Atrial Fibrillation in Heart Failure

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KEYWORDS

• Atrial fibrillation • Heart failure • Treatment • Prognosis • Antiarrhythmic therapy
• Catheter ablation • Antithrombotic therapy

KEY POINTS

- Atrial fibrillation (AF) is a marker of worse prognosis in heart failure (HF). The onset of new AF is associated with increased mortality and morbidity in HF.
- Heart rate control is non-inferior to the rhythm control strategy, and remains the first-line approach to treatment in AF with HF.
- Antithrombotic therapy for stroke prophylaxis is required in AF with HF. The availability of new, effective anticoagulants has expanded the therapeutic options.
- Non-pharmacologic strategies, such as catheter ablation procedures, are gaining wide acceptance for the treatment of AF in HF.

BACKGROUND

Chronic heart failure (HF) is a highly prevalent disorder, afflicting about 6 million individuals in the United States, with an incidence of 10 per 1000 population after age 65 years.[1] Nearly 300,000 Americans die from HF annually, and although overall survival has improved over time, mortality remains high, as roughly 50% of patients die within 5 years of diagnosis.[2] The morbidity associated with HF is also substantial, as it accounts for approximately 1 million inpatient hospitalizations and 3.5 million ambulatory care visits each year, at an estimated cost of $35 billion.[3] Mitigating the enormous public health burden exerted by HF is of paramount importance, and key to this is the recognition and management of its associated conditions or risk factors, which include atrial fibrillation (AF).

Chronic AF is the most predominant of the clinically relevant arrhythmias. The overall prevalence of AF is considerably higher in patients with HF, and has been reported to be as high as 25%.[4] AF and chronic HF (CHF) can perpetuate each other. Both

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conditions share common risk factors, such as advanced age, hypertension, diabetes mellitus, coronary artery disease, and valvular heart disease. There is also evidence of a more complex relationship between HF and AF that may be independent of these mutual predisposing factors. Because of the complex interaction between AF and HF, it is useful to review the prognostic relationship between these 2 conditions, pathophysiologic mechanisms, and appropriate therapeutic strategies for their management.

PROGNOSTIC RELATIONSHIP BETWEEN AF AND HF

CHF is the strongest predictor for the development of AF, with up to a sixfold increase in risk seen in the Framingham Study.[5] The prevalence of AF in the setting of preexisting HF increases with worsening HF symptoms: 4% in functional class I, up to 27% in functional class II to III, and 50% in functional class IV patients.[6] Even with optimal medical therapy, the onset of AF is often accompanied by cardiac decompensation and functional class deterioration in patients with HF. Hemodynamic alterations that can be observed shortly after AF onset include marked reductions in peak oxygen consumption and cardiac index, as well as increases in the severity of valvular regurgitation and cardiac chamber dimensions.[7]

AF has significant prognostic implications in patients with HF. A retrospective analysis of the Studies of Left ventricular Dysfunction (SOLVD)[8] involving more than 4200 patients with symptomatic and asymptomatic HF, showed that the presence of AF was associated with significant increases in the risks of total mortality by 32%, pump-failure death by 48%, and HF hospitalization by 38%. A similar observation was noted from the analysis of data from the Candesartan in Heart failure-Assessment of Reduction in Mortality and Morbidity (CHARM)[9] trial, which enrolled 7600 patients with symptomatic HF, 15% of whom had AF. In patients with low systolic function, AF was associated with a 29% higher risk of mortality or HF hospitalization. In those with preserved systolic function, the relative risk of adverse events is even higher at 72%. A meta-analysis of 16 studies that evaluated nearly 54,000 patients with HF showed a 40% increased risk for total mortality if AF was present.[10] The increase in adverse outcomes associated with AF was observed in both preserved and impaired ventricular HF types.

The mere presence of AF per se, while serving as a marker of poor outcomes, may not necessarily affect the prognosis of patients with HF in a direct and independent manner. For example, post hoc analysis of data from the Veterans Affairs Vasodilator-Heart Failure Trials (V-HeFT),[11] which enrolled more than 1300 patients with mild to moderate HF, found that the rates of mortality, hospitalization, and other adverse events in patients with AF were no different from those in sinus rhythm. Similarly, in severe HF, AF has not been shown to be independently associated with adverse outcomes in the Prospective Randomized Study of Ibopamine on Mortality and Efficacy (PRIME)[12] study, which enrolled more than 400 patients with advanced chronic HF.

