Atrial Fibrillation in Patients with Congestive Heart Failure

BRADLEY P. KNIGHT

From the Department of Internal Medicine, Division of Cardiology, University of Michigan Medical Center, Ann Arbor, Michigan

KNIGHT, B.P.: Atrial Fibrillation in Patients with Congestive Heart Failure. *CHF and AF are common problems that are frequently encountered together. These two disease states interact in a way that can result in a viscous cycle. This brief review will attempt to address the interaction between AF and CHF, atrial pathology and abnormal electrophysiology, clinical consequences, prognostic importance, and therapy. (PACE 2003; 26[Pt. II]:1620–1623)*

Introduction

The numbers of patients who suffer from congestive heart failure (CHF) and atrial fibrillation (AF) are increasing. Recently, there have been excellent reviews on the problem of AF in patients with CHF,[1,2] and the importance of the problem is reflected in the steadily rising number of publications on the topic. Based on a literature search using MEDLINE, the number of publications regarding AF and CHF increased over the past decade from nine publications during 1991 to 51 publications during 2000 (Fig. 1).

AF promotes CHF and vice-versa. This feedback loop can result in a downward spiral in many patients (Fig. 2), that can be interrupted by attacking each problem. This brief review will attempt to address the interaction between AF and CHF, atrial pathology and abnormal electrophysiology, clinical consequences, prognostic importance, and therapy.

Atrial Pathology and Abnormal Electrophysiology

CHF results in atrial stretch, atrial fibrosis and hypertrophy, sympathetic activation, and abnormal electrophysiology, all of which promote the development of atrial arrhythmias. There has been much emphasis on the importance of the electrical remodeling that occurs during AF and that promotes recurrent episodes of AF.[3] However, electrical remodeling may have less of a role in patients with CHF. CHF causes a reduction in Ikr and Ica, which results in an increase in refractoriness and appears to attenuate the reversible shortening of atrial refratoriness that occurs during atrial tachycardias.[4]

Two additional studies have highlighted the role of the atrial substrate in the promotion of AF in the setting of heart failure. Everett et al.[5] demonstrated, in a canine mitral regurgitation model, that the histological abnormalities that occur during chronic AF persist following cardioversion, and that the vulnerability to AF following cardioversion was more dependent on persistent structural changes than on the reversible abnormal electrophysiology. Yamada et al.[6] showed that abnormal atrial conduction, manifest as an abnormal P wave signal-averaged electrocardiogram, was a strong independent predictor of AF among patients with CHF (hazard ratio 19).

Clinical Consequences

AF acutely aggravates ventricular performance by causing loss of atrial transport. Cardiac output is often diminished further by the tachycardia that is commonly associated with AF. In addition, the irregularity of the ventricular rhythm decreases the cardiac output, independent of the ventricular rate by approximately 15%.[7]

AF can also diminish cardiac performance over time, by creating a tachycardia mediated cardiomyopathy.[8] AF with a rapid ventricular response can be the sole etiology of a nonischemic cardiomyopathy, or it can cause progressive ventricular dysfunction in a patient with a preexisting cardiomyopathy from any cause. Some studies have shown that patients with AF have a more rapid deterioration in maximum oxygen consumption over time, compared to patients with sinus rhythm. These findings argue for a closer follow-up of these patients.

Prognostic Importance of AF

Although findings regarding the effect of AF on mortality among heart failure patients have been conflicting, it is likely that the effect is negative. A study of 268 ambulatory patients referred for evaluation of severe heart failure found that AF was a univariate predictor of event-free survival.[9] Although AF was not predictive after multivariate analysis, the sample size was small and the prevalence of AF was not reported. The Studies

Address for reprints: Bradley P. Knight, M.D., University of Michigan Health System, 1500 East Medical Center Dr./B1F245, Ann Arbor, MI 48109-0022. Fax: (734) 936-7026; e-mail: bpk@umich.edu

