



presents

EAST-AFNET 4: RHYTHM CONTROL VS RATE CONTROL



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QUESTION



Is a rhythm control strategy superior to rate control in patients with recently-diagnosed atrial fibrillation?

BACKGROUND

- Rhythm control *has not* shown superiority over rate control in reducing mortality or cardiovascular events in atrial fibrillation patients with antiarrhythmic drugs (**AFFIRM, RACE**).
- Neither of these older randomized trials included catheter ablation in the rhythm control arm.
- Previous trials have included patients with established AF, who were minimally symptomatic.
- **CABANA-AF** showed no difference in rates of stroke, cardiac hospitalization, or death when comparing ablation to medical therapy in patients with at least one long-standing AF episode.

DESIGN

- n= 2789
- 135 centres from 11 European countries

QUALITY PARAMETERS

- ✓ Randomized
- ✓ Assignment concealment
- ✗ Patients and clinicians unblinded, outcome assessors blinded
- ✓ Intention-to-treat analysis
- ✗ Lost to follow-up: 7.5% overall



Early Rhythm Control Arm

- Includes anti-arrhythmic drugs and ablation.
- Patients submitted ECGs twice a week and when symptomatic, with in-person visits to escalate therapy as indicated.

At trial start: **87%** of patients started with an anti-arrhythmic drug (**43%** with a Class IC agent). **8%** had catheter ablation.



By year 2, **19%** had catheter ablation, and **46.1%** were still taking antiarrhythmic drugs.

Usual Care Arm

- Rate control therapy without rhythm control.
- **85%** were on beta-blockers.

By year 2, **7%** had catheter ablation, and **7.6%** were taking antiarrhythmic drugs.

INCLUSION CRITERIA

- AF diagnosis within 1 year of enrollment AND
1. ≥ 75 yo OR
 2. previous TIA/stroke OR
 3. met two of the following criteria: >65 yo, female, HF, HTN, DM, severe CAD, CKD, LVH (diastolic septal wall >15 mm wide), stable HF (NYHA II or LVEF $<50\%$), PAD

EXCLUSION CRITERIA

- Previous therapy failure on amiodarone
- Patients not suitable for rhythm control
- Prior AF ablation or surgical therapy
- Prosthetic mitral valve, severe mitral valve stenosis

EAST-AFNET (2020) VS AFFIRM (2002)

- EAST-AFNET's **population** only included patients with a short history of AF (median of 36 days since diagnosis), many were asymptomatic (30%). In AFFIRM, while there was no data on duration of AF since diagnosis, 64.5% of patients enrolled were experiencing a recurrent episode of AF.
- Since AFFIRM was conducted, **standard of care** for AF has changed drastically. EAST-AFNET did not routinely withdraw anticoagulation once rhythm controlled (**88%** in early rhythm, **91%** in usual care at 2 year follow-up), while patients with rhythm control in AFFIRM who achieved normal sinus rhythm could have their anticoagulation stopped, which likely increased risk of stroke/death ($\sim 70\%$ on warfarin in rhythm control vs $>85\%$ on warfarin in rate control).



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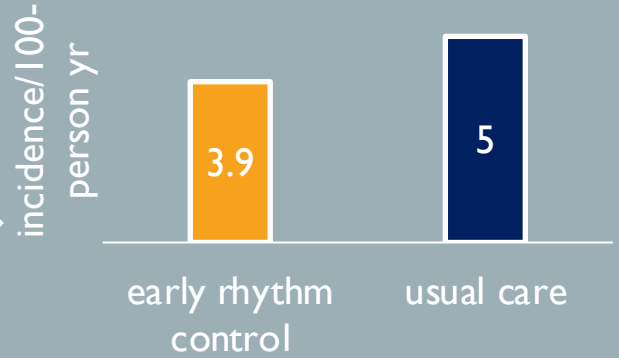


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HR: 0.79 (0.66-0.94)

PRIMARY OUTCOME:

Composite of death from CV causes, stroke (ischemic/hemorrhagic), hospitalization with worsening HF/ACS (time to event analysis)



Primary Outcomes	Incidence/100-person year	
	Early Rhythm	Usual Care
Death from CV causes	1.0	1.3
Stroke	0.6	0.9
Hospitalization with worsening of HF	2.1	2.6
Nights spent in hospital/year	0.8	1.0

Safety Outcomes	%	
	Early Rhythm	Usual Care
1° composite: stroke, death, serious AE related to rhythm control	16.6	16.0
Serious AE related to rhythm control therapy	4.9	1.4
Toxic effects of atrial fibrillation-related drug therapy	0.2	0
All-cause death	9.9	11.8

WHAT'S THE BEST RHYTHM CONTROL STRATEGY?

- Most patients in EAST-AFNET's early rhythm control arm were initiated on pharmacologic options: **36%** on flecainide, **20%** on amiodarone, **17%** on dronedarone, **7%** on propafenone, and **8%** on other anti-arrhythmic agents. However, no data is available on efficacy/safety outcomes of specific agents.
- EAST-AFNET has a considerable rate of AF ablation as well, with **8%** at enrollment and **20%** by 2 years.
- **Andrade et al.** conducted a meta-analysis of three recent RCTs comparing the use of cryoballoon ablation to antiarrhythmic drugs as first-line therapy of AF (Cryo-FIRST, EARLY-AF, STOP-AF First).
- Their findings showed that compared to antiarrhythmic drugs, cryoballoon ablation was associated with significant reductions in *atrial tachyarrhythmia recurrence* (**RR 0.61**, 95% CI 0.51-0.73, **NNT 6**), *health care use* (**RR 0.71**, 95% CI 0.56-0.90, **NNT 12**), and *hospitalization* (**RR 0.38**, 95% CI 0.23-0.63, **NNT 9**).
- Ablation was also associated with significant improvements in quality of life, at a similar rate of adverse events as antiarrhythmic drugs.

CAVEATS

- 5-year follow-up, stopped early due to efficacy in early rhythm control arm
- Open-label by necessity, single-blinded
- Compared two different strategies rather than individual medications or interventions; therefore, no comparisons can be made regarding the ideal components within a given randomized strategy in this trial

CONCLUSIONS

Early rhythm control reduced adverse cardiovascular events, including death, compared to usual care (rate-control therapy), in patients with recent AF and CV comorbidities.

GUIDELINE CHANGES:

The Canadian Cardiovascular Society 2020 guidelines suggest a rhythm control strategy be considered for most stable patients with recent-onset AF (weak recommendation; moderate-quality evidence).