

Atrial Fibrillation in Patients with Ischemic and Non-Ischemic Left Ventricular Dysfunction

Robin Ducas¹ and Vignendra Ariyaratjah²

¹Section of Cardiology Dept. of Cardiac Sciences, University of Manitoba, Winnipeg, Manitoba, Canada, ²Division of Cardiology, The Brooklyn Hospital Center, Weill Cornell Medical College, Brooklyn, New York.

Abstract

Atrial fibrillation (AF) and left ventricular dysfunction (LVD) are increasingly common clinical problems, affecting millions of people worldwide. It is well established that the presence of AF portends a poor prognosis in the setting of both ischemic and non-ischemic LVD, and frequently results in worsening clinical status. Many clinical studies and trials have attempted to address treatment options and efficacy; despite this treatment for AF in LVD is still controversial.

Introduction

With the advent of new therapies for cardiovascular disease the epidemiology of cardiovascular complications has changed. The global population is living longer, resulting in myocardial dysfunction and arrhythmia becoming growing pandemics. Impairment of left ventricular function with or without an ischemic etiology is significantly associated with the development of atrial fibrillation (AF). This is exemplified by the increasing prevalence of AF with incremental progression of New York Heart Association (NYHA) class of heart failure (HF). Ultra-structural changes in atrial myocytes leads to atrial remodeling and result in the development of multiple re-entry circuits that culminate in AF. It is therefore thought that AF is an important clinical manifestation in the setting of left ventricular dysfunction (LVD) where it serves as a precipitant and harbinger of increased mor-

bidity and mortality.¹⁻³

Epidemiology of Atrial Fibrillation and Congestive Heart Failure

Congestive HF is increasingly common, with an estimated prevalence of 20 million people worldwide; similarly, AF has the highest prevalence of all sustained arrhythmias, affecting 1.5% of the population of the United States.⁴ AF may be found in isolation; however, more often than not, AF is both a marker and cause of LVD.² The prevalence of AF in LVD ranges from 5 to 65% and appears to depend on both the severity of HF and patient age.^{5,6} The incidence of AF complicating myocardial infarction is estimated to be between 2.3 and 21%.⁷ The close association between AF and myocardial infarction relates to shared common risk factors such as age, hypertension, diabetes, coronary artery disease and HF.⁸

Corresponding Address :Vignendra Ariyaratjah, MD, 845 Garden Street, #1, Hoboken, New Jersey.

Atrial Fibrillation in Left Ventricular Dysfunction

AF has a well-established association with systolic and diastolic LVD, both with and without acute myocardial infarction (Table 1). In systolic dysfunction the prevalence of AF increases almost linearly with rising NYHA class of HF, approaching 50% at class 4 (Figure 1).⁹ Diastolic dysfunction accounts for approximately one half of new cases of HF in large clinical studies and has a similar prevalence of associated AF as seen in systolic dysfunction.^{10,11} Several mechanisms have been proposed to help explain the high incidence and prevalence of AF in the setting of LVD: 1) risk factors such as increased age, hypertension, diabetes, and coronary artery disease are common to both conditions;⁶⁻⁸ 2) AF complicates upwards of 20% of cases of myocardial infarction and is most frequently found in patients with increased age, higher Killip class, HF symptoms, increased heart rate and documented LVD;⁷ 3) Congestive HF and LVD are strong independent risk factors for development of AF both inside and outside the setting of myocardial infarction.⁷

Pathophysiology of Atrial Fibrillation

The pathophysiology of AF complicating LVD is complex and relies on a combination of factors: resultant atrial stretch, neuro-hormonal changes, reactive atrial remodeling and impairment in diastolic filling, all feed back to compromise left ventricular function.¹² Special attention must be given to the finding of left atrial enlargement as it carries important clinical and prognostic implications.^{13,14} The left atrium may be seen as a morpho-physiologic barometer of diastolic dysfunction. As described by the myocardial ischemia cascade, diastolic dysfunction precedes that of systolic, often manifesting as left atrial electrical and/or mechanical dysfunction. Such findings help to explain the similar prevalence of AF in HF patients with both systolic and diastolic dysfunction. Furthermore, in LVD, with or without an associated MI, increased left atrial size is becoming a well-recognized predictor for the development of AF, HF and all cause mortality.^{13,14 15} Prospective data from the Framingham study has shown that a 5 mm incremental increase in left atrial anterior-posterior diameter confers a 39% increased risk for the devel-