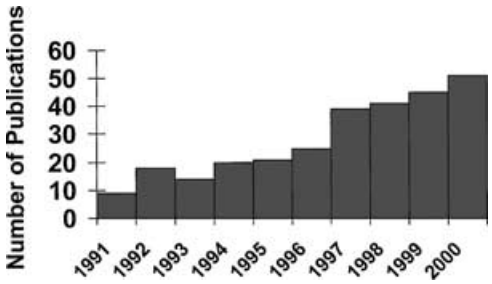

Figure 1. *The number of publications per year on atrial fibrillation and congestive heart failure over the past decade.*

of Left Ventricular Dysfunction (SOLVD) trial found that AF was associated with an increase in all-cause mortality (relative risk 1.34), and progressive pump failure death (relative risk 1.42).[10]

In the AMIOVIRT trial, which compared amiodarone to defibrillator implantation among patients with a nonischemic dilated cardiomyopathy, left ventricular ejection fraction <0.40, and asymptomatic nonsustained ventricular tachycardia, AF was an independent predictor of death due to CHF with a relative risk of 4.0.[11]

Treatment

General Considerations

The three cornerstones of therapy that apply to AF in general also apply to patients who have both AF and CHF: prevention of thromboembolism, ventricular rate control, and maintenance of sinus rhythm. CHF increases the likelihood of stroke during AF, with a relative risk of approximately 1.4.[12] Therefore, in the absence of a strong contraindication, carefully monitored treatment with warfarin is mandatory for patients with both AF and CHF.

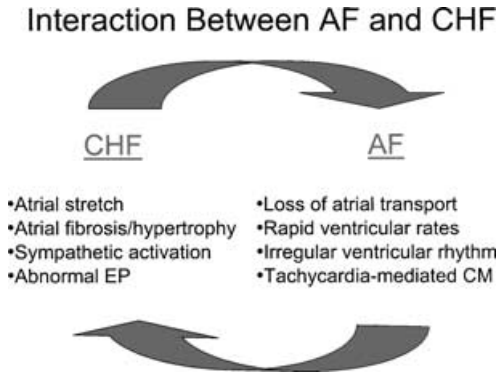

Figure 2. *Interaction between atrial fibrillation and congestive heart failure.*

The more challenging therapeutic dilemma involves the issue of rate control versus rhythm control. Patients with CHF are typically the patients who are most likely to benefit from restoration of atrioventricular synchrony, and yet can be the most difficult to keep in sinus rhythm. Two recent studies, Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) and Rate Control versus Electrical Cardioversion (RACE), found that the approach of rate control is comparable to the approach of maintaining sinus rhythm in patients with AF.[13] However, it is not clear how these findings apply to patients with symptomatic heart failure. A new study is underway that plans to compare rhythm control to rate control, exclusively among patients with CHF.[1] In the meantime, management of patients must be individualized, taking into account the duration of AF, results of prior attempts to restore sinus rhythm, likelihood of maintaining sinus rhythm, ventricular rate, risk and inconvenience of antiarrhythmic therapy, and degree of symptoms.

It is important to appreciate the benefits of standard heart failure therapy in the management of AF. Digoxin, β-blockers, and angiotensin converting enzyme (ACE) inhibitors are components of the current optimal pharmacologic therapy for heart failure. Digoxin is useful in controlling the resting ventricular rate during AF, and appears to have a neutral effect on mortality in heart failure.[14] Carvedilol provides ventricular rate control at rest and during exercise and has been shown to improve exercise duration in patients with idiopathic dilated cardiomyopathy and AF.[15] Metoprolol may prevent recurrent AF after cardioversion.[16] Although, there is currently no strong evidence that ACE inhibitors prevent AF in patients with CHF, animal studies have found that ACE inhibition attenuates the effects of pacing induced heart failure on atrial conduction, atrial fibrosis, and duration of AF.[17]

Antiarrhythmic Drug Therapy

Because the recurrence rate after electrical cardioversion of AF is high among patients with CHF, antiarrhythmic drugs are commonly prescribed in an attempt to maintain sinus rhythm. Because of proarrhythmia[18,19] and worsening of heart failure[20] with the use of sodium channel blockers in patients with ventricular dysfunction, practice patterns have shifted toward the use of potassium channel blockers.

