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REVIEW

Catheter Ablation of Atrial Fibrillation in Patients With Heart Failure—Therapy or Futility?

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Abstract

Atrial fibrillation (AF) and heart failure (HF) frequently coexist, creating a bidirectional relationship in which each condition exacerbates the other, worsening patient prognosis. This interplay also presents therapeutic challenges, as traditional pharmacological strategies for rate and rhythm control are often limited in HF. Catheter ablation (CA) is an established treatment for maintaining sinus rhythm and providing symptomatic relief in patients with AF; however, its effect on clinical outcomes and prognosis in HF populations remains under investigation. This article offers a comprehensive overview of the management of AF and HF, with a focus on the evidence surrounding CA in this population. By analysing recent randomized controlled trials (RCTs) and guideline recommendations, this review aims to provide insights into the role of CA in managing AF and HF.

Key words: atrial fibrillation; heart failure; catheter ablation

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Introduction

Atrial fibrillation (AF) and heart failure (HF) are major cardiovascular epidemics, driven by an aging population and profoundly affecting patients' lives and healthcare systems. AF and HF frequently co-exist, occurring concurrently in up to 50% of patients (Tsao et al, 2022). These conditions share a complex, bidirectional relationship, with each capable of triggering and exacerbating the other, creating a vicious cycle of worsening symptoms and poor prognosis (Santhanakrishnan et al, 2016). This interdependence underscores the need for more effective therapies for patients facing both conditions.

Managing AF in the context of HF poses unique challenges, as traditional treatments for rate and rhythm control may be limited due to differing safety and efficacy profiles (Van Gelder et al, 2024). Catheter ablation (CA) for AF is a procedure aimed at restoring normal heart rhythm by electrically isolating the pulmonary veins from the left atrium (LA), targeting AF triggers originating from these veins. Although CA is a well-established and effective treatment for symptomatic AF in the general population (Van Gelder et al, 2024), its role and long-term impact on prognosis in HF patients remain subjects of ongoing investigation. Early studies showed that CA improves left ventricle (LV) function, functional capacity, and quality of

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life (QoL) (Hunter et al, 2014; Jones et al, 2013; Prabhu et al, 2017) in patients with HF and reduced ejection fraction. Recent randomized controlled trials (RCTs) have further demonstrated their potential to decrease HF hospitalizations and mortality in selected patients (Di Biase et al, 2016; Marrouche et al, 2018; Sohns et al, 2023). Still, conflicting data and the limited generalizability of these findings to the broader HF population, including those with preserved ejection fraction, prevent its widespread clinical adoption.

This article provides an overview of the management of AF and HF, focusing on the evidence surrounding CA in this population. Relevant literature and guideline recommendations are reviewed to support clinicians in selecting appropriate patients for the procedure. Given that most studies focused on patients with heart failure with reduced ejection fraction (HFrEF; ejection fraction [EF] $\leq$40%) the data presented primarily applies to this subgroup. Heart failure with mid-range ejection fraction (HFmrEF, EF 41–49%) is grouped with HFrEF due to the similarities in clinical characteristics and treatment responses. Where relevant, distinctions in AF management between HFrEF and heart failure with preserved ejection fraction (HFpEF, EF $\geq$50%) are also discussed.

Pathophysiology of AF and HF

Shared risk factors—including advanced age, hypertension, coronary artery disease, diabetes, obesity, and chronic kidney disease—contribute to the development of both AF and HF (Maisel and Stevenson, 2003). Hemodynamic, neurohormonal, and structural factors further complicate their interaction (Fig. 1).

The pathophysiological mechanisms of AF and HF are closely linked. AF can exacerbate HF or serve as an initial trigger for its onset. The loss of atrial "kick" in systole, combined with atrioventricular (AV) dyssynchrony and an irregular ventricular rhythm, compromises diastolic filling, reduces stroke volume, and substantially decreases cardiac output by up to 25% (Daoud et al, 1996; Naito et al, 1983). Conversely, HF can initiate and sustain AF. Elevated atrial volumes and pressures in HF lead to atrial dilation, resulting in structural and electrical remodelling (Li et al, 1999). These changes create a substrate facilitating AF, which becomes more established and persistent as HF progresses. Additionally, neurohormonal activation in HF, including upregulation of the renin-angiotensin-aldosterone system and sympathetic nervous system, further promotes an arrhythmogenic environment (Sridhar et al, 2009).

Arrhythmia-Induced Cardiomyopathy (AIC) can develop due to the rapid and irregular atrial—and, consequently, ventricular—activity caused by AF (Simantirakis et al, 2012). While reductions in left ventricular ejection fraction (LVEF) can sometimes be attributed to assessment challenges during a fast ventricular rate, AF alone, independent of rate, can induce HF. Evidence shows that ventricular dilation, dysfunction, and myocardial remodelling can occur, even in patients with previously normal heart structures. AIC can manifest shortly after the onset of AF, with hemodynamic changes evident within 24 hours of sustained tachycardia. For-