Figure 1: Prevalence of Atrial Fibrillation in Studies Assessing Heart Failure

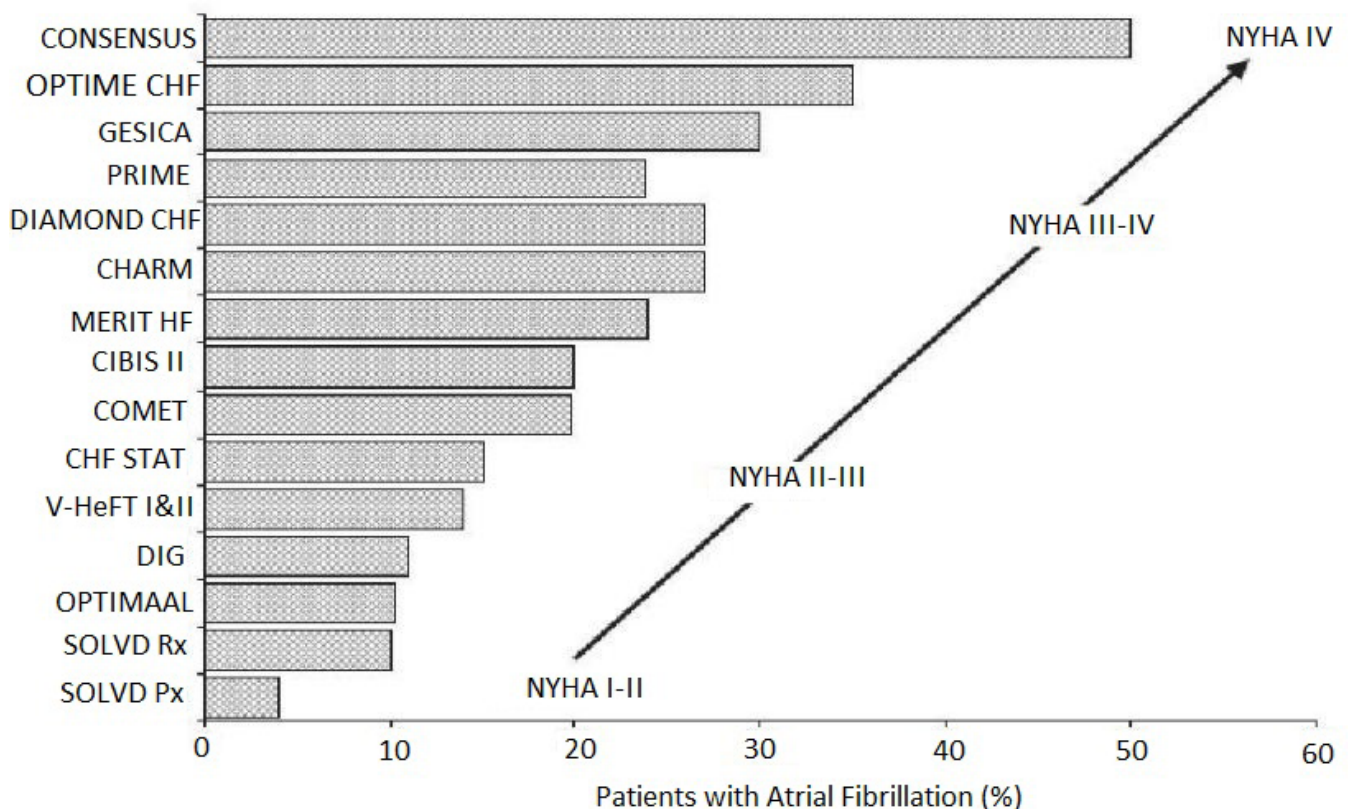


Table 1

Landmark Trials in Atrial Fibrillation and Left Ventricular Dysfunction

Study Name	Study Design	Population studied	Number of patients	Intervention	Duration	Outcome
SOLVD [22]	Single center retrospective analysis, non-prespecified variable	Patients with EF <35%, NYHA class I - III	374	Enalapril (5 to 20 mg/day) vs. Placebo	2.9 years	Decreased incidence of AF in enalapril group. Incidence of AF 5.4% in Enalapril vs. 24% in placebo group
Val-HeFT [23]	Retrospective analysis, non-prespecified variable	Patients with EF <40%, NYHA class II - IV	5010	Valsartan (160 mg BID) vs. Placebo	1.9 years	Decreased incidence of AF in valsartan group. Incidence 5.27% in valsartan group vs. 7.86% in placebo group
CHARM [25]	Prospective, randomized, double blinded Pre-specified end point of AF	Patients EF <40% or EF >40%, NYHA II - IV, no prior AF	6379	Candesartan (32 mg/day) vs. Placebo	3.2 years	Decreased incidence of AF in candesartan group. Incidence 5.6% in candesartan group vs. 6.7% in placebo group
TRACE [XX]	Retrospective analysis, non-prespecified variable	Post myocardial infarction, EF <36%, no prior AF	1577	Trandolapril (2 - 4 mg/day) vs. Placebo	2 to 4 years	Decreased incidence of AF in trandolapril group. Incidence 2.8% in trandolapril group vs. 5.3% in placebo group
CAPRI-CORN [27]	Retrospective analysis, non-prespecified variable	Post myocardial Infarction, EF <40%	1959	Carvedilol (6.25 - 25 mg BID) vs. Placebo	1.3 years	Decreased incidence of AF in carvedilol group. Incidence 2.3% in carvedilol group vs. 5.4% in placebo group
DIAMOND [7]	Retrospective analysis	NYHA III-IV or recent myocardial infarction, EF <35%	3028	Dofetilide (250 mcg-500 mcg BID) vs. Placebo	1 year	Decreased incidence of AF in dofetilide group. Probability of maintaining sinus rhythm in dofetilide group 79% vs. 42% in placebo group. No mortality benefit.
