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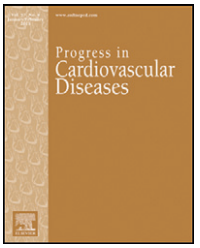

# Atrial Fibrillation and Heart Failure: Update 2015

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ABSTRACT

Heart failure (HF) and atrial fibrillation (AF) commonly coexist, adversely affect mortality, and impose a significant burden on healthcare resources. The presence of AF and HF portends a poor prognosis as well as an increased thromboembolic risk. In patients whose AF is symptomatic, rhythm restoration with either antiarrhythmic drugs or procedural therapies (*e.g.*, pulmonary vein isolation, either catheter-based or surgical) should be considered for symptom improvement, though a mortality benefit has yet to be demonstrated. Emerging evidence suggests that non-pharmacological treatment for AF (including catheter based ablation, hybrid surgical techniques, and atrioventricular node ablation with biventricular pacing) may be of value in improving HF patients' quality of life.



Atrial fibrillation (AF) is the most common sustained arrhythmia among adults.[1] Heart failure (HF) and AF often coexist. Each condition can promote the other, with an associated increase in morbidity and mortality. Together, their incidence and prevalence are on the rise, presenting a growing clinical and economic burden.[2] In order to provide optimal care, clinicians should remain abreast of relevant literature, guideline recommendations, and available therapies for their patients. In this article we review the complex relationship between AF and HF, with a focus on recent advances in management as well as emerging evidence.

## Epidemiology of HF and AF

Both AF and HF are common clinical entities. HF alone is a significant and growing epidemic, affecting nearly 5.7 million American adults.[2] The prevalence of AF is increasing as the population ages, currently affecting over 2 million people in the United States.[1] Collectively, AF and HF carry significant morbidity and mortality, while imposing a substantial adverse impact on healthcare resources. Overall, the estimated national annual cost of caring for patients with AF is approximately $26 billion.[3] Likewise, HF hospital admissions account for over 6.5 million hospital days annually,[4] and HF-related costs reach an estimated $34.4 billion each year. This total includes the cost of health care services, medications, and lost productivity.[5]

AF and HF often coexist, and when they do, they confer increased risk for hospitalization, portend lengthier inpatient stays, and increase overall morbidity and mortality.[6–10] Khazanie et al.[11] analyzed 27,829 HF admissions at 281 hospitals between 2006 and 2008, and found that pre-existing AF was associated with greater 3-year risks of all-cause mortality (HR 1.14; 99% confidence interval [CI]: 1.08–1.20), all-cause readmission (HR: 1.09; 99% CI: 1.05–1.14), HF readmission (HR: 1.15; 99% CI: 1.08–1.21), and readmission for stroke (HR: 1.20; 99% CI: 1.01–1.41), compared with no AF. There also was a greater hazard of mortality at one year

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**Abbreviations and Acronyms**

**6MWT** = 6-minute walk test

**AADs** = anti-arrhythmia drugs

**ACEIs** = angiotensin converting enzyme inhibitors

**AF** = atrial fibrillation

**ARBs** = angiotensin receptor blockers

**BB** = beta blockade

**BNP** = brain natriuretic peptide

**CA** = catheter ablation

**CHD** = coronary heart disease

**CRT** = cardiac resynchronization therapy

**CV** = cardiovascular

**CVA** = cerebral vascular accident

**HF** = heart failure

**HFpEF** = heart failure preserved ejection fraction

**HFrEF** = heart failure reduced ejection fraction

**LV** = left ventricular

**LVEF** = left ventricular ejection fraction

**NOACs** = novel oral anticoagulants

**NSR** = normal sinus rhythm

**NYHA** = New York Heart Association

**OACs** = Oral anticoagulants

**PVI** = pulmonary vein isolation

**QoL** = quality of life

**STE** = systemic thromboembolism

**VKAs** = vitamin K antagonists

among patients with new-onset AF (HR: 1.12; 99% CI 1.01-1.24) compared with no AF.