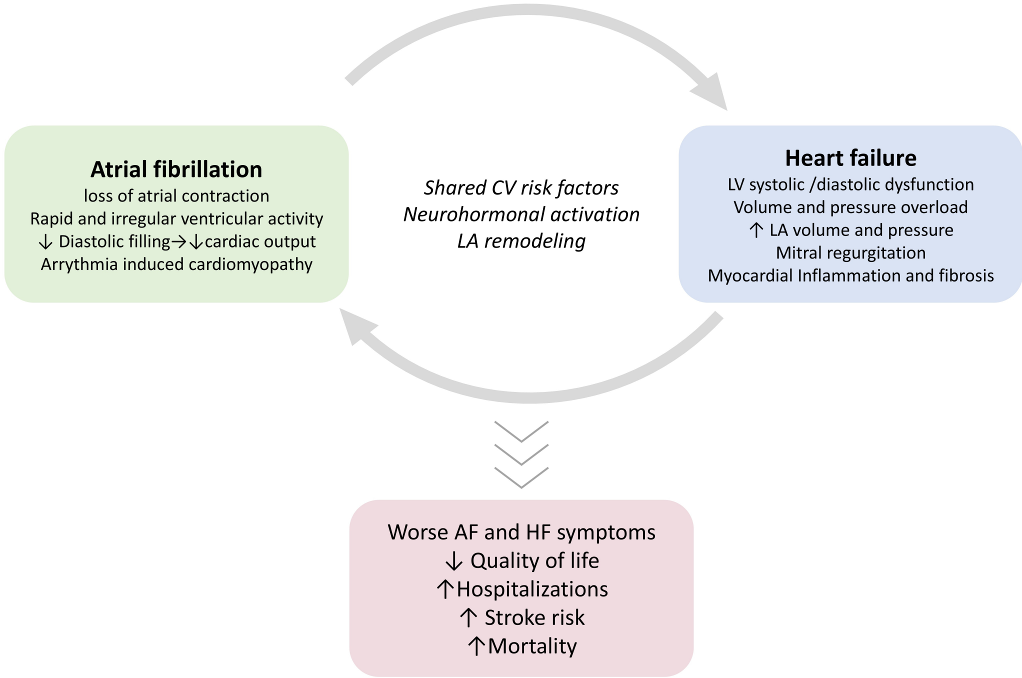

Fig. 1. Pathophysiological interactions between atrial fibrillation and heart failure. AF and HF share common risk factors and exacerbate each other through multiple mechanisms, contributing to worsening symptoms and prognosis. Figure created using Microsoft PowerPoint, Version 2410 (Build 18129.20158, developed by Microsoft Corporation, headquartered in Redmond, WA, USA). Abbreviations: AF, atrial fibrillation; CV, cardiovascular; HF, heart failure; LA, left atrium; LV, left ventricle.

tunately, this condition is often reversible with the restoration of sinus rhythm or effective rate control (Shinbane et al, 1997; Simantirakis et al, 2012).

Prevalence, Clinical Presentation, and Outcomes

Among patients with HF, the prevalence of AF increases significantly with age and worsening functional class, ranging from approximately 5% in New York Heart Association (NYHA) class I to up to 40% in NYHA class IV (De Ferrari et al, 2007; Maisel and Stevenson, 2003). AF is especially common in HFpEF. Data from the Swedish HF Registry illustrate this trend, showing an increase in AF prevalence across the HF spectrum: 53% in those with HFrEF, 60% in those with HFmrEF, and up to 65% in patients with HFpEF. The study also found that AF was associated with higher risks of mortality, HF hospitalization, and stroke across all HF subtypes (Sartipy et al, 2017). Patients with AF who develop HF have twice the risk of stroke and thromboembolism (Rohla et al, 2019) and suffer from higher all-cause mortality (Kotecha et al, 2016a). Interestingly, AF tends to precede rather than follow HF, especially in cases involving HFpEF (Santhanakrishnan et al, 2016).

The clinical picture in patients with both AF and HF is often more severe than in those with either condition alone. AF frequently serves as a trigger for acute HF episodes. Overlapping symptoms—such as dyspnea, fatigue, and exercise intolerance—can complicate the clinical assessment of AF in HF patients, particularly in HFpEF (Kotecha et al, 2016b). Determining whether AF is the primary driver of symptoms can be challenging. In such cases, AF may reasonably be considered a contributing factor to diminished cardiac function or worsening HF when no other cause is apparent.

Management of Concomitant AF and HF

Managing AF in patients with HF requires a comprehensive approach. The primary goals include controlling cardiovascular risk factors, preventing stroke, and optimizing HF management through guideline-directed medical and device therapies. Once these foundational elements are addressed, symptom management with rate or rhythm control strategies is considered (McDonagh et al, 2021; NICE, 2021; Van Gelder et al, 2024). Fig. 2 outlines a proposed management algorithm for AF and HF.

Risk Factor Management

Identifying and managing risk factors for HF and AF is essential for improving symptom control, slowing disease progression, and enhancing prognosis. The latest European Society of Cardiology (ESC) AF guidelines highlight several key targets as part of comprehensive AF management, all of which are Class I recommendations. These include maintaining blood pressure at a target of 120–129 mmHg/70–79 mmHg (or as low as reasonably achievable), achieving effective glycemic control for patients with diabetes, implementing a weight loss program with at least a 10% weight reduction for overweight patients, following a tailored exercise plan for regular moderate or vigorous activity, and reducing alcohol consumption to three or fewer standard drinks per week (Van Gelder et al, 2024). The Routine versus Aggressive Upstream Rhythm Control for Prevention of Early Atrial Fibrillation in Heart Failure (RACE) 3 trial demonstrated that in patients with AF and HF, targeted treatment of HF and related conditions—hypertension, hyperlipidemia, and obesity—with angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs), mineralocorticoid receptor antagonists (MRAs) and statins, combined with physical activity and cardiac rehabilitation, was more effective at maintaining sinus rhythm at one year compared to standard treatment (Rienstra et al, 2018).

Optimization of HF Treatment

Guideline-directed therapies for HF should be optimized for all patients, as certain treatments may help prevent AF and improve outcomes in those with both conditions. Beta-blockers, ACE inhibitors, and MRAs—all Class I recommendations for HFrEF—are associated with a reduced incidence of AF. While ACE inhibitors and beta-blockers are proven to reduce mortality in HF patients with sinus rhythm, evidence is limited on whether these benefits extend to those with AF (Newman et al, 2024). Nonetheless, these therapies remain essential in HF management, offering additional advantages such as managing comorbidities and alleviating AF symptoms. Angiotensin receptor-neprilysin inhibitors (ARNi) have shown mortal-