STAT-CHF [37]	Prospective, randomized, double blinded control trial	NYHA II - IV, EF <40%, patients with and without baseline AF	667 (564 no baseline AF, 103 with AF)	Amiodarone (target 300 mg QID) vs. Placebo	4.5 years	Of patients without baseline AF decreased incidence of AF in amiodarone group. Incidence 4.1% in amiodarone group vs. 8.4% in placebo group. Of patient with pre-existing AF increased conversion to sinus rhythm with amiodarone 31.3% vs. 7.7% placebo

opment of new AF.¹⁶ These findings are supported by the Cardiovascular Health Study which demonstrated subjects initially in sinus rhythm with a left atrial anterior-posterior diameter >50 mm had a four fold risk of developing new onset AF.¹⁷

In the setting of HF the underlying cause of AF has been attributed to stretching of the atria secondary to increased volume and pressure. This "atrial stretch" activates stretch-mediated channels, which enhance calcium binding to myo-filaments. This in turn induces calcium currents that produce delayed after-depolarizations and an increase in triggered activity, which act as a potent substrate for AF.¹⁸ Atrial stretch is also associated with slow-

ing of electrical conduction and increased refractoriness throughout the atria, which together may promote re-entry and propagation of AF. The presence of chronic atrial stretch, as seen in HF, results in calcium overloading of the atrial myocytes, further propagating abnormal electrical activity. Persistent AF results in atrial remodeling where ultra-structural changes in atrial myocytes occur via increased cell volume, misalignment and loss of contractile elements, gap-junction remodeling and electrophysiological changes at the cellular level. These AF-induced ultra-structural changes promote multiple re-entry circuits, continued AF-induced changes, and lead to impaired diastolic filling. Thus, atrial remodeling becomes

the structural substrate for cellular changes favoring the propagation of further AF.^{12,19}