The prognostic role of AF in HF was later clarified in the post hoc analysis of data from the Carvedilol Or Metoprolol European Trial (COMET), which enrolled more than 3000 patients with symptomatic systolic HF, 20% of whom had AF at baseline. Univariate analysis showed that patients who were in AF on baseline electrocardiography had significantly higher risks of all-cause and cardiovascular mortality and hospitalization rates over a 5-year period (**Fig. 1**). After adjustment for patient-related variables (eg, age and gender), however, the presence of AF at baseline was no longer independently associated with mortality. Serial electrocardiography was performed

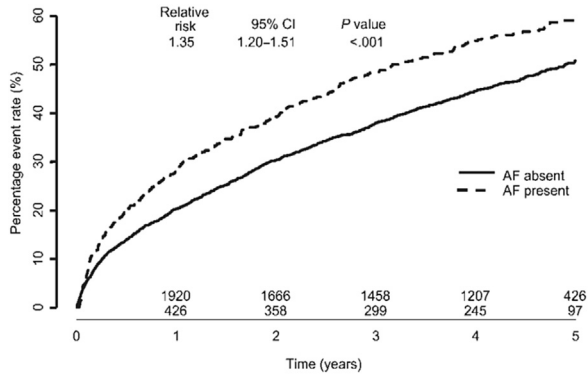


Fig. 1. Cardiovascular mortality or hospitalization for worsening heart failure by baseline atrial fibrillation in the COMET trial.

throughout the COMET follow-up period to screen for subsequent development of AF. Of the nearly 2500 patients who were in sinus rhythm at baseline, 580 developed new-onset AF during the study. In this subset of patients, new-onset AF was an independent predictor of subsequent all-cause mortality and remained so regardless of treatment and changes in functional class over time.[13] In summary, although preexisting chronic AF has not been definitively shown to independently affect the mortality or morbidity rates in patients with HF, the onset of new AF is certainly associated with adverse outcomes in chronic HF.

PATHOPHYSIOLOGIC MECHANISMS

Under normal circumstances, atrial systole may contribute up to 25% of the cardiac output. In the setting of ventricular dysfunction, the atrial contribution to the total cardiac output could be as high as 50%. The onset of AF abolishes the "atrial kick" leading to reductions in cardiac output, peak oxygen uptake, and exercise tolerance.[14,15] When the failing heart is subjected to these adverse hemodynamic conditions, cardiac decompensation occurs.

In addition, the onset of AF also decreases cardiac output and worsens HF through other mechanisms. AF may cause valvular regurgitation, which causes reduction in forward blood flow. Rapid ventricular rates during periods of uncontrolled AF lead to inadequate ventricle filling time and decrease in stroke volume.[16–18] An irregular ventricular response, in itself and independent of heart rate, causes a drop in cardiac output, increase in pulmonary wedge pressure, and elevation of right atrial pressure.[19]

In patients with normal baseline ventricular function, the chronic rapid heart rates associated with AF can produce a distinct, reversible type of severe biventricular HF called "tachycardia-induced cardiomyopathy." On a hemodynamic level, the incessant tachycardia seen in AF impairs myocardial compliance and shortens the ventricle filling times, leading to a reduction in cardiac output and subsequent development of symptomatic HF. Higher heart rates and longer tachycardia duration generally lead to more severe HF. Ultrastructural cardiac remodeling occurs, characterized by cytoskeletal alteration, matrix metalloproteinase disruption, depletion of high-energy stores, and induction of abnormal calcium handling. The negative remodeling process is also accompanied by neurohormonal derangements, such as increased sympathetic response and activation of the renin-angiotensin system (RAS).[20–22]

In patients with HF with sinus rhythm at baseline, the ultrastuctural and neurohormonal aberrations that are induced by cardiac dysfunction produce a favorable substrate for the development and maintenance of atrial and ventricular arrhythmias, including AF. High intracardiac volumes and pressures in HF can cause mechanical stretching of the atria, which is associated with shortening of the atrial refractory period, prolongation of atrial conduction times, increased frequency of interatrial conduction blocks, and heightened atrial irritability.[23,24] Stimulation of the sympathetic nervous system and high catecholamine levels that are features of chronic HF not only increase the ventricular rate response in AF, but may cause abnormalities of atrial action potentials and automaticity that can trigger arrhythmogenesis as well.[25] Parasympathetic hyperinnervation is part of a complex autonomic remodeling process seen in HF, and contributes significantly to the maintenance of AF.[26] HF is also accosted by activation of the RAS system and increased angiotensin-II expression, which induce atrial interstitial fibrosis, creating areas of slowed conduction and heterogeneity in repolarization that serve as substrates for AF generation.[25,27] In the failing atrium, profound calcium dysregulation and ion channel remodeling within the atrial cardiomyocyte enhance arrhythmogenesis and promote triggered activity in AF.[28]