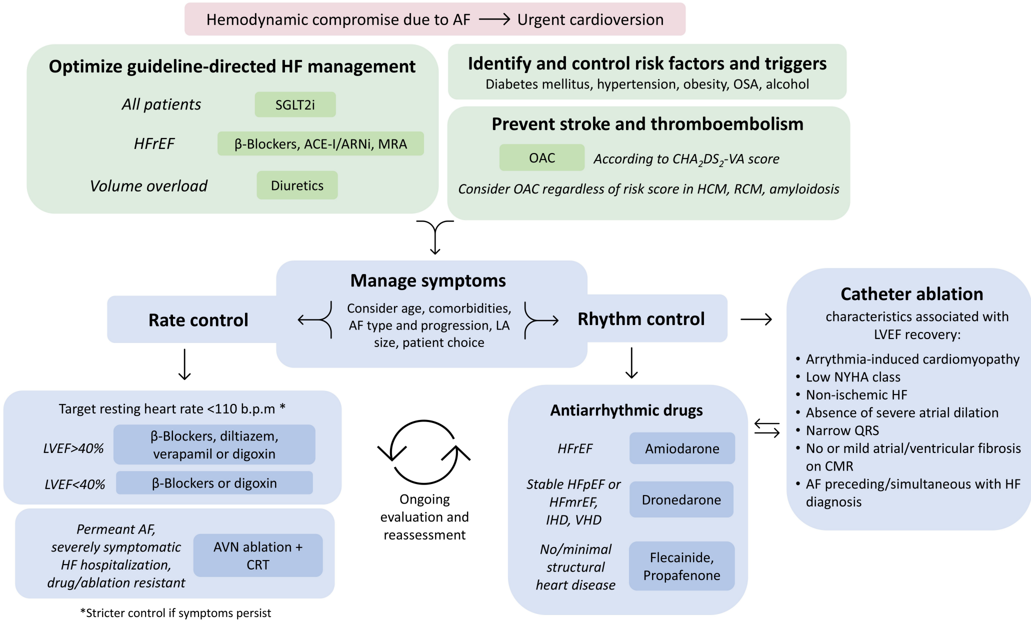

Fig. 2. Management of atrial fibrillation and heart failure. An integrated approach to managing AF and HF based on the 2024 European Society of Cardiology (ESC) and 2023 American College of Cardiology/American Heart Association/American College of Chest Physicians/Heart Rhythm Society (ACC/AHA/ACCP/HRS) guideline. Figure created using Microsoft PowerPoint, Version 2410 (Build 18129.20158, developed by Microsoft Corporation, headquartered in Redmond, WA, USA). Abbreviations: ACE-I, angiotensin-converting enzyme inhibitors; AF, atrial fibrillation; ARNi, angiotensin receptor-neprilysin inhibitors; AVN, atrioventricular node; b.p.m., beats per minute; CMR, cardiac magnetic resonance; CRT, cardiac resynchronization therapy; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; OAC, oral anticoagulation; OSA, obstructive sleep apnea; RCM, restrictive cardiomyopathy; SGLT2i, sodium-glucose cotransporter 2 inhibitors; VHD, valvular heart disease; CHA_2DS_2-VA, Congestive heart failure, Hypertension, Age $\geq$75 years, Diabetes, Stroke/TIA/thromboembolism, Vascular disease, and Age 65–74 years.

ity benefits in HFrEF patients, regardless of whether they are in sinus rhythm or AF (Newman et al, 2024). Sodium-glucose cotransporter 2 (SGLT-2) inhibitors are now recommended as first-line therapy for HF and AF across all LVEF ranges. Although they have not consistently proven effective in preventing AF in HF patients, data from multiple large RCTs show that they reduce cardiovascular mortality and HF hospitalizations in patients with both AF and HF (Newman et al, 2024; Pandey et al, 2021).

The established benefits of cardiac resynchronization therapy (CRT) for reducing symptoms and mortality in eligible HFrEF patients in sinus rhythm may not fully apply to those with AF as a rapid and irregular rhythm can interfere with effective biventricular pacing. This limitation is highlighted by a large U.S. registry which found that two-thirds of patients with persistent or permanent AF failed to achieve a high rate of biventricular pacing, a factor associated with an increased risk of death (Ousdigian et al, 2014). Ensuring consistent biventricular capture is therefore essential, and in some cases, AV node ablation may be necessary to achieve this (Glikson et al, 2021).

Stroke Prevention

AF and HF are independent risk factors for thromboembolism, and their combination markedly elevates this risk (Kang et al, 2017). Based on the CHA_2DS_2-VA risk score (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes, Stroke/TIA/thromboembolism, Vascular disease, and Age 65–74 years), oral anticoagulation should be considered for all AF patients who exhibit symptoms and signs of HF or have documented LVEF ≤40% (Van Gelder et al, 2024). Direct oral anticoagulants are preferred over warfarin, except in cases where the patient has severe mitral stenosis or a mechanical valve prosthesis, for which vitamin K antagonists are advised.

Notably, specific cardiomyopathies, such as hypertrophic cardiomyopathy, cardiac amyloidosis, and restrictive cardiomyopathy, carry an especially high stroke risk. Consequently, the ESC guidelines on the management of cardiomyopathies recommend prophylactic anticoagulation for patients with AF in these specific groups, regardless of their CHA_2DS_2-VA score or presence of clinical HF (Arbelo et al, 2023).

Rate and Rhythm Control in AF and HF—General Considerations

For many years, the primary goals of rate and rhythm control have been symptom relief and improved QoL; routine rhythm control was not recommended. This was based on early RCTs showing no prognostic benefit of rhythm over rate control, both in the general AF population and in those with HF (Freudenberger et al, 2007; Hagens et al, 2005). The Atrial Fibrillation and Congestive Heart Failure (AF-CHF) trial, one of the largest RCTs comparing rate to rhythm strategy in HF patients (LVEF <35% or with symptoms of HF), found no survival benefit associated with antiarrhythmic therapy, primarily using amiodarone. Notably, patients in the rhythm control group experienced higher hospitalization rates, particularly in the first year, likely due to repeated cardioversions and adjustments in antiarrhythmic therapy (Roy et al, 2008). Several factors may explain the findings of these early trials. First, rhythm control largely depended on antiarrhythmic drugs (AADs), whose potential benefits were often offset by side effects. Second, many studies included patients with persistent or long-standing AF, where AADs were less effective.