Effect on Cardiac Function

AF can impair myocardial function through four primary mechanisms. Principally, heart rate response to AF at either extreme is the most clinically obvious complication seen in HF. Rapid ventricular response may compromise cardiac output by impairing diastolic filling time, while slow ventricular response may result in symptomatic bradycardia and syncope. Although the exact incidence is not known, prolonged and sustained elevation in heart rate can result in tachycardia-induced cardiomyopathy.²⁰ Secondly, the irregularity of the ventricular response, independent of rate, has been shown to decrease cardiac output while increasing both right atrial and pulmonary capillary wedge pressures.²⁰ Third, loss of the atrial systolic contribution to ventricular filling is associated with impaired diastolic filling, elevated atrial pressures and reduced stroke volume, which may lead to a 20% decrease in cardiac output.²¹ The loss of "atrial kick" directly impacts cardiac function and is most detrimental when complicating HF with LVD. The sufficiently delayed, mis-timed or total absence of left atrial contractions seen in AF ineffectively contributes to left ventricular ejection fraction and severely impairs left ventricular filling capacity. During AF, left ventricular filling is further impaired when the left atrial emptying is obstructed by an incompletely open or closed mitral valve. The fourth complication of AF and arguably the most deleterious is that the resultant reduced ventricular function can feedback into a maladaptive neuro-hormonal cascade. Excessive production of catecholamines, vasoconstrictors and adrenergic stimulants all result in further deleterious effects in the setting of LVD. Through electrical, mechanical and neuro-hormonal activation, AF creates the perfect storm of physiologic inefficiency.

Studies and Clinical Trials in Heart Failure

The Framingham Heart Study was a large prospective study and has contributed greatly to our understanding of the etiology of AF. During the 38-year study period 2090 men and 2641 women without a prior diagnosis of AF were followed;

there were 562 incident cases of AF. Independent risk factors for AF were found to be age, diabetes, hypertension, HF and valvular heart disease. This study clearly demonstrated the increasing incidence of AF with age, approximately doubling for every increment decade. The attributed risk of AF from HF was 10-12%, translating into an odds ratio of 4.5 in women and 5.9 in men of developing AF in the presence of HF. The attributed risk of AF from myocardial infarction was 1-5%.⁶ The Framingham study was the first large prospective investigation showing a clear association between HF and AF. The authors even speculate that the study may underestimate the risk of AF in HF as the impact of HF may be attenuated by its correlation with other variables/risk factors in their multivariate model.⁶ More recent data from the Framingham study reported by Wang et al. examined 1470 patients who developed AF, HF or both, over a 47-year period, and the association of these conditions with mortality. There were 708 patients with HF who subsequently developed AF (5.4% / year). Wang et al. found an increased mortality in individuals with AF or HF who subsequently developed the other disorder. Patients with pre-existing AF who developed HF had a hazard ratio for mortality of 2.7 in men and 3.7 in women; conversely, patients with pre-existing HF who developed AF had a hazard ratio for death of 1.6 for men and 2.1 for women.¹

Growing evidence from large clinical trials has shown that the presence of AF complicating LVD is associated with increased mortality. The SOLVD prevention and treatment trials examined 6517 patients with HF (ranging from asymptomatic to NYHA Class III) with ejection fraction < 35% over a 3-year follow up period. The results demonstrated that the presence of AF was a statistically significant, independent predictor of all cause mortality (35% vs. 23% in patients without AF).³ A retrospective analysis of the SOLVD trial composed of patients enrolled at the Montreal Heart Institute looked specifically at the effect of enalapril on the occurrence of new AF. This retrospective, single center sub-study examined 374 patients with left ventricular ejection fraction < 35%, and varying degrees of symptoms (NYHA I to III). Half of these patients were randomly assigned to receive enalapril and followed for approximately 3-years. This analysis demonstrated a decreased incidence of new AF in patients with systolic dysfunction chronically treated with enalapril (an angioten-

sin converting enzyme inhibitor [ACEi]). The reported incidence of AF was 5.4% in the ACEi arm and 24% in the placebo arm (RR 0.22, 95% CI 0.11-0.44).²¹ Interestingly, this study also demonstrated a greater risk reduction for development of AF in asymptomatic patients with impaired systolic function treated with enalapril compared to placebo (3.2% vs. 24.6% in the placebo arm).²¹

