

Advances in the management of atrial fibrillation in congestive heart failure

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Abstract

Atrial fibrillation, a common problem in patients with heart failure, is associated with increased mortality and morbidity. Pharmacological as well as invasive management and the endpoints of such management are complex. Recent randomized trials indicate that a rate-control strategy, along with anticoagulation treatment with warfarin, when appropriate, has a similar outcome in terms of mortality and morbidity as rhythm control, and could, therefore, be considered as the primary management strategy for atrial fibrillation in patients with heart failure.

Introduction and context

Atrial fibrillation and heart failure are emerging and co-existing cardiovascular disease epidemics of the new millennium [1]. Both affect each other and both are associated with substantial mortality and morbidity. Atrial fibrillation, present in 10-40% of patients with heart failure, is associated with adverse clinical consequences, including excess risk of death, hemodynamic decompensation, exacerbation of heart failure, impaired functional capacity, and risk of stroke [1-7]. The adverse impact of atrial fibrillation in heart failure has been attributed to the presence of irregular and/or excessive ventricular rates, lack of atrial contribution to ventricular filling, and the toxicity of therapies prescribed to control rate, to control rhythm, and to reduce the risk of stroke. In addition to anticoagulation, rate control [drugs or atrioventricular (AV) junctional ablation] is probably the only option for permanent atrial fibrillation, but the optimal strategy for managing paroxysmal and persistent atrial fibrillation in heart failure remains uncertain. Given adverse prognostic implications and postulated hemodynamic consequences, aggressive re-establishment and maintenance of sinus rhythm with antiarrhythmic drugs and/or ablation has been advocated, and frequently attempted, in the hope of achieving better outcomes [8]. On the other hand, interventions to

attempt to maintain sinus rhythm may be ineffective, temporary, and potentially toxic.

Recent advances

Available data show no benefit for a routine rhythm-control strategy for management of atrial fibrillation [9-11] but only a small minority of the patients enrolled had systolic dysfunction. A recent prospective, multicenter, randomized clinical trial, termed the Atrial Fibrillation and Congestive Heart Failure (AF-CHF) trial [12], confirms this same finding in the heart failure population. The AF-CHF trial randomized 1,376 patients with paroxysmal or persistent atrial fibrillation, a left ventricular ejection fraction < 35%, and New York Heart Association (NYHA) functional class III or IV heart failure, to a rate-control strategy (using beta-blockers and/or digoxin with AV junctional ablation if drugs were ineffective) or a rhythm-control approach (amiodarone along with electrical cardioversion as needed). The rhythm-control group was associated with a substantial increase in sinus rhythm but no obvious benefit was seen during the 37 ± 19-month follow-up. Death from cardiovascular causes, adjusted for baseline differences, was the same in both groups. Secondary outcomes, including death from any cause, stroke, and worsening

heart failure, were also similar in both groups. Hospitalizations were greater in the rhythm-control group.

It is unclear whether a better therapy to maintain sinus rhythm would have had a better outcome. Given the currently reported success rates of atrial fibrillation ablation, it is unlikely that ablation would be better than the rhythm-control strategy (that is, amiodarone) used in the AF-CHF trial.

In regard to pharmacologic therapy to maintain sinus rhythm, amiodarone appears to be the most potent [13]. Only amiodarone and dofetilide have been shown to have a neutral effect on survival when compared to placebo [4,14–17], but these drugs may have long-term toxicity. Dronedarone, a congener of amiodarone (with its multichannel-blocking abilities, but without its iodine-related moiety), seemed appealing in this regard.

The recently reported Anti-arrhythmic Trial with Dronedarone in Moderate to Severe Congestive Heart Failure Evaluating Morbidity Decrease (ANDROMEDA), compared dronedarone with placebo in atrial fibrillation patients who had heart failure and a left ventricular ejection fraction < 35% [18]. The study was terminated prematurely after enrolling 627 patients (310 taking dronedarone and 317 taking placebo) over a 7-month period (median follow-up of 2 months) as mortality was significantly increased in the dronedarone arm (8.1 versus 3.8% in the placebo arm). This excess mortality was predominantly due to deaths from worsening heart failure and was greatest in patients with the most severe left ventricular dysfunction. Treatment with dronedarone was the most powerful predictor of death after adjustment for other risk factors. This study dealt a blow at efforts to develop a safe and effective antiarrhythmic drug to use for atrial fibrillation in heart failure.

Although previous studies indicate that atrial fibrillation is independently associated with increased mortality in heart failure, in reality, atrial fibrillation may simply be a marker of poor prognosis, as these heart failure patients may be more ill. Thus, the rhythm by itself may not need treatment except to manage adverse consequences – that is, exacerbation of heart failure and risk of thromboembolism – in selected patients. Available evidence supports this thesis.

Adjunctive therapies, including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), statins, and omega-3 fatty acids, may also help prevent atrial fibrillation in heart failure patients. Modulation of the renin-angiotensin system by ACEIs has been shown to attenuate arrhythmogenic atrial

structural remodeling in experimental models of heart failure [19]. A meta-analysis of randomized clinical trials showed that use of both ACEIs and ARBs significantly reduced (relative risk reduction = 44%) the incidence of atrial fibrillation in patients with systolic heart failure [20]. Both statins and omega-3 fatty acids have been thought to have favorable effects on atrial structural remodeling in heart failure [21,22], but the exact mechanisms as well as the magnitude of their beneficial effects remain unclear.

Implications for clinical practice

It is time to rethink the widely held belief that restoration and maintenance of sinus rhythm using antiarrhythmics and serial electrical cardioversions benefits patients with systolic dysfunction and heart failure. A strategy aimed at sinus rhythm does not improve cardiovascular and all-cause mortality, risk of stroke, and worsening of heart failure [12]. Instead, it can result in repeated cardioversions, hospitalization from drug-related side effects, and even increased mortality, as shown with the use of dronedarone [18].

Whether invasive attempts at rhythm control, such as by ablation, will improve outcomes, remains to be seen. At present, rate control with appropriate anticoagulation should be considered as the primary strategy to manage atrial fibrillation in patients with heart failure. Beta-blockers with or without digoxin should be first-line rate-control agents but multiple drug combinations and even AV junctional ablation may be needed [23]. In regard to anticoagulation, no substitute exists for warfarin, although direct thrombin inhibitors are being tested [24]. Rhythm control should only be pursued in those highly symptomatic heart failure patients who have rapid uncontrolled atrial fibrillation that fails to respond to standard rate-control therapy and for selected patients who are shown to have worsening heart failure symptoms and/or poor quality of life attributable to atrial fibrillation, despite adequate rate control.

Abbreviations

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; AV, atrioventricular.

Competing interests

The authors declare that they have no competing interests.

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