In contrast, the landmark recent Early Treatment of Atrial Fibrillation for Stroke Prevention Trial (EAST-AFNET) 4 yielded different results. Patients with newly diagnosed AF were randomized to early rhythm control or standard care, primarily involving rate control. Early rhythm control, which included AAD therapy and ablation in approximately 19% of participants, led to a statistically significant 21% reduction in the composite endpoint of cardiovascular death, stroke, heart failure hospitalization, or acute coronary syndrome (Kirchhof et al, 2020). Sub-analysis of patients with symptomatic HF or reduced LV function indicated a similar benefit, particularly in HFpEF cases (Rillig et al, 2021). Additionally, large registries have shown that early rhythm control improves cardiovascular outcomes, including hospitalization and death, whereas delaying treatment for a year or more diminishes these benefits (Dickow et al, 2022; Kim et al, 2021). These findings suggest that early rhythm control may be the preferred approach for managing newly diagnosed AF in both the general population and patients with HF; further trials are needed to validate this approach. Furthermore, recent evidence indicates that rhythm control via ablation reduces hospitalizations and mortality in HF patients (as discussed later), prompting a shift toward recommending it as first-line therapy for selected HF patients in current guidelines (Joglar et al, 2024; Van Gelder et al, 2024).

Numerous factors can influence the choice between rate and rhythm control, including patient age, comorbidities, suspected AIC, AF type and progression, LA size, and individual patient preferences. It is important to note, that rate and rhythm control are not mutually exclusive and may be combined, with the strategy potentially evolving over time. Whenever possible, these decisions should be guided by clinical trial evidence and guideline recommendations (Joglar et al, 2024; Van Gelder et al, 2024).

Rate and Rhythm Control in AF and HF—Specific Recommendations

In cases of acute or worsening hemodynamic instability likely due to AF, immediate electrical cardioversion is recommended. Intravenous amiodarone may also be used for acute rate control in AF patients with advanced HF or cardiogenic shock (Delle Karth et al, 2001; Hofmann et al, 2004). For stable patients with newly diagnosed AF, rate control is typically chosen as the initial approach. If symptoms persist despite achieving adequate rate control, a rhythm control strategy is usually considered. However, in symptomatic patients, when the cause of symptoms is unclear (whether due to AF or HF itself) or when heart dysfunction is suspected to result from AIC, restoring sinus rhythm is recommended as a first step to clarify the clinical picture and improve both symptoms and heart function.

Long-term rate control in HFrEF is usually achieved with beta-blockers, with digoxin used less frequently (Van Gelder et al, 2024). Non-dihydropyridine calcium channel blockers (ND-CCBs) should be avoided in HFrEF due to their negative inotropic effect, which can worsen HF (Goldstein et al, 1991). For rate control in stable patients with LVEF $>$40%, guidelines suggest beta-blockers, ND-CCBs, or digoxin as Class I options (Van Gelder et al, 2024). The optimal heart rate for AF-HF patients remains unclear, as HF patients were under-represented in studies comparing lenient and strict rate control, such as RACE-2 (Van Gelder et al, 2010). Generally, a target heart rate below 110 bpm is accepted, with stricter control ($<$80 bpm) advised for cases of rate-related cardiac dysfunction or in patients with CRT to ensure adequate biventricular pacing (Joglar et al, 2024; Van Gelder et al, 2024).

In patients with severe, symptomatic, permanent AF and a history of HF hospitalizations, a combination of AV node ablation and CRT may be beneficial, based on findings from the Ablate and Pace in Atrial Fibrillation plus Cardiac Resynchronization Therapy (APAF-CRT). This strategy was associated with reduced HF symptoms and hospitalizations, along with improved survival compared to pharmacological rate control alone. Notably, the APAF-CRT trial population had a narrow

QRS complex, a median age of 73 years, included nearly 50% women, and demonstrated benefits regardless of baseline ejection fraction, suggesting this may be a viable option even for HFpEF patients. However, the small sample size (n = 133) limits the interpretation of the mortality difference between groups, and larger trials are needed to confirm a mortality benefit definitively (Brignole et al, 2021)

Rhythm control can be achieved through either medication or ablation therapy. Using AADs in HF is particularly challenging due to potential adverse effects, including an elevated risk of pro-arrhythmia in patients with structural heart disease. Amiodarone is the most effective drug for maintaining sinus rhythm, with evidence supporting similar efficacy in patients with and without LV dysfunction (Cadrin-Tourigny et al, 2014). It is the only recommended AAD for HFrEF, though its extensive extracardiac toxicity and wide range of drug interactions may limit its utility (Van Gelder et al, 2024). Dronedarone, which has a better safety profile than amiodarone, can be used in patients with HFpEF or mildly impaired LV function but is less effective at reducing AF burden. Due to an increased mortality risk, it is contraindicated in patients with unstable HF or in those in NYHA class III or IV (Hohnloser et al, 2010; Køber et al, 2008). Class Ic AADs, such as flecainide and propafenone, are appropriate only for patients with normal heart function. These drugs should be avoided in individuals with impaired LV function, severe LV hypertrophy, or coronary artery disease, as they carry a risk of life-threatening arrhythmias in these populations (Joglar et al, 2024; Van Gelder et al, 2024).

AF Ablation in HF Patients

Catheter ablation of AF is a widely recognized and effective treatment for maintaining sinus rhythm. The procedure involves isolating the pulmonary veins either through radiofrequency ablation or cryoablation, to block the ectopic activity that triggers AF. CA has been shown to be superior to AADs in preventing arrhythmic recurrences in both the general population with AF and patients with HF (Chen et al, 2020; Di Biase et al, 2016). Additionally, studies in the general AF population indicate that CA is more effective than AADs in delaying the progression from paroxysmal to persistent and long-standing AF (Andrade et al, 2021; Packer et al, 2020). When performed by experienced clinicians, CA is generally safe, with a complication rate of 2–3% and a mortality rate of approximately 0.05% (Benali et al, 2023). Some evidence suggests that HF patients may experience higher rates of complications and post-ablation mortality (Cheng et al, 2019; Ruzieh et al, 2019).

