

Attaining sinus rhythm mediates improved outcomes with early rhythm control therapy of atrial fibrillation

August 29 2022, by Angelika Leute



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The EAST—AFNET 4 (Early Treatment of Atrial Fibrillation for Stroke Prevention) trial investigated whether rhythm control therapy—with

antiarrhythmic drugs or atrial fibrillation ablation—delivered within one year after AF diagnosis improves outcomes. The main study result, published in 2020, demonstrated a clinical benefit of early rhythm control therapy for patients with AF and comorbidities: ERC with antiarrhythmic drugs and/or AF ablation reduced the primary outcome, a composite of cardiovascular death, stroke, and hospitalization for worsening heart failure or acute coronary syndrome, in 2,789 patients with early AF and cardiovascular risk factors compared to usual care (UC) over a 5-year follow-up time.

Professor Eckardt explains that "the EAST—AFNET 4 trial demonstrated that systematic early rhythm control reduced cardiovascular outcomes by 21% compared to usual care. But it was not yet known which components of early rhythm control therapy contributed to the outcome reduction. To identify possible mediators of the observed treatment effect, we scrutinized the EAST—AFNET 4 trial dataset for factors of early rhythm control that were associated with reduced cardiovascular outcomes."

All participants of the EAST—AFNET 4 trial were examined in a study visit at 12 months after randomization. At that time, 90% of study patients (1257/1395 randomized to early rhythm control and 1260/1394 randomized to usual care) had not reached the first primary outcome. The data of these patients were incorporated into the mediator analysis.

Fourteen potential mediators of early rhythm control were identified at the 12-month visit. Of these, sinus rhythm at 12 months explained 81% of the treatment effect compared to usual care during the remainder of follow-up (4.1 years). In patients not in sinus rhythm at 12 months, early rhythm control did not reduce future cardiovascular outcomes (HR 0.94, 95% CI [0.65-1.67]). Inclusion of AF recurrence in the model only explained 31% of the treatment effect, and inclusion of systolic blood pressure at 12 months only 10%, respectively. Within the

EAST—AFNET 4 trial, a total of 340/1395 (24%) patients randomized to early rhythm control therapy underwent AF [ablation](#). There was no difference in outcomes in patients who underwent AF ablation compared to those who did not undergo AF ablation.

Professor Eckardt summarizes the findings: "Successful rhythm control therapy, estimated by the presence of sinus rhythm at 12 months after randomization, mediates most of the reduction in cardiovascular outcomes achieved by early rhythm control in the EAST—AFNET 4 trial. Based on these results, clinicians implementing early rhythm control should aim for early and sustained restoration of sinus rhythm in patients with recently diagnosed AF and cardiovascular comorbidities. Further population-based investigations and clinical trials of AF management strategies may help to clarify the role of AF ablation and antiarrhythmic drug therapy for outcome reduction in patients with recently diagnosed AF and comorbidities."

Since the publication of the main study result in 2020, different subgroup analyses of the EAST—AFNET 4 study data have been performed. One described the different, variable treatment patterns of [antiarrhythmic drugs](#) and AF ablation used in the trial, applied within guideline recommendations. Other subgroup analyses demonstrated the prognostic benefit of early rhythm control in patients with AF and [heart failure](#), in patients with asymptomatic AF, in patients with different AF patterns, and in patients with high comorbidity burden.

The research was published in *European Heart Journal*.

More information: L Eckardt et al, Attaining sinus rhythm mediates improved outcome with early rhythm control therapy of atrial fibrillation: the EAST—AFNET 4 trial, *European Heart Journal* (2022). [DOI: 10.1093/eurheartj/ehac471](https://doi.org/10.1093/eurheartj/ehac471)

Provided by Kompetenznetz Vorhofflimmern e.V. (AFNET)

Citation: Attaining sinus rhythm mediates improved outcomes with early rhythm control therapy of atrial fibrillation (2022, August 29) retrieved 11 May 2023 from <https://medicalxpress.com/news/2022-08-sinus-rhythm-outcomes-early-therapy.html>

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