ATRIAL FIBRILLATION AND HEART FAILURE: THE GROWING EPIDEMIC

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Atrial fibrillation (AF) and congestive heart failure (HF) are among the most common medical conditions and are associated with significant morbidity. These two conditions share similar risk factors, with each predisposing to the other, and frequently coexisting with additive adverse prognosis. AF is associated with both systolic HF (HFREF) and preserved/ diastolic HF (HFPEF). Much evidence has amassed regarding the relationships between these two disorders, which have emerged as major cardiovascular epidemics.

Epidemiology

AF is the most common arrhythmia seen in clinical practice with an overall prevalence of 1%. During the past two decades, hospital admissions for AF have increased by 66% for a number of reasons: aging of the population, rising prevalence of chronic heart disease and more frequent diagnosis as a result of increased monitoring. The lifetime risk for developing AF after the age of 40 is 26% for men and 23% for women. Moreover, the presence of AF confers a five-fold increased risk of stroke, a significantly increased risk of dementia and an almost two-fold increased risk of death. Furthermore, the incidence of AF is rising. It is estimated that the prevalence of AF will increase 2.5 fold by 2050 affecting nearly six million Americans. This upward trend is also consistently seen in Europe and elsewhere. This rising incidence of AF presents a significant healthcare burden as it accounts for an increasing proportion of hospitalizations. Health care costs are approximately five times greater for individuals with AF than for those without AF.

HF is a highly prevalent clinical syndrome with diverse etiologies and defined by characteristic symptoms and physical findings. HF which affects 2-3% of the population is a major cause of morbidity and mortality in most countries and is the leading cause of hospitalization in older patients. HF affects approximately 10% of men and 8% of women older than 60 years. Echocardiography is often performed in patients with HF to measure the left ventricular ejection fraction (EF) and to determine if systolic function is reduced (systolic HF – HFREF) or preserved/diastolic (preserved HF – HFPEF). Several epidemiologic studies have recently shown that more than 50% of older patients who present with symptoms of HF have preserved left ventricular systolic function (HFPEF). After the age of 40, the lifetime risk of developing HF is over 20%. HF portends a grave prognosis, with over half of individuals dying within five years of diagnosis; though with guideline driven therapy, survival for HFREF may be improving. HF accounts for a significant proportion of the healthcare budget, with an estimated cost of $34.8 billion in 2008 in the US.

Prevalence of af and hf

The association between AF and HF was appreciated almost a century ago. While the causative relationship between the two has not been fully determined, their co-existence may be explained in part by the presence of common risk factors viz. age, hypertension, diabetes, obesity, valvular, ischemic and non-ischemic structural heart disease. These factors are associated with myocardial cellular and extracellular alterations, electrophysiological and neurohormonal changes that combine to create an environment that predispose the heart to both HF and AF.

Among HF trials and registries, the prevalence of AF increases with the severity of HF from less than 5% in patients with functional Class NYHA I to nearly 50% in individuals

with functional Class NYHA IV. When AF occurs in the presence of HF, it is associated with worse prognosis. There is with no differences between the cause of HF (preserved or reduced ejection fraction) in developing AF.

AF may facilitate either the development or the progression of heart failure in several ways. An increased resting heart rate and the exaggerated heart rate response to exercise results in shorter diastolic filling time leading to reduced cardiac output. The irregularity of the ventricular response further affects this. The loss of effective atrial contraction also contributes. This loss of atrial contraction is even more important in those individuals who have diastolic dysfunction rather than those with systolic dysfunction.

Conversely, HF can increase the risk for the development of AF in several ways. An increased left ventricular filling pressure is a hallmark feature of the HF hemodynamic profile, which can be the result of either systolic (HFREF) or diastolic dysfunction (HFPEF). This elevation of the left ventricular filling pressure is transmitted to the left atrium which will lead to macroscopic and microscopic changes in this chamber facilitating AF. The atrial pressure may be further elevated with development of mitral regurgitation as the result of left ventricular remodeling.