RCTs Evaluating Ablation in HFrEF

Numerous trials have investigated the efficacy and prognostic impact of AF ablation in HF patients, particularly those with HFrEF. Key findings from these studies are summarized below and in Table 1. Early and small RCTs primarily focused on the impact of CA on left ventricular function in patients with HFrEF and persistent AF, often comparing it to rate control strategies. These studies largely found that CA led to greater improvements in LVEF, functional capacity, exercise tolerance, peak oxygen consumption, and QoL (Hunter et al, 2014; Jones et al, 2013; Khan et al, 2008).

Table 1. Summary of key clinical trials evaluating catheter ablation in patients with heart failure.

Study	Sample size	Follow up (month)	Study population	Comparison group	Results	Major limitations
PABA-CHF (Khan et al, 2008)	81	6	LVEF ≤40% NYHA II–III Persistent/paroxysmal AF	AVN ablation + BiV pacing	Ablation improved the composite outcome of LVEF, 6MWT, and QoL scores compared to the control	Small sample size Short follow up
MacDonald, 2011	41	6	LVEF ≤35% NYHA II–IV Persistent AF	Rate control - beta-blockers and/or digoxin	No significant difference in LVEF change or secondary outcomes (NT-proBNP, 6MWT, QoL)	Low procedural success rate High procedural complication rate (15%)
ARC-HF (Jones et al, 2013)	52	12	LVEF ≤35% NYHA II–IV Persistent AF	Rate control - beta-blockers and/or digoxin	Ablation significantly increased peak oxygen consumption compared to rate control and also improved QoL and BNP levels as secondary outcomes	Small sample size Short follow up Extensive ablation strategy used
CAMTAF (Hunter et al, 2014)	50	12	LVEF <50% NYHA II–IV Persistent AF	Rate control	Ablation significantly improved LVEF compared to rate control. Secondary outcomes, including peak oxygen consumption and QoL were also better in the ablation group	Small sample size Short follow up
AATAC (Di Biase et al, 2016)	203	24	LVEF <40% NYHA I–III ICD or CRT-D Persistent AF	Amiodarone	Ablation reduced the primary outcome of AF burden and secondary outcomes of unplanned hospitalizations and mortality compared to amiodarone	Variable in procedural technique among centres Many patients underwent extensive and/or repeat ablation
CAMERA-MRI (Prabhu et al, 2017)	68	6	LVEF ≤45% NYHA II–IV Persistent AF Idiopathic cardiomyopathy	Rate control	Ablation significantly improved LVEF (measured by cardiac MRI) compared to control. Absence of LGE was associated with greater LVEF improvement and normalization post-ablation	Small sample size Short follow up
CASTLE-AF (Marrouche et al, 2018)	363	37.8	LVEF ≤35% NYHA II–IV ICD or CRT-D Paroxysmal/persistent AF Failure, intolerance, or refusal to AAD	Medical therapy (rhythm or rate control)	Ablation reduced the primary composite outcome of all-cause mortality or HF hospitalization. Secondary outcomes, including all-cause mortality, HF hospitalizations, and cardiovascular mortality, were also significantly reduced	Highly selected population Failure to reach target sample size Low statistical power High rate of crossover between groups Substantial exclusions and loss to follow-up

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Table 1. Continued.

Study	Sample size	Follow up (month)	Study population	Comparison group	Results	Major limitations
AMICA (Kuck et al, 2019)	202	12	LVEF ≤35% NYHA II–III ICD or CRT-D Persistent/Long-standing AF	Medical therapy (rhythm or rate control)	No significant difference in the primary endpoint of LVEF improvement or secondary outcomes, including NT-proBNP, 6MWT, or QoL	Terminated early for futility 12% of patients could not be assessed for primary outcome due to unanalyzable/missing data
RAFT-AF (Parkash et al, 2022)	411	37.4	NYHA II–III HF High-burden paroxysmal/persistent AF Elevated NT-proBNP	Rate control	No significant difference between groups in the primary composite outcome of all-cause mortality and HF events. Secondary endpoints showed improvements in LVEF, 6MWT, NT-proBNP levels, and QoL with ablation	Terminated early due to futility, low recruitment, lower-than-expected event rate Serious adverse events occurred in 50% of both groups
CASTLE-HTx (Sohns et al, 2023)	194	18	LVEF ≤35% NYHA II–IV Referred for heart transplant/LVAD Presence/indication for cardiac implantable device Paroxysmal/persistent AF	Guideline-directed medical therapy	Ablation reduced the composite outcome of death, LVAD implantation, or urgent heart transplantation compared to medical therapy. Secondary outcomes showed individual reductions in all-cause mortality and LVAD implantation with ablation	Small, single-center study Highly selected population Few major events with a very large effect size raised reproducibility concerns

Abbreviations: AAD, antiarrhythmic drugs; AF, atrial fibrillation; AVN, atrioventricular node; BiV, biventricular; BNP, B-type natriuretic peptide; CRT-D, cardiac resynchronization therapy with a defibrillator; HF, heart failure; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; LVAD, left ventricular assist device; MRI, magnetic resonance imaging; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; QoL, quality of life; 6MWT, 6-minute walk test; AATAC, Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device; CAMERA-MRI, Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction; CASTLE-AF, Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction and Atrial Fibrillation; AMICA, Atrial Fibrillation Management in Congestive Heart Failure With Ablation; RAFT-AF, Randomized Ablation-Based Rhythm-Control Versus Rate-Control Trial in Patients With Heart Failure and Atrial Fibrillation; CASTLE-HTx, Catheter Ablation for Atrial Fibrillation in Patients with End-Stage Heart Failure and Eligibility for Heart Transplantation; PABA-CHF, Pulmonary Vein Antrum Isolation versus AV Node Ablation with Bi-Ventricular Pacing for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure; ARC-HF, A Randomized Trial to Assess Catheter Ablation Versus Rate Control in the Management of Persistent Atrial Fibrillation in Heart Failure; CAMTAF, Catheter Ablation Versus Medical Treatment of Atrial Fibrillation in Heart Failure.