Amiodarone appears to be the most useful antiarrhythmic drug to manage AF in patients with CHF, and can be safely initiated on an outpatient basis. The Survival Trial of Amiodarone Therapy in Congestive Heart Failure (STAT-CHF) trial randomized patients with heart failure to amiodarone

or placebo, and included 103 patients who were in AF. A significantly higher number of patients with AF who were randomized to amiodarone converted to sinus rhythm compared to placebo (31 vs 8%).[21] The patients who converted to sinus rhythm had improved survival compared to those who remained in AF. Although this finding is intriguing, it does not prove that restoration of sinus rhythm leads to an improvement in mortality in patients with heart failure, because patients in the study with more severe heart disease may have been less likely to convert to sinus rhythm.

It is tempting to consider d,l-sotalol as an alternative to amiodarone for the treatment of AF in patients with heart failure, given the low risk of organ toxicity compared to amiodarone, and the benefits of β-blockade in heart failure. However, there are little data to support the use of sotalol in the presence of symptomatic ventricular dysfunction, and there is evidence that the risk of proarrhythmia from sotalol due to torsades de pointes is increased in the presence of CHF.[22] Furthermore, a recent study found amiodarone to be twice as effective as sotalol in maintaining sinus rhythm.[23] This study, however, did not include patients with New York Heart Association (NYHA) class III or IV heart failure symptoms.

Dofetilide has been shown to be safe and effective in restoring sinus rhythm in patients with CHF. In the Danish Investigations of Arrhythmia and Mortality on Dofetilide (DIAMOND) substudy, dofetilide was associated with a higher AF conversion rate compared to placebo (59 vs 34%).[24] However, the use of dofetilide is problematic because it must be initiated in the hospital, requires careful monitoring of the QT interval to reduce the risk of torsades de pointes, and, in the United States, can only be prescribed by an approved physician.

Nonpharmacologic Therapy

Several nonpharmacologic therapies are available for the management of AF in patients with CHF. For patients in whom the ventricular rate cannot be controlled and sinus rhythm cannot be maintained, catheter ablation or modification of the atrioventricular junction has been shown to improve symptoms, and often improves ventricular function.[25] The advantages of atrioventricular node modification, compared to complete ablation, include cost savings,[26] minimization of pacemaker dependency, and avoidance of the adverse hemodynamic effects associated with right ventricular pacing. However, complete ablation and pacemaker implantation is more commonly performed, because it is more definitive and eliminates the irregularity of the ventricular rhythm. More work is need to develop techniques, like His-bundle pacing[27] and electrical vagal stimulation that control the ventricular rate and preserve normal His-Purkinje activation.

Nonpharmacologic options for rhythm control include catheter ablation, the surgical maze procedure, an implantable atrial defibrillator, and multisite pacing. Much of the experience with segmental pulmonary vein ablation has been with patients who have minimal structural heart disease.[28] It is possible that the pulmonary veins are less important in the genesis of AF in patients with CHF. In addition, segmental pulmonary vein isolation appears to be less useful in the presence of persistent compared to paroxysmal AF.[28] Other atrial ablation options like circumferential pulmonary vein isolation may be more useful for patients with structural heart disease and persistent AF.[29]

Conclusion

CHF and AF interact to create a downward spiral that adversely affects functional capacity and longevity. Until trials that compare rate control to rhythm control among patients with CHF have been completed, treatment decisions must be individualized. To be effective, treatment aimed at maintaining sinus rhythm must address the abnormal atrial substrate associated with CHF, which appears to be an important factor in the development of AF in these patients.

Antiarrhythmic drugs to maintain sinus rhythm should be limited to amiodarone and dofetilide. Given the limitations of drug therapy in the treatment of AF in patients with CHF, nonpharmacologic therapies need to be explored further. Atrioventricular junction ablation can be useful for patients whose ventricular rate cannot be controlled. Better nonpharmacologic techniques are needed to maintain sinus rhythm and to control the ventricular rate during AF, while preserving normal ventricular activation.

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