Approximately 40% of individuals presenting with either HF or AF will develop clinical evidence of the other condition given time.

Prognosis of comorbid af and hf

While substantial morbidity and mortality is attributable to each of these individual conditions, the concomitant presence of AF and HF identifies individuals with a higher risk for death than with either condition alone. Of note, the development of the second is associated with a worse prognosis irrespective of which condition developed first. In the Framingham Heart Study, the presence of AF and HF was associated with twice the cardiovascular mortality compared to those with sinus rhythm. In a meta-analysis of mortality of randomized controlled trials of chronic HF, (with impaired or preserved left ventricular function) the mortality rate was worse in those individuals who had or developed AF compared to those who were in sinus rhythm. Thus, AF is a negative prognostic marker in patients with HF. Furthermore, several studies have found that new onset AF in patients with HF is associated with clinical deterioration and poor prognosis.

Therapeutic considerations: af and hf

The evidence on AF or HF treatments is generalizable to patients presenting with both conditions.

Thromboembolism prophylaxis

Thromboembolism prophylaxis, ventricular rate control and restoration of sinus rhythm when indicated are the goals of AF therapy. Clinical trials have consistently shown the benefits of anticoagulation in AF, which is a powerful risk factor for stroke and thromboembolism. The presence of AF in those with HF more than doubles the risk of stroke. Generally, warfarin is advisable for the prevention of events in patients with HF.

Heart failure therapy

Pharmacological agents are commonly used in the management of patients with systolic HF to both prevent AF and to reduce its recurrence in patients with concomitant AF and HF. This reinforces the shared mechanisms of these diseases. Both ACE inhibitors and angiotensin receptor blockers are effective in preventing the onset of AF. In a meta-analysis of randomized trials assessing the use of an angiotensin converting enzyme inhibitor or angiotensin receptor blocker, the relative risk of developing AF among patients treated with either medication was reduced by 28%. The greatest benefit was seen amongst those individuals who had severe left ventricular systolic dysfunction.

A systemic review of randomized placebo controlled trials in patients with HF demonstrated the addition of beta- blocker to the ACE inhibitor therapy was associated with a relative reduction of 27% in the incidence of AF over an average follow up of 1.4 years. With regards to outcome, however, beta-blockade therapy reduces mortality in HF patients with sinus rhythm, but not in those with AF.

Rate or rhythm control

Ventricular rate control in patients with AF and HF is recommended as first line therapy in the acute phase. AF with rapid ventricular response can lead to systolic HF whereas restoration of sinus rhythm or appropriate rate control can reverse this process. Controversy exists as to whether patients with HF respond better to rhythm restoration or ventricular rate control. Randomized controlled trials of patients with predominantly persistent and symptomatic AF have demonstrated no advantage of a rhythm control strategy comprised of antiarrhythmic drug therapy and electrical cardioversion over a rate control strategy ie. a ventricular rate control strategy is not inferior to rhythm control with regards to cardiovascular morbidity and mortality. Most of these studies, however, had only a small subset with chronic HF.

In the AF and chronic HF trial (AF-CHF), 1376 patients (mean EF<35%) were randomized to either a rate or rhythm control strategy. There was no difference observed between the two strategies during the follow up period (47 months) with regards to death from cardiovascular causes, symptoms, functional status, quality of life and left ventricular function. Thus it is appropriate to pursue ventricular rate control in most patients with both conditions, if symptoms related to AF are acceptable.