THERAPEUTIC STRATEGIES: RATE VERSUS RHYTHM CONTROL OF AF IN HF

Although most of the landmark trials on AF therapy have shown that the therapeutic strategy of rhythm-control (conversion to and maintenance of sinus rhythm using antiarrhythmic agents) generally had no clinical advantage over that of simple rate control (AF is not actively converted to sinus rhythm, but heart rate [HR] is maintained at a specified target range), retrospective analyses of early major trials in HF pointed toward favorable outcomes with rhythm control.

For example, 103 patients with HF with baseline AF who enrolled in the Congestive Heart Failure: Survival Trial of Antiarrhythmic Therapy (CHF-STAT)[29] were randomized to treatment with either amiodarone or placebo. Of those treated with amiodarone, 31% converted to sinus rhythm. After 4 years of follow-up, significantly lower mortality rate was noted in patients with HF with baseline AF who subsequently converted to sinus rhythm on amiodarone compared with nonresponders. Also, subgroup analysis of data from 261 patients with AF with mild to moderate HF who enrolled in the Rate-Control Efficacy in Permanent Atrial Fibrillation (RACE)[30] trial showed improved survival, less frequent HF hospitalization, and lower adverse events with rhythm control compared with rate control. A similar observation was seen in the post hoc analysis of patients with HF enrolled in the Danish Investigations of Arrhythmia and Mortality on Dofetilide (DIAMOND),[31] 506 of whom had baseline AF. The study showed that the restoration and maintenance of sinus rhythm in patients with HF with AF was associated with significant reductions in mortality and hospitalization rates.

A small prospective study (CAFÉ-II)[32] randomized 61 patients with chronic HF and persistent AF into either rhythm-control or rate-control treatment approaches. After 1 year of follow-up, the trial found improved ventricular function and better quality of life in the rhythm-control group. The clinical benefit of rhythm control, however, was not demonstrated in the landmark Atrial Fibrillation in Congestive Heart Failure (AF-CHF) trial.[33] In this study, nearly 1400 patients with AF and concomitant HF were randomized to either rhythm-control or rate-control strategies. After 3 years of follow-up, the trial found no difference in the rates of mortality and major cardiovascular events in either group (**Fig. 2**). Probably contributing to the lack of net clinical

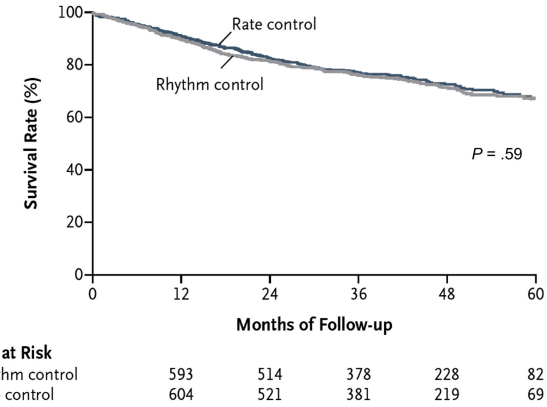


Fig. 2. A comparison of Kaplan-Meier estimates of death from cardiovascular causes in patients with atrial fibrillation and heart failure treated with rhythm-control or rate-control strategies in the AF-CHF trial.

benefit of the rhythm-control approach is the suboptimal efficacy and relative toxicity of the antiarrhythmic drugs that were used.

RATE-CONTROL APPROACHES

Pharmacologic Rate Control

Beta adrenergic blocking agents are the preferred HR-modulating drugs for AF because of their established cardioprotective effects in the setting of HF. Bisoprolol, metoprolol succinate, and carvedilol have demonstrated mortality benefit in HF,[34] and have been shown to provide effective rate control in patients with AF with HF. The current guidelines also recommend digoxin as a first-line agent in the control of HR in patients with AF with systolic dysfunction and HF.[35] In the presence of adequate beta blockade, digoxin does not appear to be significantly effective; however, in cases when adequate doses of beta blocker are not tolerated or contraindicated, digoxin should be considered the first-line therapy.