A sub-study of the Val-HeFT trial examined the incidence of AF complicating HF (EF <40%) in 5010 patients followed for more than 23 months. The use of valsartan resulted in a 37% relative risk reduction in AF. This trial also reported that the development of AF conferred a 40% increase in all-cause mortality and a 38% increase in the combined endpoint of death, sudden death with resuscitation, hospitalization due to HF, or administration of intravenous inotropic or vasodilator drugs for >4 hours without hospitalization.²²

The CHARM series of trials were the first to prospectively evaluate the effect of angiotensin II receptor blockers (ARBs) on cardiovascular outcomes in patients with HF and AF. In addition, the CHARM trials also included patients with preserved ejection fraction (>40%), giving further insight into the effects of AF in diastolic HF. The CHARM series were large, sequential prospective studies that included 7599 patients with symptomatic HF with both impaired and preserved ejection fraction. The baseline incidence of AF was approximately 18%. Over a 38 month follow-up period AF was found to be an independent predictor of all-cause mortality regardless of ejection fraction (37% vs. 28% for ejection fraction <40%, 24% vs. 14% for ejection fraction >40%).²³ A sub-study of CHARM followed 6379 patients without pre-existing AF for 38 months, and found the use of candesartan was protective against the development of new AF regardless of ejection fraction. This work demonstrated a 6.2% incidence of new AF in their patient population, with 5.6% in the candesartan group and 6.7% in the placebo group (p = 0.039).²⁴ Interestingly these results mirror that of the SOLVD data, indicating that blockade of angiotensin effect may help prevent AF clinically.

Mountantonakis et al reported their results from a large, multicenter study in the United States focusing on AF in acute HF hospitalizations. In this study 99 810 patients admitted to 255 hospitals with new or decompensated HF from January 1 2005 to December 21 2010 were followed. They found, in patients hospitalized with HF that AF was present in approximately 31% of cases, with 21% having a new diagnosis of AF. The finding of AF during admission for HF was independently associated with longer hospital stays, discharge to an institution other than home and increased in-hospital mortality.²⁵

Considerations in Acute Heart Failure

Acute decompensated HF creates an ideal environment for development of AF, via left atrial stretch from compromised diastolic function to increased sympathetic drive and effects from inotropic medications. Once established, AF may then go on to further undermine ventricular function. Precautions to prevent AF in these acute HF patients have not been explicitly studied; however, data from many clinical trials would favor the use of ACEi or ARB and beta-blockers in the more stable cohort. Judicious use of inotropic medications may limit the occurrence of supra-ventricular arrhythmias, but their avoidance is not always possible. Extrapolating data from physiologic studies, treatment of volume overload and minimizing atrial stretch in the congested state may improve diastolic pressures and decrease AF induction. Once diagnosed, divergent strategies may be implemented to manage AF, through either rate or rhythm control. AF may be treated through cardioversion or with anti-arrhythmics to try and maintain sinus rhythm and optimize ventricular function and cardiac output. Rate controlling medications such as beta-blockers and calcium channel blockers are not ideal in decompensated HF as they carry negative inotropic effects.

Studies and Clinical Trials in Myocardial Infarction

AF is commonly found in the peri-infarction period as well as in the post-discharge setting and was originally thought to complicate 2.3 to 21% of cases. A recent review by Schmitt et al. dem-

onstrates clearly that AF after myocardial infarction is associated with adverse clinical outcomes regardless of treatment for myocardial infarction.⁷ The CHARISMA study used implantable loop recorder monitoring over a 2 year period to evaluate the long-term development of AF post discharge in 271 patients with myocardial infarction and ejection fraction <40%. The study found an impressive 39.3% incidence of new AF, with the highest incidence in the first 2 months post infarction (16%). In patients who developed AF, over 50% had episodes lasting >30 seconds which were associated with a statistically significant increased risk of major cardiovascular events (re-infarction, stroke, hospitalization for HF and cardiac death). The high incidence of AF in the CHARISMA study is likely due to the identification of asymptomatic AF by implantable loop recorder that may have been missed by other studies, as more than 90% of patients who developed AF were entirely asymptomatic.⁸