The optimal ventricular rate in patients with AF is 60-80 bpm at rest and 92-115 bpm during moderate exercise. Therefore, adequate rate control cannot be determined by resting ECGs alone and should be assessed with 24 hour Holter monitoring or by the evaluation of the chronotropic response during exercise. Beta-blockers should be the first choice for rate control in patients with chronic HF and AF. Beta-blockers are the most effective rate control agents and improve the long term survival in patients with systolic HF. In patients with HF and preserved left ventricular EF (HFPEF), non-dihydropyridine calcium-channel blockers (verapamil and diltiazem) could also be considered as they are effective rate controlling agents. This approach, however, should be avoided in patients who have very reduced left ventricular function (HFREF) because of the negative inotropic effect of these drugs.

Digoxin can be used for ventricular rate control in patients with AF and chronic systolic HF. Digoxin slows the ventricular rate at rest, but not during exercise in patients with AF. Combination with beta-blocker improves ventricular rate control, reduces symptoms and may improve left ventricular function.

Amiodarone is also effective for ventricular rate control of AF in patients with chronic HF. It is also the most efficacious anti-arrhythmic drug for maintain sinus rhythm. However, because of its potential non cardiac toxicity, it is considered a second line drug for rate control after beta-blockers and digoxin are proven ineffective.

Atrioventricular node ablation and pacemaker rhythm

In patients with symptomatic AF and rapid ventricular response that is refractory to pharmacological therapy, radiofrequency atrioventricular (AV) nodal ablation with implantation of a single right ventricular pacemaker lead for permanent pacing is effective for the achievement of rate control. This is referred to as the "ablate and pace" approach. Long term right ventricular pacing can be associated with progressive left ventricular dysfunction, whereas cardiac resynchronization therapy (CRT) with biventricular pacing results has improved both symptoms and mortality in patients (NYHA class III and IV) with systolic HF, who are in sinus rhythm and have a prolonged QRS duration. This approach

has been utilized in a few patients with HF and AF. The degree of improvement with CRT compared to those individuals who are in sinus rhythm is mild at best. The benefits of CRT in such patients were maximized when the biventricular pacing was induced nearly 100% of the time by AV node ablation.

Catheter ablation of af

The effect of maintaining sinus rhythm in patients with AF and HF requires further study. While trials have shown an equivalent outcome for pharmacological rhythm or rate control, the results may be due to the inability of the antiarrhythmic drugs to maintain sinus rhythm long term and to the adverse effects of the drugs themselves. One of the therapeutic options for AF is a curative catheter ablation. Catheter-based techniques to isolate the pulmonary veins from the surrounding left atrium has been shown to be effective in maintaining sinus rhythm long term without need for antiarrhythmic drugs. Subjects in these trials were typically without structural heart disease. Study of patients with AF and HF who have had such ablation has shown improvement in left ventricular EF. However, the number of such patients remains small. Moreover in many of these patients the problem was more related to ventricular rate control. Despite promising initials results, there are no data that demonstrate that catheter ablation improves survival in patients with HF. Definitive trials to assess outcomes are required before this becomes an accepted mode of therapy in these patients. Indeed, definitive trials assessing the effectiveness of AF ablation as compared with an ablate and ventricular pacing strategy are required.

Conclusion

AF and HF are amongst the most common cardiac disorders in our society. They share many risk factors, frequently co-exist and identify individuals who are at high risk of cardiovascular morbidity. AF occurs in more than half of the patients with HF, while HF occurs in more than one-third of those with AF. The pathological mechanisms of AF in patients with HF are complex and potentially involve elements of reentry, triggered activity and enhanced automaticity. It is unlikely that the treatment strategy aimed at any one of these mechanisms alone will restore sinus rhythm. Therapies directed towards HF may protect the heart from developing AF. A rhythm control strategy consisting of antiarrhythmic drugs and electrical cardioversion in stable patients with AF and HF adds no benefit to a rate control strategy. Newer therapies aimed at restoring sinus rhythm such as catheter ablation for AF and rate control therapies such as AV node ablation with biventricular pacing have emerged as potential alternatives to conventional rate and rhythm control strategies. Future trials are necessary to delineate the role of such therapies in the multitude of patients with these co-morbid conditions.

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