Strict Versus Lenient Rate Control

Traditionally, treatment targets for HR for AF have been defined to range between 60 and 80/min at rest and 80 to 110/min with moderate exercise. These arbitrary goals are often difficult to accomplish, especially in patients with HF, and have been recently challenged by the results of the Rate Control Efficacy in Permanent Atrial Fibrillation (RACE-II) trial.[36] The study enrolled more than 600 patients with AF, 10% of whom had previous hospitalization for HF, who were randomized to either lenient (target resting HR <110/min) or strict rate control (target HR <80/min at rest, <110/min on moderate exercise). After 3 years of follow-up, there was no significant difference seen in the composite rates of death, HF hospitalization, or major cardiovascular events between the 2 groups (**Fig. 3**). However, specific data on patients with HF were not released and the long-term effect of the lenient rate control approach on systolic function was not evaluated, so the results of the RACE-II trial cannot be extrapolated to the general HF population with AF at this time.

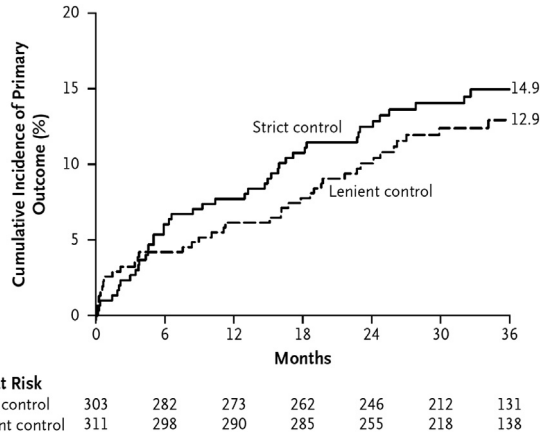


Fig. 3. Kaplan-Meier estimates of the cumulative incidence of major adverse cardiac events in patients with atrial fibrillation treated with either strict or lenient rate-control strategies in the RACE-II trial.

Target Heart Rate in CHF

The optimal HR goal for HF treatment has not yet been defined, although previous studies have highlighted the prognostic role of HR in patients with HF. For example, post hoc analyses of the CIBIS-I (Cardiac Insufficiency Bisoprolol Study)[37] and COMET[38] found that HR assessed a few months after initiating beta-blocker therapy had an independent prognostic value for subsequent outcomes in patients with HF. Recent data suggest that HR may be a suitable modifiable target in HF therapy. Subgroup analysis of the BEAUTIFUL trial (Morbidity-Mortality Evaluation of the I_f Inhibitor Ivabradine in Patients With Coronary Disease and Left Ventricular Dysfunction),[39] involving nearly 5500 patients with systolic dysfunction, found that those with resting HR above 70/min had a 34% higher risk of mortality and a 53% higher frequency of HF hospitalization compared with patients with resting HR below 70/min.

Subsequently, a rate-control strategy in patients with HF was tested in the Systolic Heart Failure Treatment with the I_f inhibitor Ivabradine Trial (SHIFT)[40] using the novel selective sinus-node inhibitor ivabradine. In this trial, more than 6500 patients with HF (8% of whom had AF) with resting HR above 70/min were randomized to treatment with either placebo or ivabradine, dose adjusted to maintain HR between 50 and 60/min. After nearly 2 years of follow-up, the study showed that HR reduction with ivabradine was associated with a 26% reduction in HF deaths and 24% decrease in hospitalization for worsening HF. Whether or not the results are applicable to the general AF population with HF remains unclear. Furthermore, it is important to note that ivabradine, which primarily works by its action on I_f channels in the sinus node, has no effect on atrioventricular (AV) nodal conduction and, as such, does not appear to be useful in controlling ventricular rate in patients with AF.

