



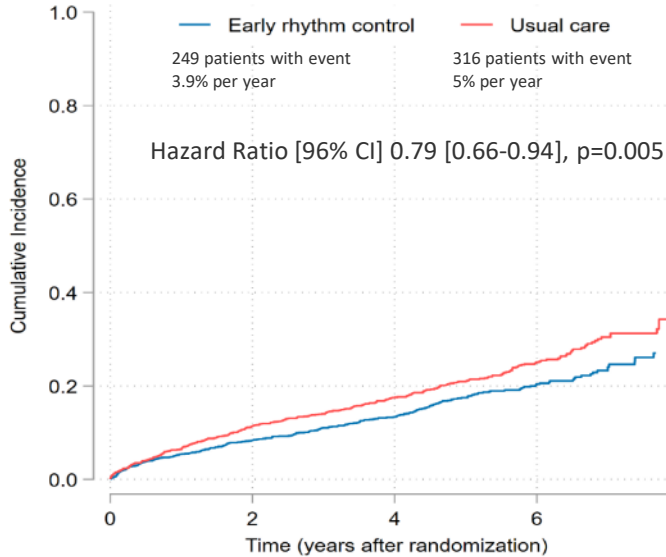
ATRIAL FIBRILLATION
NETWORK

EAST - AFNET 4

Subanalysen



EAST-AFNET 4



Patients at risk	0	2	4	6	8
Early rhythm control	1395	1193	913	404	26
Usual care	1394	1169	888	405	34

Cost-effectiveness of early rhythm control vs. usual care in atrial fibrillation care: an analysis based on data from the EAST-AFNET 4 trial

Heart failure patients

Circulation ORIGINAL RESEARCH ARTICLE

Early Rhythm Control Therapy in Patients With Atrial Fibrillation and Heart Failure

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ABSTRACT: Lower atrial rhythm control therapy in patients with heart failure and atrial fibrillation improves cardiovascular outcomes. Additional treatment is needed to reduce these benefits, especially in patients with heart failure and preserved left ventricular ejection fraction.

OBJECTIVES: This prespecified substudy of the randomized EAST-AFNET 4 trial (early treatment of atrial fibrillation for stroke prevention) assessed the effect of systematic early rhythm control therapy (RCT) using an antiarrhythmic drug or catheter ablation compared with usual care (allowing rhythm control therapy to improve symptoms) on the primary outcome of the trial and on additional secondary outcomes in patients with heart failure, defined as heart failure symptoms, New York Heart Association class II or III, or left ventricular ejection fraction (LVEF) <50%.

RESULTS: This analysis included 730 patients (50% female, median age 71.0 [64.6, 76.0] years, 78% with ischaemic LVF). The majority of patients (n=487) had heart failure and preserved LVEF (LVEF ≥50%) (mean LVEF 61 ± 16.5%). The others had heart failure with midrange ejection fraction (n=211) (LVEF 40%–49%, mean LVEF 44.1 ± 22.9%) or heart failure with reduced ejection fraction (n=132) (LVEF <40%) (mean LVEF 31.6 ± 8.6%). Over the 5.1 year median follow-up, the composite primary outcome of cardiovascular death, stroke, or hospitalization for worsening of heart failure or atrial tachycardia syndrome occurred less often in patients randomly assigned to RCT (n=162) than in 162 patients who were assigned to usual care (n=184) (13.0% vs 15.0%, respectively; hazard ratio, 0.74 [95% CI, 0.57–0.97], p=0.03). The primary safety outcome (death, stroke, or serious adverse events related to rhythm control therapy) occurred in 71 (11.3%) patients with heart failure randomly assigned to RCT and in 87 (10.9%) patients with heart failure randomly assigned to usual care (hazard ratio, 0.85 [95% CI, 0.67–1.07], p=0.18). LVEF improved in both groups (LVF: increase of 0.5 year: RCT, 5.8% [1.9%]; usual care, 3.4% [1.8%], p=0.03). LVEF also improved the composite outcome of death or hospitalization for worsening of heart failure.

CONCLUSIONS: Rhythm control therapy reduces clinical benefit when initiated within 1 year of diagnosing atrial fibrillation in patients with signs or symptoms of heart failure.