The TRACE trial was the first large randomized clinical trial to demonstrate a decreased incidence of AF due to ACEi use in the post-myocardial infarction setting. The trial followed for 2-4 years 1746 patients post-myocardial infarction with left ventricular ejection fractions <40% and found a 55% relative risk reduction in the incidence of AF with the use of trandolapril compared to placebo (2.5% absolute risk reduction). The TRACE study also demonstrated a statistically non-significant trend towards increased mortality in patients who developed AF.²⁶

In the CAPRICORN trial the use of beta-blockers in addition to ACEi was shown to decrease the incidence of new onset AF after acute myocardial infarction. This study enrolled 1959 patients post myocardial infarction with LVD, with 98% already on ACEi therapy. A relative risk reduction of approximately 58% in AF with use of beta-blocker in addition to ACEi was reported, (absolute risk reduction 3.1).²⁷

Treatment

Prevention and Treatment of Underlying Disease

Several studies have suggested treatments that

may over the long term prevent AF in patients with HF and post-infarction. Neuro-hormonal activation and angiotensin II play a large role in the pathophysiology of atrial remodeling. Elevated angiotensin II levels in AF cause successive phosphorylation events that stimulate mitogen-activated protein kinases which in turn promote atrial remodeling through myocyte hypertrophy, fibroblast proliferation, increased intracellular collagen and cellular apoptosis.²⁸ ACEi, ARBs and beta-blockers have been found to reduce the incidence of new AF in large clinical trials; however, in the acute setting the occurrence of AF may not be preventable. Strategies to manage new onset acute AF once present include: cardioversion, anti-arrhythmic medications such as amiodarone, digoxin and beta-blockers. Despite the management of AF in the acute setting, its mere presence portends adverse clinical outcomes and patients with AF need to be followed and managed accordingly. Although most patients with myocardial infarction and HF have other indications for ACEi/ARB or beta-blocker use, these medications play more than one role in health maintenance and further disease progression prevention.

General Approach

There exists much debate in the optimal treatment of AF in the setting of LVD. Opposing schools of thought argue for and against rate and rhythm control. The concept of rhythm control seems attractive as it theoretically confers the advantages of atrial-ventricular synchrony, optimization of diastolic filling as well as physiologic rate control. Despite the physiologic superiority of sinus rhythm, its maintenance has not translated into improved outcomes in clinical trials. Several major clinical trials including HOT CAFÉ, STAF, PIAF, RACE, and AFFIRM were unable to show superiority of rhythm control.²⁹⁻³³ In general, trends toward increased survival and lower cardiovascular complications were seen in the rate control groups. The paucity of data supporting rhythm control for AF management has been scrutinized and generated much criticism related to trial design, inability to truly maintain sinus rhythm and inadequate anticoagulation for stroke prevention.³⁴ In a sub-group analysis of the AFFIRM trial the authors report benefit conferred by rhythm control in patients with HF and LVD. Interestingly,

patients with impaired ventricular systolic function had improved survival with re-establishment and maintenance of sinus rhythm. The retrospective “on treatment” analysis of the AFFIRM trial demonstrated a considerable reduction in the risk of death (hazard ratio 0.53) in the presence of sinus rhythm.³⁵ The more recent AF-CHF trial was a large multicenter randomized trial that compared rhythm to rate control in patients with left ventricular ejection fraction <35%, symptoms of HF and a history of AF. The trial enrolled 1376 patients and followed them over a 37-month period, with the primary outcome being death from a cardiovascular cause. The study found no significant difference in primary outcome in the rhythm vs. rate control strategy. The patients in the rhythm control group remained in sinus rhythm 75-80% of the time on repeat assessments; however, the patients in the rhythm control group were more likely to be re-hospitalized compared to their rate control counterparts. Interestingly, the study demonstrated no trend toward increased rate of death or stroke associated with rhythm control. The authors explain this finding by their exclusion of patients on class I antiarrhythmics and more frequent anticoagulant use in the rhythm control group (88%) compared to other studies.³⁶ The results from the AF-CHF trial suggest a rate control strategy be considered as the primary approach in patient populations with HF and LVD.