Unlike most studies, which included diverse HF causes (mainly ischemic), the Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction (CAMERA-MRI) trial focused on patients with idiopathic cardiomyopathy, excluding those with significant coronary artery disease or other clear causes of LV dysfunction. CA led to significantly greater improvements in LVEF, assessed by cardiac magnetic resonance imaging (MRI), than rate control, along with reductions in chamber size, B-type natriuretic peptide (BNP) levels, and NYHA class. This suggests that AF-related cardiomyopathy is not solely rate-dependent, as adequate rate control did not reverse LV dysfunction in the control group; factors like ventricular irregularity and neurohormonal activation may also contribute. Additionally, the study found that the absence of late gadolinium enhancement (LGE) was linked to greater LVEF improvement, suggesting that MRI assessment of myocardial viability may help predict CA benefits (Prabhu et al, 2017).

The Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device (AATAC) trial compared CA to amiodarone in individuals with persistent AF and symptomatic HFrEF. In the ablation group, the primary outcome of freedom from AF recurrence at 24 months was higher, and secondary outcomes demonstrated a 45% relative reduction in unplanned HF hospitalizations and a 56% relative reduction in mortality compared to the amiodarone group (Di Biase et al, 2016). Although it was not designed to assess clinical outcomes, it was one of the first RCTs to suggest a positive prognostic impact of AF ablation in HF patients. Notably, many patients in the study underwent extensive ablation, and the protocol allowed for multiple procedures in the ablation group without a standardized approach for repeat ablation. Furthermore, variability in procedural technique was observed among centres.

Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction and Atrial Fibrillation (CASTLE-AF) stands as a landmark study evaluating hard clinical outcomes in symptomatic AF patients (both paroxysmal and persistent) with LVEF $<35\%$ and NYHA class II–IV. To be included, patients needed either prior failure of AAD therapy or a reluctance to take AADs, along with an implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy with a defibrillator (CRT-D) to monitor AF recurrence. Participants were randomized to receive either CA or medical therapy. Outcomes showed that the primary composite endpoint of death or HF hospitalization was significantly lower in the ablation group (28.5% vs. 44.6%; $p = 0.007$), with secondary reductions in all-cause and cardiovascular mortality (Marrouche et al, 2018). While the positive findings from this trial have influenced the latest AF management guidelines, several limitations should be considered when applying them to real-world settings. The CASTLE-AF study population was highly selective, with only 398 of 3013 patients assessed for eligibility ultimately enrolled for randomization. Interestingly, a U.S. administrative database study of nearly 290,000 patients found that only 7.8% met the CASTLE-AF eligibility criteria (Dickow et al, 2022). Unlike the general HF population, the ablation group in the study had a median age of 64 years, 87% of participants were men, and the median LVEF was 32%, with most patients (58%) classified as NYHA class II. Notably, subgroup analysis revealed that patients with LVEF <25%, NYHA class >II, diabetes, or age >65 years did not show significant benefit from ablation. Other limitations included low statistical power due to a low number of primary outcome events and a high rate of loss to follow-up. Notably, the mortality benefit of ablation only emerged at 3 years, with about half of the participants still under follow-up.

In contrast to the positive findings of CASTLE-AF, the Randomized Ablation-Based Rhythm-Control Versus Rate-Control Trial in Patients With Heart Failure and Atrial Fibrillation (RAFT-AF) did not demonstrate a significant prognostic benefit of catheter ablation. This trial compared CA to rate control in HF patients (NYHA class II–III) with elevated levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP) and high-burden paroxysmal or persistent AF. Although significantly more patients in the ablation group maintained sinus rhythm (85% vs. 13% at 24 months), there was no significant difference in the primary composite outcome of all-cause mortality and HF events. Event rates were numerically lower in the CA group, particularly among patients with EF ≤45%. The study was terminated early due to low enrollment and apparent futility, potentially reducing the study's power to detect a statistically significant result. Also, as differences in primary outcomes only became apparent after 18 months (similarly to CASTLE-AF in which mortality difference was apparent only after 2 years), a longer study duration might have yielded different results. Improvements in secondary outcomes, including LVEF, QoL, NT-proBNP, and exercise tolerance, were observed in the ablation group; Yet, these findings remain exploratory due to the lack of adjustment for multiple comparisons (Parkash et al, 2022).

Another negative study, the Atrial Fibrillation Management in Congestive Heart Failure With Ablation (AMICA) trial, was also terminated early due to futility and showed no benefit of CA over best medical therapy in improving LVEF at 1 year or in secondary outcomes, including the 6-minute walk test, QoL, and NT-proBNP. Patients in this study had persistent or longstanding persistent AF and LVEF <35%. However, the AMICA population included sicker HF patients compared to other studies. Specifically, compared to the CASTLE-AF population, the AMICA ablation group included more patients with longstanding persistent AF, a lower LVEF (27.6% vs. 32.5%), and a higher proportion of patients in NYHA class III or IV (60% vs. 31%). These differences were proposed as an explanation for the negative findings, suggesting that patients with advanced HF are less likely to benefit from AF ablation. The study's short follow-up might also explain these negative findings as longer time might be necessary for reverse remodelling to occur and LVEF to improve in severe HF (Kuck et al, 2019).

