Heart Failure; N Engl J Med 2018; 378(5): 417–427 (modified)

Abbreviations:

AF, atrial fibrillation; ATP, antitachycardia pacing; CAD, coronary artery disease; CI, confidence interval; CRT-D, cardiac resynchronization therapy defibrillator; HF, heart failure; HR, hazard ratio; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; QoL, quality of life; VF, ventricular fibrillation; VT, ventricular tachycardia.