## Pathophysiology of AF and HF

AF and HF share several common risk factors and commonly occur together.[6–10,12–19] The complex underlying mechanisms that lead to the development of AF in HF patients, and the converse relationship, have been partially described. In patients with HF, there is evidence to support structural, neurohormonal, and electrical atrial remodeling—each of which may encourage the development of AF.[20–26] The development of AF in HF appears to be a multifactorial process, including early atrial enlargement, conduction heterogeneity from intra-atrial fibrosis, ion channel dysregulation, and autonomic remodeling (see Fig 1).[27–30] This causative relationship also works in the opposite direction: AF can induce electrical and hemodynamic deterioration and can cause tachycardia-mediated cardiomyopathy, resulting in HF.[31–33] Through induction of a rapid ventricular response or altered diastolic ventricular function, AF also can cause HF symptoms even in patients with intact LV systolic function.

## Anticoagulation

The presence of AF in patients with HF increases the risk of stroke and systemic thromboembolism (STE) when compared to those without AF.[34] Likewise, AF can lead to left ventricular (LV) dysfunction, which in turn can compound the stroke risk. The risk of STE when HF is combined with AF is well described, and the clinical burden of STE events with regard to morbidity and mortality is substantial.[35] As described initially by the Framingham Heart Study investigators, the presence of HF carries a fourfold risk of STE events per year.[36] Other studies, including the Stroke Prevention in Atrial Fibrillation study (SPAF), have also demonstrated that LV dysfunction is a particularly significant independent risk factor for cerebral vascular accident (CVA).[37–43]

Risk stratification schemes such as the $CHADS_2$ and $CHA_2DS_2$-VASc scores divide patients into low, intermediate, and high-risk groups and are invaluable in assessing the need for anticoagulation.[44–47] Recently the American Heart Association/American College of Cardiology/Heart Rhythm Society AF guidelines have promoted the utility of the $CHA_2DS_2$-VASc over the $CHADS_2$ score to identify patients who are at truly low risk for STE events.[48] Additionally, the $CHA_2DS_2$-VASc score takes into consideration risk factors that were not previously accounted for (*i.e.*, female sex, age 65–75 years, vascular disease).[49] Patients at high stroke risk (*i.e.*, $CHA_2DS_2$-VASc $\geq 2$) clearly benefit from anticoagulation with oral anticoagulants (OACs; either vitamin K antagonists [VKAs] or the novel oral anticoagulants [NOACs; see below]). Patients at intermediate risk ($CHA_2DS_2$-VASc score of 1) are eligible for either aspirin alone or OAC therapy.[48] In AF patients with HF as their only risk factor, however, there is some evidence to suggest that therapy with OAC may be superior to aspirin alone (see below).

Recent data from smaller series of patients suggest that among intermediate-risk patients with AF, VKAs may be superior to antiplatelet agents alone for CVA protection, without a significant difference in major bleeding.[50] In a study of such patients, Gorin et al.[51] reported a lower rate of CVA and mortality with VKA (RR = 0.42, 95% CI 0.29–0.60, $p < 0.0001$). Overall, VKAs are known to be superior to antiplatelet regimens in intermediate-risk patients, but this has not been specifically described in patients with HF.[52]

Importantly, the independent risk of stroke in patients with HF complicating AF may be underestimated by commonly used risk stratification schemes. Specifically, similarly scored individual risk factors for STE events in AF do not imply exactly equivalent actual additional risk.[37–40,53,54] Notably, in the Framingham Heart Study, HF carried a fourfold risk of STE events per year, whereas hypertension and coronary heart disease (CHD) implied only three times and twice the risk, respectively.[36] Thus, many experienced clinicians elect to anticoagulate patients with HF as their only $CHA_2DS_2$-VASc risk factor, using either VKA or a NOAC, if the bleeding risk is low. When making this decision, the HAS-BLED score can be utilized to assess the bleeding risk of anticoagulation.[55]

Clinical trials assessing the risk of STE events in AF have used various definitions for the diagnosis of HF. To date, clinical risk scores do not differentiate between clinical HF with preserved ejection fraction (HFpEF) and LV systolic dysfunction with or without HF symptoms.[44–46,48] Attempts have been made to correlate risk with the level of systolic dysfunction, but the results are mixed.[56–58] However, these data are confounded by inequalities in comorbid clinical factors that sway the results. From the best available evidence, it appears that there is no difference between HFpEF and LV systolic dysfunction in terms of CVA/STE