REGISTRATION: URL: <https://www.clinicaltrials.gov/ct2/show/study/NCT01988892>; URL: <https://www.clinicaltrials.gov/ct2/show/study/NCT01988892>; Unique Identifier: 2010-021299-20.

KEY WORDS: atrial tachycardia syndrome, antiarrhythmic agents, atrial fibrillation, atrial fibrillation ablation, controlled clinical trial, death, heart failure, stroke

Early Rhythm Control in Patients With Atrial Fibrillation and High Comorbidity Burden

Asymptomatic patients

ESC European Society of Cardiology ORIGINAL RESEARCH ARTICLE

Systematic, early rhythm control strategy for atrial fibrillation in patients with or without symptoms: the EAST-AFNET 4 trial

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OBJECTIVES: The EAST-AFNET 4 trial (early treatment of atrial fibrillation for stroke prevention) was a randomized controlled trial comparing systematic, early rhythm control therapy (RCT) with usual care (allowing rhythm control therapy to improve symptoms) in patients with or without symptoms of atrial fibrillation. The primary outcome was the composite of cardiovascular death, stroke, or hospitalization for worsening of heart failure or atrial tachycardia syndrome. Secondary outcomes included quality of life, mortality, and safety. The trial was prespecified in the EAST-AFNET 4 protocol.

RESULTS: The trial included 1709 patients (50% female, median age 71.0 [64.6, 76.0] years, 78% with ischaemic LVF). The majority of patients (n=487) had heart failure and preserved LVEF (LVEF ≥50%) (mean LVEF 61 ± 16.5%). The others had heart failure with midrange ejection fraction (n=211) (LVEF 40%–49%, mean LVEF 44.1 ± 22.9%) or heart failure with reduced ejection fraction (n=132) (LVEF <40%) (mean LVEF 31.6 ± 8.6%). Over the 5.1 year median follow-up, the composite primary outcome of cardiovascular death, stroke, or hospitalization for worsening of heart failure or atrial tachycardia syndrome occurred less often in patients randomly assigned to RCT (n=162) than in 162 patients who were assigned to usual care (n=184) (13.0% vs 15.0%, respectively; hazard ratio, 0.74 [95% CI, 0.57–0.97], p=0.03). The primary safety outcome (death, stroke, or serious adverse events related to rhythm control therapy) occurred in 71 (11.3%) patients with heart failure randomly assigned to RCT and in 87 (10.9%) patients with heart failure randomly assigned to usual care (hazard ratio, 0.85 [95% CI, 0.67–1.07], p=0.18). LVEF improved in both groups (LVF: increase of 0.5 year: RCT, 5.8% [1.9%]; usual care, 3.4% [1.8%], p=0.03). LVEF also improved the composite outcome of death or hospitalization for worsening of heart failure.

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Early rhythm-control therapy for atrial fibrillation in patients with a history of stroke: a secondary analysis of the EAST-AFNET 4 trial

Treatment patterns

ESC European Society of Cardiology ORIGINAL RESEARCH ARTICLE

Anticoagulation, therapy of concomitant conditions, and early rhythm control therapy: a detailed analysis of treatment patterns in the EAST-AFNET 4 trial

Andreas Metzner^{1,2}, Anna Sörns^{3,4}, Axel Brandes^{4,5}, Günter Breithardt^{4,7}, A. John Camm^{8,9}, Harry J.G.M. Crijns^{10,11}, Lars Eckardt^{12,13}, Arif Elvan¹⁰, Andreas Goette^{6,11,12}, Laurent M. Haegeli^{12,14}, Mein Heidebuchel¹⁵, Josef Kautzner^{16,17}, Karl-Heinz Kuck^{18,19}, Luis Mont^{18,19}, G. André Ng²⁰, Lukasz Szumowski²¹, Sakis Themistoclakis²², Isabelle C. van Gelder^{23,24}, Panos Vardas²⁵, Karl Wegscheider^{26,27}, Stephan Willems^{28,29}, and Paulus Kirchhof^{30,31,32}

OBJECTIVES: The EAST-AFNET 4 trial (early treatment of atrial fibrillation for stroke prevention) was a randomized controlled trial comparing systematic, early rhythm control therapy (RCT) with usual care (allowing rhythm control therapy to improve symptoms) in patients with or without symptoms of atrial fibrillation. The primary outcome was the composite of cardiovascular death, stroke, or hospitalization for worsening of heart failure or atrial tachycardia syndrome. Secondary outcomes included quality of life, mortality, and safety. The trial was prespecified in the EAST-AFNET 4 protocol.

