Best of the HRS Scientific Sessions 2008

Highlights From the Heart Rhythm Society Scientific Sessions, May 14-17, 2008, San Francisco, CA

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The Heart Rhythm Society (HRS) meeting was held in San Francisco on May 14-17, 2008. A wide spectrum of presentations, abstracts, and clinical trials were presented covering the entire field of electrophysiology. We have provided this review of the HRS 2008 meeting to present some of the highlights that we believe may have direct impact on clinical cardiology practice.

The ATHENA Trial

The Effects of Dronedarone on Cardiovascular Outcomes in High-Risk Patients With Atrial Fibrillation or Atrial Flutter (ATHENA) was a placebo-controlled, double-blind, parallel-arm trial.[1] The primary endpoint was the efficacy of dronedarone 400 mg bid compared with placebo for the prevention of cardiovascular hospitalization or death from any cause in patients with atrial fibrillation (AF) or atrial flutter. Dronedarone and amiodarone have similar molecular structures, but dronedarone, a benzofuran analog of amiodarone, lacks the iodine component that is largely responsible for amiodarone's multiple end-organ toxicities, which hit the lungs, thyroid, eyes, and other organs.

A total of 4628 patients were randomized from more than 550 sites in 37 countries. Compared with placebo, patients receiving dronedarone had a 24% reduction in cardiovascular hospitalizations or death over 21 months of follow-up ($P < .001$) (Table 1). There was also a significant reduction of 30% in the risk of death due to cardiovascular causes compared with placebo ($P = .03$), which was driven primarily by a significant 45% reduction in the incidence of death due to arrhythmias ($P = .01$). There was no significant difference in overall mortality.

In terms of safety, the rate of drug discontinuation was similar between the 2 cohorts, with adverse event rates of 72% for dronedarone and 69% for placebo. (This difference was not significant.) There was a greater incidence of increased serum creatinine with dronedarone (4.7%) compared with placebo (1%). Dronedarone increases serum creatinine by inhibiting tubular excretion of creatinine without adversely affecting renal function. Investigators were encouraged to continue angiotensin-converting enzyme inhibitor therapy in the face of moderate rises in creatinine. Rates of side effects, such as thyroid dysfunction and respiratory complications, were no different between dronedarone

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Table 1
Dronedarone Versus Placebo in the ATHENA Trial

Endpoint*	Hazard Ratio	*P* Value
Time to first CV hospitalization or death from any cause	0.76	< .001
All-cause mortality	0.84	NS
CV mortality	0.71	.034
CV hospitalization	0.75	< .001
Death from cardiac arrhythmia	0.55	.01
Cardiac nonarrhythmic death	0.95	NS

*The mean follow-up was 21 months.
ATHENA, Effects of Dronedarone on Cardiovascular Outcomes in High-Risk Patients With Atrial Fibrillation or Atrial Flutter; CV, cardiovascular; NS, not significant.
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and placebo. Because of its enhanced safety profile compared with amiodarone, dronedarone may end up being a much better option in patients requiring long-term antiarrhythmic treatment, such as those with AF.

The HERS Trial: Statins and Atrial Fibrillation

In the Heart and Estrogen-Progestin Replacement Study (HERS), the prevalence and incidence of AF was determined in 2673 women with coronary disease at initiation and again at an average of 4.1 years of follow-up.[2]

Women with AF were less likely to be taking a statin as compared with women without AF (22% vs 37%). Among patients without AF at baseline, those taking statins were 55% less likely than those not taking statins to develop AF during the study, after adjusting for race, age, and risk factors such as history of revascularization/myocardial infarction and heart failure (hazard ratio, 0.45; $P = .004$). These results may be an added inducement for women with known coronary artery disease to be compliant with their prescribed statins.

The INCREMENTAL Study

The Randomized Comparison of Targeted Versus Usual Left Ventricular Lead Placement (INCREMENTAL) study evaluated the impact of a targeted lead placement strategy proximate to the site of the latest mechanical activation based on tissue Doppler imaging versus usual lead placement in patients undergoing cardiac resynchronization therapy (CRT).[3] Patients were stratified by the etiology of their cardiomyopathy: ischemic versus nonischemic. The primary endpoint of this study was defined as survival for at least 6 months, at least a 10% reduction in left ventricular (LV) end systolic volume, and improvement in heart failure symptoms of 1 class.

Successful LV lead placement in the area of the target site was achieved in 80% of the targeted placement cohort versus 44% of the usual lead placement cohort. CRT response was related to the proximity of the LV lead to the target site ($P < .01$). A trend towards an improved rate of CRT response was observed in the targeted group ($P = .07$). Although response rates did not differ in patients with nonischemic cardiomyopathies, those with ischemic cardiomyopathies had a significantly higher CRT response rate when in the targeted cohort (69%) than in the usual placement cohort (37%) ($P < .017$).

The use of tissue Doppler imaging to help identify optimal LV lead placement may be more important in patients with ischemic cardiomyopathy in order to avoid placement in infracted/nonviable zones that would not respond to pacing. In patients with nonischemic cardiomyopathy, this approach may not be as relevant because wider zones of pacer lead placement still have a positive impact on resynchronization and clinical response.