Rate Control

The foundation of a rate control strategy is based on slowing conduction through the atrio-ventricular (AV) node. Commonly employed pharmacologic agents for such an approach include beta-blockers and calcium channel blockers. However, as previously alluded to, such agents must be used judiciously in patients with impaired left ventricular function. There is no standard method for rate control; goals recommended by the AHA/ACC include target heart rates of 60 to 80 beats per minute at rest, and 90 to 115 beats per minutes with exercise.³⁷ The optimal pharmacologic regimen is highly patient specific but usually requires multiple agents. Beta-blockers and calcium channel blockers are considered class I recommendations by the AHA/ACC in both acute and chronic settings. In cases of chronic and decompensated HF

the AHA/ACC further recommends the use of digoxin and/or amiodarone due to fewer negative inotropic effects.³⁷

Rhythm Control

Antiarrhythmic medications have had a controversial role in the management of AF. The goal of maintaining sinus rhythm in an effort to improve survival and morbidity has been questioned due to numerous clinical trials showing its ineffectiveness.^{29,30,32,33} Despite this, the pathologic states created by LVD with AF are as individual as the patients they affect. In some cases, maintenance of sinus rhythm may be the goal of care; as such, selection of an antiarrhythmic medication is important in trying to minimize adverse effects. However, in the patient population with structural heart disease the Singh-Vaughn-Williams class IA and IC drugs are problematic, due in part to their reduced efficacy and pro-arrhythmic predisposition. Amiodarone is a class III antiarrhythmic that has a long track record for both its efficacy and relative safety. Despite the fact that protracted use of amiodarone risks numerous side effects with no proven benefit in mortality, its ability to maintain sinus rhythm in patients with HF has been shown repeatedly. Data from the STAT-CHF trial demonstrated an increased conversion to sinus rhythm using amiodarone compared to placebo (31.3% vs. 7.7%). In this study patients were less likely to develop AF on amiodarone, and if AF did develop the frequency of its recurrences was decreased.³⁸ Newer antiarrhythmics such as dronedarone, also a class III antiarrhythmic, initially showed promise for maintenance of sinus rhythm; however, findings from the ANDROMEDA study showed an increase in mortality in patients with HF and LVD.³⁹

Dofetilide, a class III antiarrhythmic, has been shown to decrease the incidence of AF in patients with HF as well as myocardial infarction. The DIAMOND studies looked at 3028 patients with severe HF or recent myocardial infarction treated with dofetilide vs. placebo and demonstrated increased likelihood of maintaining sinus rhythm at 1 year (79% vs. 42%). The DIAMOND study also showed the utility of dofetilide in preventing new onset of AF (1.98% vs. 6.55% in placebo arm). Although dofetilide had no effect on all-

cause mortality, the DIAMOND study did show improved survival in patients who maintained sinus rhythm.²

Non-Pharmacologic Approach

The feasibility of either rate or rhythm control may not always be possible in some patients and therefore mechanical control of rhythm may be required. Arguably, the definitive treatment for rate and rhythm control is AV node ablation and implantation of a permanent pacemaker. This strategy is highly successful but exposes patients to procedural risks and ventricular pacing dependence. In the setting of LVD, right ventricular pacing may undermine ventricular synchrony and affect cardiac output.⁴⁰ Such undesirable effects of right ventricular pacing may be mitigated with the use of cardiac resynchronization therapy (CRT); however, the efficacy of this strategy has not been well tested.