Nonpharmacologic Rate Control

If drug therapy is unsuccessful or not tolerated, nonpharmacologic approaches to AF rate control can be performed, such as transcatheter ablation of the AV node or His bundle or modification of the AV nodal conduction. In transcatheter AV node ablation, a complete heart block is created with the use of direct current or radiofrequency

energy, electrically separating the atria from the ventricles. A permanent pacing device is subsequently implanted to adequately control the ventricular rate.[41] Alternatively, radiofrequency energy can be used to modify, rather than completely abolish, AV nodal conduction. Ablation of one of the 2 electrical pathways within the AV node can reduce the number of impulses that successfully reach the infranodal conduction system and the ventricles. This precludes the need for permanent pacemaker implantation, although procedural success rate is lower compared with complete AV node ablation.[42]

AV nodal ablation could have a favorable effect in patients with HF on cardiac resynchronization therapy (CRT) and concomitant AF. In this group of patients, a small study found lower rates of mortality and adverse outcomes, as well as greater functional class improvement, in those who underwent AV nodal ablation compared with those given drug therapy for AF rate control.[43] However, larger randomized trials are required to confirm this observation before this approach is considered.

RHYTHM CONTROL STRATEGY

Pharmacologic Rhythm Control

Although in general, rhythm control is not superior to simple rate control in patients with HF with AF, this approach may be worthwhile in individuals who are symptomatic during AF episodes even if HR is adequately controlled. For this indication, amiodarone or dofetilide may be used for pharmacologic rhythm control of AF in the setting of HF. If concurrent coronary disease or significant left ventricle hypertrophy is present, however, dofetilide is contraindicated, leaving amiodarone as the sole agent of choice in these cases.[34] Although amiodarone is a well-tested therapy that has been used in a number of clinical trials, including in patients with HF, it does have its limitations because of significant drug-drug interactions (especially with polypharmacy in patients with HF) and HF-related alterations in the volume of distribution and overall drug metabolism and elimination.

Dronedarone

The relative dearth of safer and more tolerable antiarrhythmic drugs in AF therapy has led to the development of the novel agent dronedarone, a derivative of amiodarone that has a shorter half-life and is devoid of iodine moiety to reduce toxicity. In the general AF population, the incidence of major adverse effects with dronedarone was similar to placebo and 20% lower compared with amiodarone.[44] In patients with advanced HF, however, the Antiarrhythmic Trial with Dronedarone in Moderate to Severe CHF Evaluating Morbidity Decrease (ANDROMEDA)[45] found a twofold excess in mortality with dronedarone compared with placebo, primarily because of worsening HF, prompting the early termination of this study after just 2 months of clinical follow-up. On the other hand, the ATHENA trial (A Placebo-Controlled, Double-Blind, Parallel Arm Trial To Assess the Efficacy of Dronedarone 400 mg Bid for the Prevention of Cardiovascular Hospitalization or Death from Any Cause in Patients With Atrial Fibrillation/Atrial Flutter) enrolled more than 4600 patients with AF, 21% of whom had HF with functional class II or III symptoms. The study found that dronedarone therapy was associated with significant reductions in morbidity and mortality in patients with AF.[46] The seemingly conflicting findings of these 2 trials have led some to hypothesize that dronedarone possibly increases mortality among patients with advanced and recently decompensated HF, but reduces those same adverse events in patients with less severe heart failure. Currently, the drug carries a Black Box Warning listing severely symptomatic or recently decompensated HF as a contraindication to dronedarone therapy.

Nonpharmacologic Rhythm Control

The track record of current antiarrhythmic drug therapy is rather disappointing. On the contrary, the alternative nonpharmacologic interventions that are available for the maintenance of sinus rhythm in patients with AF and HF have been promising. The Cox-Maze procedure, a major open-heart surgical technique, involves placing multiple incisions within the atria to interrupt reentry pathways. It has an excellent efficacy in the general AF population (90% freedom from AF at 10 years), with a 1.4% early operative mortality rate.[47] Although often avoided in high-risk patients with HF, the Cox-Maze procedure, when performed in the setting of severe systolic dysfunction, was associated with significant improvements in ejection fraction, functional class, and quality of life. The efficacy of this surgical procedure remains high at 86% without increasing operative risk in patients with HF.[48] With recent modifications in surgical technique, the procedure is now being performed in a simpler, minimally invasive fashion (eg, mini-Maze), resulting in less incidence of perioperative morbidity while achieving comparable efficacy as the classic Cox-Maze procedure.[49]