The most recent trial, Catheter Ablation for Atrial Fibrillation in Patients with End-Stage Heart Failure and Eligibility for Heart Transplantation (CASTLE-HTx) focused on patients with end-stage HF who were referred for heart transplantation or left ventricular assist device (LVAD) implantation and had LVEF <35%, symptomatic HF, and impaired functional capacity. Notably, patients were required to be clinically stable at the time of randomization. The ablation group was compared to AF medical therapy (including both rate and rhythm control). The trial was terminated early due to the overwhelming efficacy observed in the CA arm, showing a significant reduction in the primary composite outcome of all-cause mortality, LVAD implantation, or urgent heart transplantation compared to medical therapy (8% vs. 30%; $p < 0.001$) at a median follow-up of 18 months (Sohns et al, 2023). Despite these promising results, the study has been criticized and should be interpreted with caution. First, it was a small, single-center, and unblinded study. Second, CA showed a much larger effect on outcomes than previously reported in other studies. Although CA reduced AF burden by only 30% at one year, it was associated with nearly a 70% reduction in all-cause mortality compared to the control group, raising concerns about methodology and reproducibility. Lastly, the study population may not accurately represent true end-stage HF. The ablation group had a median age of 62 years, a median LVEF of 29%, and one-third of patients were classified as NYHA class II. Most patients did not undergo the comprehensive assessments typically required for this classification. Notably, the 1-year mortality rate even in the control group was also significantly lower than expected for end-stage HF, suggesting the inclusion of more stable patients with less advanced disease (Mewton et al, 2024).

Collectively, these studies suggest that CA can reduce all-cause mortality and hospitalizations in HF patients compared to medical therapy alone (Chen et al, 2020; Simader et al, 2023; Zhang et al, 2024). Reduced AF burden, improved LVEF, and enhanced biochemical markers of HF with CA indicate that maintaining sinus rhythm may promote structural remodelling, ultimately contributing to a better prognosis. This highlights the importance of preserving physiological atrial function for overall cardiac health. Nevertheless, based on these studies, it is not yet possible to provide definitive recommendations for the use of ablation in the broader HF patient population due to several limitations. These include small sample sizes, open-label designs, and variable control groups. Additionally, most studies had follow-up periods of less than a year, restricting the evaluation of CA's long-term effects on LV function and prognosis. Most importantly, as previously mentioned, the inclusion of highly selected patient populations limits the applicability of these findings to real-world settings (McMurray et al, 2014; Vaduganathan et al, 2022). Two additional important considerations should be noted. First, QoL was inconsistently reported in larger studies, which primarily focused on mortality and hospitalization rates. From a patient perspective, both mortality and QoL are critical, as patients often prioritize maintaining functional status and well-being, even when survival remains unchanged. Second, only a few trials have been conducted in the modern era of the "four pillars" of HFrEF therapy: beta-blockers, ARNi, mineralocorticoid receptor antagonists, and SGLT-2 inhibitors. The introduction of these therapies has significantly improved HF management and outcomes, potentially altering the context in which AF ablation is evaluated.

Trials Evaluating Ablation in HFrEF

HFpEF represents nearly half of all HF cases and is expected to become the predominant form. Registry data show that AF is more strongly associated with the development of HFpEF than HFrEF (Santhanakrishnan et al, 2016). Additionally, AF occurs in two-thirds of HFpEF patients at some point in the disease course and is associated with increased mortality risk (Zakeri et al, 2013). Due to its overlapping clinical features with AF, HFpEF is often underdiagnosed and undertreated in patients with both conditions. There is a significant gap in the literature regarding the clinical outcomes of CA in HFpEF, as no dedicated prospective RCTs have been conducted in this group. Most of the available evidence comes from registry and observational data, suggesting that in patients with HFpEF, CA reduces AF recurrences (Aldaas et al, 2021; Yamauchi et al, 2021) and lowers the risk of cardiovascular events compared to drug therapy, similar to its effects in HFrEF (Ishiguchi et al, 2022; von Olshausen et al, 2022).

A recently published, small, randomized trial was the first to evaluate CA in strictly defined HFpEF patients confirmed by hemodynamic criteria. Compared to medical therapy, patients undergoing CA showed significant improvements in hemodynamic parameters, including peak pulmonary capillary wedge pressure, cardiac output, and NT-proBNP levels, along with symptom relief and enhanced exercise capacity. Notably, half of the patients in the CA arm no longer met invasive hemodynamic criteria for HFpEF post-ablation, suggesting a possible reversal of cardiac dysfunction (Chieng et al, 2023). While the study's small sample size of 31 patients limits the strength of its conclusions, it nonetheless provides proof-of-concept for the physiological benefits of CA in this population.

Post-hoc analysis of the Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) trial provides one of the largest sources of data on HFpEF, including 778 patients with symptomatic HF, most of whom are considered to have preserved heart function. The study found that CA reduced AF burden and improved survival and QoL compared to medical therapy. However, this analysis has been debated, as HF was not clearly characterized or objectively confirmed; diagnoses were based on symptoms and functional status, which may have been related to AF rather than HF. Additionally, LVEF data was available for only 73% of patients diagnosed with HF (Packer et al, 2021).

Further research, including dedicated and adequately powered prospective RCTs, is needed to determine whether CA improves prognosis in this growing patient population.

Ongoing Clinical Trials

Several ongoing trials aim to address unanswered questions and bridge the knowledge gaps mentioned earlier. The Cryoballoon/Radiofrequency Ablation of Atrial Fibrillation Versus Medical Treatment for Heart Failure (CRAAFT-HF) trial (ClinicalTrials.gov: NCT06505798), a collaboration between the British Heart Rhythm and British Heart Failure Societies, will evaluate the prognostic effects of CA in patients with LVEF $<50\%$. Its primary outcomes include all-cause mortality and urgent cardiovascular hospitalizations at 2 years, with QoL also being assessed. With planned enrollment of 1200 patients, the inclusion criteria are designed to reflect a more "real-world" HF population, also incorporating patients treated with contemporary guideline-directed medical therapy for HF.

The DanAblate-HF trial (ClinicalTrials.gov: NCT06560047) investigates whether early CA in HFrEF patients (clinically assessed and with LVEF <50%) diagnosed with AF within the past 12 months is superior to standard guideline-directed treatment for AF and HF. Primary outcomes include hospitalization for worsening HF and cardiovascular mortality at 1 year. This trial also represents a large-scale effort, with a planned enrollment of 1600 patients.