Newer techniques for pulmonary vein isolation (PVI) are gaining popularity for treatment of AF in the LVD population. A retrospective study by Chen et al. looked at 377 patients undergoing catheter based PVI, with 94 having LVD (LVEF <40%). This study demonstrated sinus rhythm was maintained in 73% of patients with LVD vs. 87% of controls at 14 months of follow-up ($p = 0.03$). The patients with LVD experienced a non-significant increase in LVEF and a significant improvement in quality of life after PVI. Complication rates were similar between groups and included a 1% risk of pulmonary vein stenosis.⁴¹ A small prospective study done by Hsu et al. followed 58 patients with LVEF < 45% (NYHA class 2 or higher) and 58 controls, all treated with catheter based PVI. This study showed modest success in maintaining sinus rhythm at mean follow-up of 1 year after PVI without antiarrhythmic medication (69% of LVD patients vs. 78% of controls; $p = 0.34$). The patients with LVD had a significant improvement in LVEF (21 +/- 13%; $p < 0.001$), decreased left ventricular systolic and diastolic dimensions, improved exercise capacity, symptoms and quality of life after PVI. Complication rates were similar between groups ranging from 2 to 3% and included tamponade and stroke.⁴² Despite enthusiasm over a true "cure" for AF, PVI carries with it procedural risk and no guarantee of long-term sinus rhythm

maintenance. Further long-term studies may help to clarify the true durability of this procedure in a population at such high risk of recurrence.

Anticoagulation

Anticoagulation in patients with LVD is a substantial topic in and of itself. Needless to say the goal of anticoagulant therapy is reduction in risk of stroke. Due to the electrical and mechanical disarray of the atria during AF, blood circulating through the atria may remain static, predisposing to formation of clot. Atrial thrombus is a well-established risk factor for stroke in patients with AF. Most patients with LVD and HF fulfill criteria for long-term anticoagulation due to the increased risk of thrombo-embolism, regardless of the rate or rhythm control strategy employed.

Complications and Risk of Treatment

Though there are increasing treatment options for AF in LVD, iatrogenic complications are not infrequent and may in turn exacerbate matters. Clinicians must always consider the risks and benefits of each treatment, as many medications used to treat AF frequently have unwanted side effects. Chronotropic medications may result in negative inotropic effects in the LVD population while antiarrhythmics used to maintain sinus-rhythm are fraught with pro-arrhythmic risk. Non-pharmacologic procedures should also be approached with caution as both CRT and PVI are not universally successful and carry with them procedural risk.

Future Directions

Ongoing research into therapy for AF brings with it insights into the management of patients with AF and LVD. The CABANA study, pioneered by the Mayo Clinic, has been designed to compare percutaneous left catheter ablation of AF to pharmacologic therapy (rate or rhythm control). The CABANA study is a randomized trial aiming to include 3000 patients. The primary end point of the study being reduction in total mortality.^{43,44} A subset of the study patients enrolled will have HF and LVD; as such study findings may provide a better understanding into the management of AF in this patient population.

Conclusions

AF frequently complicates LVD and myocardial infarction resulting in physiologic turmoil compromising ventricular function. In a somewhat self-fulfilling prophecy, AF results in cellular changes that further propagate AF and ventricular dysfunction. Once present, AF portends increased morbidity and mortality, though it is not always clear if it is simply a marker of worsening hemodynamic function or the instigator. Treatment for AF comprises a multifaceted approach: 1) blockade of the neuro-hormonal changes in the atria; 2) control of ventricular rate and/or rhythm; 3) anticoagulation to reduce risk of stroke. The best treatment approach is far from universal and treatment efficacy is also variable. Ongoing and future research into therapy for AF brings with it new understanding into the management patients with LVD and AF. New therapies are more and more frequently employing mechanical techniques as therapeutic intervention for AF. In time we will gain insight into this more invasive approach and its long-term success in patients with pre-existing and ongoing myocardial dysfunction. As the population ages, more people develop and survive with LVD, ensuring that AF will continue to be an ongoing complication. Indeed, when considering the management of AF, an ounce of prevention may be well worth a pound of cure.

Disclosures

No disclosures relevant to this article were made by the authors.

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