Transcatheter AF ablation is a safer and less invasive alternative to the surgical approaches. Like the Cox-Maze procedure, the transcatheter approach aims to interrupt reentry pathways and isolate the pulmonary veins and arrhythmogenic AF foci by placing multiple ablation lines within the atria. It has been shown to be safe and effective in patients with HF, although some operators are still reluctant to perform the procedure in these patients because of technical concerns. The PABA-CHF (Pulmonary Vein Antrum Isolation vs AV Node Ablation With Bi-Ventricular Pacing for Treatment of Atrial Fibrillation in Patients With Congestive Heart Failure)[50] trial randomized more than 80 patients with drug-resistant AF and symptomatic systolic HF to either transcatheter pulmonary vein isolation (PVI) or AV nodal ablation with permanent pacing. After 6 months of follow-up, patients who underwent PVI had significantly higher improvements in ejection fraction, functional capacity, and quality of life. Freedom from AF was achieved in 78% of patients after PVI, with no periprocedural deaths reported.

The popularity of transcatheter AF ablation has dramatically increased over the past few years, and is now considered a part of the standard therapies for patients with AF who have failed drug therapy. The large, multicenter, randomized CASTLE-AF (Catheter Ablation vs Standard Conventional Treatment in Patients With Left Ventricular Dysfunction and Atrial Fibrillation) trial is currently ongoing, with the objective of comparing transcatheter AF ablation versus conventional medical treatment in terms of mortality and morbidity in patients with AF and HF. Until then, ablation techniques remain as second-line alternatives to pharmacologic therapy in the rhythm-control approach to patients with AF with HF.[51]

NON-ANTIARRHYTHMIC THERAPY

Non-antiarrhythmic therapeutic alternatives to the conventional antiarrhythmic drugs in AF management have been explored, but their clinical utility is still a subject of debate. Retrospective and epidemiologic data suggest that statins, omega-3 fatty acids, antioxidants, anti-inflammatory agents, and ranozaline may favorably alter the natural course of AF by modulating the underlying structural, electrophysiologic, and neurohormonal substrates that fuel atrial arrhythmogenesis.[52] Data from small-scale studies and experimental models suggest that these alternative therapies may be of benefit in the setting of HF as well.[53–55] However, the clinical efficacy of these therapeutic alternatives for patients with AF and HF has never been corroborated in large randomized trials, and their role in actual practice remains undefined.

The RAS inhibitors have been the mainstay of HF pharmacotherapy owing to their well-established mortality and morbidity benefit. This class of non-antiarrhythmic agents has recently attracted interest because of its potential role in AF management. A meta-analysis of 23 randomized trials involving more than 87,000 patients who were treated with RAS blockers showed a 33% reduction in the risk of AF in those who received angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ARBs). Patients with HF appeared to derive the most benefit from these agents.[56] However, these observations were not substantiated by the results of the recently concluded ACTIVE-I (Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events) trial,[57] which randomized more than 9000 high-risk patients with AF (32% of whom had HF) to treatment with either placebo or the ARB irbesartan. After 4 years of follow-up, the study found no difference in the composite rates of cardiovascular events, hospitalizations, mortality, and stroke between groups, implying that RAS blockade does not provide additional therapeutic benefit in patients with AF. Of note, the study found a lower incidence of HF hospitalizations in the treatment arm. Specific data on the subset of patients with HF have not been released, but RAS inhibitors remain an integral part in the management of these patients even though the effect on AF has not been convincing.

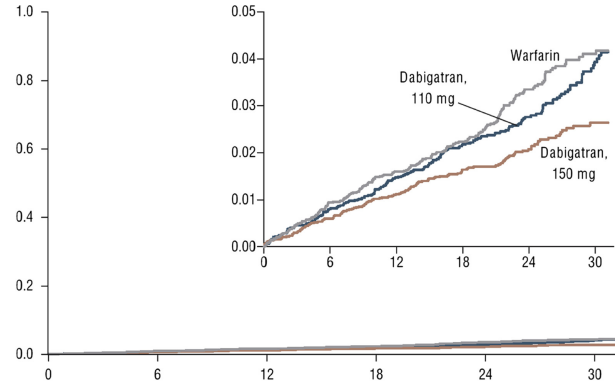
ANTITHROMBOTIC THERAPY

HF is a major risk factor for thromboembolic events in AF, and, thus, antithrombotic therapy is required in these patients whether a rhythm-control or rate-control treatment approach is chosen. Oral anticoagulation with warfarin has been the mainstay of stroke prophylaxis in AF. Patients with AF with HF who do not have any of the other CHADS2 risk factors (eg, hypertension, age older than 75 years, diabetes, and stroke) may be given aspirin as an alternative, although oral anticoagulation is preferred.[34]