Two trials are currently evaluating the long-term clinical outcomes of CA in patients with HFpEF. CABA-HFPEF (ClinicalTrials.gov: NCT05508256) focuses on comparing CA to usual medical care in individuals with heart failure with preserved ejection fraction (HFpEF) or mildly reduced ejection fraction (HFmrEF). Its primary outcome includes a composite of cardiovascular death, stroke, and total (first and recurrent) unplanned cardiovascular hospitalizations for heart failure or acute coronary syndrome. In the Catheter Ablation in Atrial Fibrillation Patients With HFpEF (STABLE-SR) IV trial (ClinicalTrials.gov: NCT06125925), researchers are investigating whether radiofrequency catheter ablation offers superior outcomes compared to AADs in AF patients with HFpEF who are on optimized therapy for heart failure.

Guideline Recommendations and Patient Selection for Ablation

The newly published ESC 2024 Guidelines on AF management recommend ablation for HF patients as follows:

• For selected patients with HFrEF: Ablation should be considered to improve survival and reduce HF hospitalizations (Class of Recommendation [COR] IIa, Level of Evidence [LOE] B).

• For patients with a high likelihood of tachycardia-induced cardiomyopathy: Ablation is recommended regardless of symptoms, to reverse LV dysfunction (COR I, LOE B).

Additionally, ablation is suggested within a shared decision-making framework for all AF patients, regardless of whether they have HF, to manage symptoms and to reduce AF progression. It is recommended as first-line therapy for paroxysmal AF or as second-line therapy after failure or intolerance of drug therapy (Van Gelder et al, 2024).

Similarly, the 2023 American College of Cardiology/American Heart Association/American College of Chest Physicians/Heart Rhythm Society (ACC/AHA/ACCP/HRS) Guidelines for the Diagnosis and Management of AF recommend ablation as a first-line therapy for patients with HFrEF who are on guideline-directed medical therapy and are likely to benefit from the procedure, with the goal of improving symptoms, QoL, and prognosis (COR I, LOE A).

It should be noted that in contrast to the AF guidelines, the ESC HF guidelines do not provide similar recommendations for ablation, as they note that the positive effects of ablation on mortality and hospitalization were based on a relatively small number of events in RCTs, preventing definitive conclusions or recommendations (McDonagh et al, 2021).

In the context of HFpEF, the ESC guidelines do not provide specific recommendations for CA, stating that its prognostic value in this population is less well-established compared to HFrEF (Joglar et al, 2024). The ACC/AHA/ACCP/HRS Guidelines do include a specific recommendation suggesting that ablation may be useful for appropriate patients with symptomatic AF and HFpEF, when there is a reasonable expectation of benefit, with the goal of improving symptoms and QoL (COR IIa, LOE B-NR) (Joglar et al, 2024)

To maximize the benefits of AF CA in HFrEF patients, careful patient selection is essential. A 2024 Collaborative Consensus Statement by leading Heart Rhythm Societies on CA of AF identifies specific characteristics associated with LVEF recovery in patients with impaired LV systolic function. These include the absence of severe atrial dilation (LA volume index $<$50 mL/m^2), lower NYHA class, non-ischemic HF etiology, a narrow QRS complex, and the absence of atrial or ventricular fibrosis as detected by cardiac MRI. Additionally, the consensus paper suggests that patients with simultaneous AF and HF diagnosis, or those in whom AF precedes HF diagnosis, are more likely to experience LVEF normalization and resolution of HF symptoms following ablation. Post-cardioversion improvements in functional status and/or ventricular function can also help identify patients with underlying AIC who are likely to respond favourably to CA (Tzeis et al, 2024). It should be noted that even patients with less favorable characteristics for AF ablation may still experience improvements in heart function and prognosis. Ultimately, decisions should be individualized and involve shared decision-making with the patient.

Discussion

The concurrence of AF and HF presents a common clinical challenge characterized by unique pathophysiological interactions and poorer outcomes. Patients with both conditions require a nuanced therapeutic approach that addresses multiple aspects of treatment. The evidence outlined in this article supports CA as superior to medical therapy in reducing AF burden and promoting LV remodelling, with promising effects on reducing mortality and hospitalisation rates in HF patients. Nevertheless, questions persist regarding the durability of these prognostic benefits across a broader, real-life population, including sicker patients with advanced HF and those with HFpEF. Further investigation is crucial to ascertain whether these patients will enjoy both improved QoL and extended survival. Fully integrating AF ablation into clinical practice for HF will require robust evidence from larger, well-designed RCTs that incorporate current evidence-based optimal medical therapy to establish clear guidelines for its use.

Conclusion

CA is an important therapeutic option for managing AF in HF, particularly in patients with reduced EF, to improve symptoms and LV function. Awareness of current evidence is essential for selecting appropriate patients, in whom ablation may be offered as first-line therapy to improve survival and reduce hospitalizations.

Ongoing evidence from well-designed trials will be crucial to further guide its integration into broader HF populations and clinical practice.

Key Points

- Atrial fibrillation (AF) and heart failure (HF) frequently co-exist, sharing a complex bidirectional relationship, exacerbating each other and worsening patient prognosis.
- Randomized trials in heart failure with reduced ejection fraction (HFrEF) have demonstrated that catheter ablation (CA) improves left ventricular function and functional capacity. Recent data also indicate reduced hospitalizations and mortality.
- However, these trials involve highly selected populations and have limitations that affect their generalizability, often excluding patients with preserved ejection fraction.
- Ongoing trials in real-world populations receiving optimal modern HF therapy will determine whether these findings are reproducible for hard endpoints, such as cardiovascular hospitalizations and mortality.
- Currently, CA should be selectively used as a first-line treatment for HF patients, guided by clinical trial evidence and factors associated with favourable outcomes.

Availability of Data and Materials

This article is based on a comprehensive review of the literature on this topic. The reference list includes all sources used, and all relevant data and materials are provided in the manuscript.

Author Contributions

PDL and YBBG planned and designed the article. YBBG composed the original draft, and PDL reviewed and edited it. Both authors contributed to significant editorial changes, participated sufficiently in the work, and read and approved the final manuscript. They agree to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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