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TOPIC COLLECTION: ATRIAL FIBRILLATION UPDATES

Letter from the Editor

Understanding and knowledge of atrial fibrillation (AF) treatment continues to expand in 2020.

The EAST-AFNET 4 trial, recently published in the *New England Journal of Medicine*, showed that an aggressive early approach to maintaining normal sinus rhythm in patients with new onset AF led to a reduction in the composite endpoint of cardiovascular death, stroke, and hospitalization with heart failure or acute coronary syndrome. The trial was terminated early because of the demonstrated benefits of an aggressive early rhythm control approach. Patients in the rhythm control group were treated predominantly with antiarrhythmic agents, including a mix of Class IC and III agents. At 1 year, 8% underwent AF ablation, and at 2 years, 20% had undergone AF ablation.

The benefits of ablating AF in heart failure patients was determined by Turagam and colleagues, who conducted a meta-analysis of the six randomized control trials of ablation in heart failure. While the results were primarily driven by the Castle-AF trial, all six trials pointed in the same direction for endpoints of mortality, hospitalizations, quality of life, 6-minute walk test, and left ventricular ejection fraction. Also recently published are January and colleagues' updates to the AHA/ACC AF guidelines. Among other important changes, female sex was downgraded as a risk factor, aspirin was no longer recommended, and direct acting oral anticoagulants were preferred over warfarin. Finally, a decision aid was developed and published online for anticoagulation of patients with AF. This online calculator, developed by Mayo Clinic researchers, is simple, straightforward, and easily understandable, with clear visuals portraying the risks and benefits of anticoagulation.

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ORIGINAL ARTICLE

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

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ABSTRACT

BACKGROUND

Despite improvements in the management of atrial fibrillation, patients with this condition remain at increased risk for cardiovascular complications. It is unclear whether early rhythm-control therapy can reduce this risk.

METHODS

In this international, investigator-initiated, parallel-group, open, blinded-outcome-assessment trial, we randomly assigned patients who had early atrial fibrillation (diagnosed ≤1 year before enrollment) and cardiovascular conditions to receive either early rhythm control or usual care. Early rhythm control included treatment with antiarrhythmic drugs or atrial fibrillation ablation after randomization. Usual care limited rhythm control to the management of atrial fibrillation–related symptoms. The first primary outcome was a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome; the second primary outcome was the number of nights spent in the hospital per year. The primary safety outcome was a composite of death, stroke, or serious adverse events related to rhythm-control therapy. Secondary outcomes, including symptoms and left ventricular function, were also evaluated.

RESULTS

In 135 centers, 2789 patients with early atrial fibrillation (median time since diagnosis, 36 days) underwent randomization. The trial was stopped for efficacy at the third interim analysis after a median of 5.1 years of follow-up per patient. A first-primary-outcome event occurred in 249 of the patients assigned to early rhythm control (3.9 per 100 person-years) and in 316 patients assigned to usual care (5.0 per 100 person-years) (hazard ratio, 0.79; 96% confidence interval, 0.66 to 0.94; P=0.005). The mean (±SD) number of nights spent in the hospital did not differ significantly between the groups (5.8±21.9 and 5.1±15.5 days per year, respectively; P=0.23). The percentage of patients with a primary safety outcome event did not differ significantly between the groups; serious adverse events related to rhythm-control therapy occurred in 4.9% of the patients assigned to early rhythm control and 1.4% of the patients assigned to usual care. Symptoms and left ventricular function at 2 years did not differ significantly between the groups.

CONCLUSIONS

Early rhythm-control therapy was associated with a lower risk of adverse cardiovascular outcomes than usual care among patients with early atrial fibrillation and cardiovascular conditions. (Funded by the German Ministry of Education and Research and others; EAST-AFNET 4 ISRCTN number, ISRCTN04708680; ClinicalTrials.gov number, NCT01288352; EudraCT number, 2010-021258-20.)

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*A complete list of the EAST-AFNET 4 investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Benefits of Ablating Atrial Fibrillation in Heart Failure Patients

Results of a meta-analysis of six randomized, controlled trials in patients with reduced left ventricular ejection fraction

Atrial fibrillation (AF) frequently accompanies heart failure, particularly with reduced ejection fraction (HFrEF). A rhythm control strategy theoretically offers the potential for clinical benefit, but antiarrhythmic agents have not been proven to improve outcomes. Catheter ablation of AF might provide clinical benefit without the toxicities of antiarrhythmic agents but might involve procedural risks. In the randomized, controlled CASTLE-AF study (*NEJM JW Cardiol* Apr 2018 and *N Engl J Med* 2018; 378:417), patients receiving ablation had reductions in mortality and admissions for heart failure. The current researchers conducted a meta-analysis of six randomized, controlled trials, including CASTLE-AF, of AF ablation in patients with HFrEF.

In the 775 patients, ablation compared with physician-directed medication (including rate-controlling agents or antiarrhythmic agents) was associated with lower rates of all-cause mortality (9.0% vs. 17.6%) and HF hospitalizations (16.4% vs. 27.6%). AF ablation was also beneficial in improving left ventricular ejection fraction, 6-minute walk distances, and quality of life. The two approaches had no significant differences in adverse events.