RESULTS: The trial included 1709 patients (50% female, median age 71.0 [64.6, 76.0] years, 78% with ischaemic LVF). The majority of patients (n=487) had heart failure and preserved LVEF (LVEF ≥50%) (mean LVEF 61 ± 16.5%). The others had heart failure with midrange ejection fraction (n=211) (LVEF 40%–49%, mean LVEF 44.1 ± 22.9%) or heart failure with reduced ejection fraction (n=132) (LVEF <40%) (mean LVEF 31.6 ± 8.6%). Over the 5.1 year median follow-up, the composite primary outcome of cardiovascular death, stroke, or hospitalization for worsening of heart failure or atrial tachycardia syndrome occurred less often in patients randomly assigned to RCT (n=162) than in 162 patients who were assigned to usual care (n=184) (13.0% vs 15.0%, respectively; hazard ratio, 0.74 [95% CI, 0.57–0.97], p=0.03). The primary safety outcome (death, stroke, or serious adverse events related to rhythm control therapy) occurred in 71 (11.3%) patients with heart failure randomly assigned to RCT and in 87 (10.9%) patients with heart failure randomly assigned to usual care (hazard ratio, 0.85 [95% CI, 0.67–1.07], p=0.18). LVEF improved in both groups (LVF: increase of 0.5 year: RCT, 5.8% [1.9%]; usual care, 3.4% [1.8%], p=0.03). LVEF also improved the composite outcome of death or hospitalization for worsening of heart failure.

CONCLUSIONS: Rhythm control therapy reduces clinical benefit when initiated within 1 year of diagnosing atrial fibrillation in patients with signs or symptoms of heart failure.

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KEY WORDS: atrial tachycardia syndrome, antiarrhythmic agents, atrial fibrillation, atrial fibrillation ablation, controlled clinical trial, death, heart failure, stroke

Presenting Pattern of Atrial Fibrillation and Outcomes of Early Rhythm Control Therapy

Attaining sinus rhythm mediates improved outcome with early rhythm control therapy of atrial fibrillation: the EAST-AFNET 4 trial

EAST-AFNET 4 genetic substudy

2789 participants underwent randomisation
2389 participants offered DNA sampling
1567 participants with analyzable DNA sample

5 year follow-up, centrally adjudicated outcomes (CV death, stroke, heart failure hospitalizations), Analysis of interaction with early rhythm control and associations with outcomes

PRS AF vs **PRS Stroke**

HR [95% CI]	Primary outcome EAST-AFNET 4	HR [95% CI]	Stroke
HR 0.99 (0.88 – 1.11)	Primary outcome EAST-AFNET 4	HR 1.13 (1.0 – 1.27)	Stroke
HR 1.10 (0.83 – 1.45)	Stroke	HR 1.00 (0.75 – 1.34)	Heart Failure Hospitalization
HR 1.00 (0.86 – 1.17)	Heart Failure Hospitalization	HR 1.23 (1.05 – 1.43)	Recurrent AF
HR 1.08 (1.0 – 1.16)	Recurrent AF	HR 1.04 (0.97 – 1.12)	Stroke

Incident disease

HR [95% CI]	Stroke	Heart Failure Hospitalization	Recurrent AF
HR 1.08 (1.06 – 1.11)	Stroke	HR 1.08 (1.06 – 1.10)	Recurrent AF
HR 1.15 (1.14 – 1.17)	Stroke	HR 1.15 (1.14 – 1.17)	Recurrent AF

1. Early rhythm control effectively reduces cardiovascular outcomes across the spectrum of genetic AF and stroke risk.
2. Genetic stroke risk is associated with heart failure, but not associated with stroke in this well-anticoagulated cohort.
3. Our observations call for further research into the interactions between genetic stroke and AF risk and heart failure.

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