Omega-3 Fatty Acids and Atrial Fibrillation

Evidence from several studies has suggested that docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) in the form of fish or fish oil supplements decreases triglycerides, lowers blood pressure slightly, and reduces the risk of death, myocardial infarction, ventricular arrhythmias, and strokes in people with known heart disease. This study examined a total of 46,704 participants from the Women's Health Initiative (WHI), after excluding women with AF at baseline or women in the diet modification interventional arm, to determine if there was a relationship between omega-3 fatty acid intake and AF.[4] The total amount of omega-3 intake was estimated using a Food Frequency Questionnaire.

There did not seem to be an association between dietary omega-3 fatty acid intake and the incidence of AF, even when taking into account baseline risk factors or the amount of omega-3 intake.

The 5A Study

There is a known occurrence of AF during the acute phase following AF

Table 2
Recommended Empiric Antiarrhythmic Therapy in the 5A Trial

Clinical Setting	Agent (minimum dosage)
Normal LV function, no obstructive CAD	Propafenone (450 mg/d) or flecainide (200 mg/d)
Normal LV function, with CAD	Sotalol (160 mg/d)
Abnormal LV function	Sotalol (160 mg/d) or dofetilide (500 μg/bid)*

*Adjusted according to creatinine clearance and corrected QT interval.
5A, Antiarrhythmics After Ablation of Atrial Fibrillation; LV, left ventricular; CAD, coronary artery disease.
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ablation. Whether patients who have undergone ablation would benefit from the addition of antiarrhythmic therapy or are at proarrhythmic risk during the periprocedure period was examined in the Antiarrhythmics After Ablation of Atrial Fibrillation (5A) study.[5]

The 5A study randomized adults undergoing ablation by pulmonary-vein isolation for paroxysmal AF who had previously demonstrated tolerance to antiarrhythmic therapy and had not been on amiodarone for at least 3 months. Patients with paroxysmal AF undergoing ablation were randomized to receive either a class I or III antiarrhythmic drug (AAD) (n = 49) or no AAD (n = 52) beginning the evening of the ablation and continued for a 6-week period. Antiarrhythmics were given in an unblinded fashion and consisted of class 1C agents in patients without structural heart disease or of dofetilide or sotalol in those with structural heart disease (Table 2). In the no-AAD group, drugs that blocked the atrioventricular node could be prescribed. All patients wore a rhythm monitor with transmission on a routine daily basis, in addition to symptomatic transmission for 4 weeks following the ablation.

Patients were evaluated at 6 weeks. The primary endpoint of the study was a composite of intolerance to AAD requiring drug cessation and clinically significant atrial arrhythmias, defined as: 1) lasting longer than 24 hours, 2) requiring AAD initiation or change, and/or 3) requiring hospitalization or cardioversion. The authors found that the use of class I or III antiarrhythmic drugs seemed to reduce the incidence of clinically significant AF during the 6-week period following ablation. How this result translates into a long-term effect is beyond the scope of this trial but worthy of study.

Antithrombotic Therapies in Atrial Fibrillation Patients at Risk of Stroke

The $CHADS_2$ Score provides an estimate of stroke risk in patients with nonrheumatic AF by assigning points to the following stroke risk factors: diabetes, hypertension, congestive heart failure, age (> 75 years), and prior cerebral ischemia. In this study, researchers retrospectively reviewed the records of 1502 patients and identified 422 patients with a $CHADS_2$ score of 1, which designates intermediate risk of a cerebral ischemic event.[6] Patients with $CHADS_2$ scores of 1 were studied because there are no guidelines recommending a specific stroke prophylaxis approach

Main Points

- In patients who require long-term antiarrhythmic treatment, dronedarone may prove to be a better option than amiodarone due to its enhanced safety profile.
- After 4 years of follow-up, women with coronary artery disease who took statins were 55% less likely to develop atrial fibrillation than those not taking statins.
- The use of tissue Doppler imaging to help identify optimal left ventricular lead placement may be more important in patients with ischemic cardiomyopathy than with nonischemic cardiomyopathy in order to avoid placement in infracted/nonviable zones that would not respond to pacing.
- In patients who have undergone ablation, the use of class I or III antiarrhythmic drugs seemed to reduce the incidence of clinically significant atrial fibrillation during the 6-week period following the procedure.
- In patients with nonrheumatic atrial fibrillation who were at intermediate risk of a cerebral ischemic event, those taking warfarin had fewer ischemic stroke events and lower all-cause mortality than those taking antiplatelet therapy.

in this group. Of the patients identified, 143 were taking warfarin, 169 received antiplatelet agents, and 110 were taking neither. The primary endpoint of this analysis was ischemic stroke.

During an average follow-up period of 18 months, patients taking warfarin had fewer ischemic stroke events than patients taking antiplatelet therapy (5.4% vs 11.8%; $P < .05$). All-cause mortality was also lower in the warfarin group compared with the antiplatelet group (0.6% vs 3.3%; $P = .08$). There was no significant increase in intracranial hemorrhage and major bleeding in the warfarin group. This analysis, although retrospective in nature, does support consideration of anticoagulation with warfarin over antiplatelet therapy in patients at intermediate risk of stroke. ■

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