COMMENT

The CASTLE-AF trial, the largest of the six studies in the meta-analysis, has provoked much discussion, and the trial has both supporters and detractors. Still, other trials in the meta-analysis show benefits leaning in the same direction. This meta-analysis is a nice summation of the various trials, and the forest plots of the varied endpoints are informative. I expect that this meta-analysis — while not the last word in addressing AF in HFrEF patients — will move some detractors to support AF ablation. ***— Mark S. Link, MD***

Turagam MK et al. Catheter ablation of atrial fibrillation in patients with heart failure: A meta-analysis of randomized controlled trials.
Ann Intern Med *2019 Jan 1; 170:41.*
(https://doi.org/10.7326/M18-0992)

Update to the Atrial Fibrillation Guideline: A Focus on Anticoagulation Strategies

Changes in the guideline reflect the increased data on direct-acting oral anticoagulants.

Note to readers: The language in the third and fourth bullet points has been updated since the original online publication of the Guideline Watch.

Sponsoring Organizations: American College of Cardiology, American Heart Association, and Heart Rhythm Society (AHA/ACC/HRS)

Target Audience: General cardiologists and cardiac electrophysiologists

Background and Objective

The guideline task force has updated key aspects of the 2014 ACC/AHA/HRS atrial fibrillation (AF) guideline, especially with regards to new data on direct anticoagulants.

Key Points

- Female sex, if the only risk factor, does not confer a CHA_2DS_2-VASc score of 1. Female sex adds to the score only when another risk factor is present. Oral anticoagulants are recommended for patients with AF and elevated CHA_2DS_2-VASc scores — ≥2 in men and ≥3 in women.
- For patients with low CHA_2DS_2-VASc scores, aspirin is no longer recommended. Oral anticoagulants might be reasonable for men with CHA_2DS_2-VASc score of 1 and women with CHA_2DS_2-VASc score of 2.
- Direct-acting oral anticoagulants (DOACs) are preferred over warfarin, except in certain cases such as valvular heart disease.
- Valvular heart disease is now defined more narrowly as moderate-to-severe mitral stenosis or a mechanical heart valve. For patients with AF who have mechanical heart valves or moderate-to-severe mitral stenosis, warfarin, not DOACs, is recommended.
- In end-stage renal disease, apixaban is a reasonable alternative to warfarin.
- Percutaneous left atrial appendage (LAA) occlusion may be considered in patients with AF who have heightened risks for stroke and contraindications to long-term anticoagulation.
- In specific patients with symptomatic AF and heart failure with reduced ejection fraction (HFrEF), catheter ablation may be reasonable as it could lower mortality and HF hospitalizations.
- The update clarifies the use of anticoagulants in AF patients undergoing percutaneous coronary intervention (PCI) with stenting.
  - For triple therapy, choosing clopidogrel over prasugrel for the $P2Y_{12}$ inhibitor is reasonable.
  - The guideline strengthens its preference for dual therapy with warfarin and clopidogrel (i.e., "it is reasonable to choose" it) over triple therapy.
  - Dual therapy can involve rivaroxaban or dabigatran.

What's Changed

Important changes include the preference of DOACs to warfarin, the dropping of female sex as a risk factor in CHA_2DS_2-VASc scores, clarifications to triple therapy in patients undergoing PCI, and recommendations for LAA occlusion devices and catheter ablation in patients with HFrEF.

COMMENT

Several randomized, controlled trials published since the 2014 guidelines serve as the basis for this important update, which primarily changes recommendations regarding DOACs. These changes will potentially affect many of our patients, and our shared-decision discussions will be informed by these modified recommendations. ***— Mark S. Link, MD***

January CT et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. **Circulation** *2019 Jan 28; [e-pub]. (https://doi.org/10.1161/CIR.0000000000000665)*

"Anticoagulation Choice Decision Aid" for Patients with Atrial Fibrillation

A shared decision-making tool improved some quality measures.

The effectiveness of shared decision-making (SDM) for patients with atrial fibrillation (AF) who are at high risk for stroke and who are considering anticoagulation therapy is unclear. An Anticoagulation Choice Decision Aid tool is available that is designed to facilitate SDM for such patients. In this randomized trial, researchers assessed various measures of this tool's effectiveness.

Study participants were 244 clinicians plus 922 adult patients (mean age, 71) with nonvalvular AF who were at high risk for thromboembolic events (CHA_2DS_2-VASc score ≥1 for men or ≥2 for women) and who were starting or reviewing anticoagulant therapy. Participants were randomized to usual care or to usual care plus the SDM tool.

A significantly higher proportion of clinicians were satisfied after SDM encounters than after usual-care encounters (88% vs. 62%). Clinicians' involvement of patients in decision-making was significantly greater in the intervention arm than in the usual-care arm (adjusted mean between-arm difference, 4.2 points [score range, 0–100]). Researchers found no differences in treatment decisions or encounter duration (≈32 minutes) between groups.

COMMENT

Although this tool didn't affect ultimate treatment decisions, it did improve SDM quality and clinician satisfaction without prolonging encounters. In my view, those outcomes alone justify the use of this tool for patients with atrial fibrillation who are weighing benefits and harms of anticoagulation.

— Paul S. Mueller, MD, MPH, FACP

Kunneman M et al. Assessment of shared decision-making for stroke prevention in patients with atrial fibrillation: A randomized clinical trial. **JAMA Intern Med** *2020 Jul 20; [e-pub]. (https://doi.org/10.1001/jamainternmed.2020.2908)*