Warfarin, although highly effective, has many limitations, including slow onset of action, significant drug-drug and food-drug interactions, and narrow therapeutic window. This is further complicated by the pharmacokinetic and pharmacodynamic alterations that are associated with HF. A reduction in the volume of distribution and impairment in drug clearance may result from HF-related end-organ hypoperfusion, as well as congestion of the liver and gut.[58] Thus, maintenance of optimal anticoagulation is particularly challenging with warfarin in patients with HF.

Dabigatran

Over the past decade, more effective and efficient alternatives to warfarin have been explored, which led to the emergence of dabigatran, a direct oral thrombin inhibitor that has a rapid onset of action, less food and drug interaction, and more predictable anticoagulation response, which permits fixed dosing without the need for coagulation monitoring. The clinical efficacy and safety of dabigatran was evaluated in the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy)[59] trial, which randomized more than 18,000 high-risk patients with AF into treatment with either warfarin or dabigatran (in 2 separate dosing arms of 110 mg or 150 mg twice daily). After 2 years of follow-up, the study found that low-dose dabigatran had similar antithrombotic efficacy in preventing thromboembolic events but had significantly lower rates of bleeding compared with warfarin. High-dose dabigatran, on the other hand, was associated with a significant 34% lowering of embolic events compared with warfarin without increasing bleeding risk (**Fig. 4**). As such, dabigatran is now considered an important alternative to warfarin, and the practice guidelines have been recently updated to reflect the addition of dabigatran as a first-line option for anticoagulation for high-risk patients with AF, which include those with HF.[60]



Warfarin	6022	5862	5718	4593	2890	1322
Dabigatran, 110 mg	6015	5862	5710	4593	2945	1385
Dabigatran, 150 mg	6076	5939	5779	4682	3044	1429

Fig. 4. Cumulative hazard rates of stroke or systemic embolism in patients with atrial fibrillation treated with warfarin or dabigatran in the RE-LY trial.

Dual Antiplatelet Therapy

In patients who are unsuitable for warfarin therapy, the ACTIVE-A trial, which enrolled more than 7500 high-risk patients with AF, found that dual antiplatelet therapy using combination aspirin and clopidogrel was 28% more effective than aspirin monotherapy in preventing stroke. There was, however, a higher incidence of major bleeding events seen with dual antiplatelet therapy. The revised AF guidelines point out that dual antiplatelet therapy may be considered in patients who cannot safely sustain anticoagulation using warfarin.[51] In those who are otherwise candidates for oral anticoagulation, the ACTIVE-W trial[61] has clearly demonstrated the superiority of warfarin over combination aspirin-clopidogrel in the prevention of thromboembolic events.

SUMMARY

HF and AF are highly prevalent disorders that exert tremendous burden to the health care system. Presence of chronic AF is a marker of worse prognosis in patients with CHF, and the onset of new AF in those with chronic HF is associated with increased morbidity and mortality. This may be because of the numerous hemodynamic impairments associated with the arrhythmia, as well as the accompanying adverse ultrastructural and neurohormonal processes that ultimately lead to cardiac decompensation. Pharmacologic rhythm control has been shown to have no clinical advantage over simple rate control in patients with AF, including those with HF. The use of the new, relatively safer antiarrhythmic agent dronedarone has also resulted in net harm in the setting of HF. A lenient approach to HR is now considered a viable strategy in the general AF population, although its safety in patients with HF is still unclear. Improvements in procedural techniques have resulted in increased efficacy and safety of the surgical and interventional approaches (eg, Maze procedure and transcatheter AF ablation/PVI) to the maintenance of sinus rhythm in patients with AF with HF. As such, their popularity has recently skyrocketed. Until more data establishing their superiority are available, however, these invasive procedures remain as alternative therapies to the first-line pharmacologic rhythm control. Patients with HF are at high risk for AF-related systemic thromboembolic events. The emergence of dabigatran as a more practical alternative

to warfarin in AF thromboprophylaxis has been a cause of excitement recently. All of these advances in drug development, nonpharmacologic modalities, and therapeutic strategies have been instrumental in reducing the negative impact of AF and HF.

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