

The management in the patients with atrial fibrillation and dilated cardiomyopathy

Abstract

Atrial Fibrillation (AF) not only maintains itself but also becomes closely linked with Left Ventricular (LV) dysfunction, creating a complex clinical picture for clinicians. Furthermore, Dilated Cardiomyopathy (DCM), marked by LV dysfunction and chamber dilation, adds another layer of complexity to patient management. The coexistence of AF and DCM poses significant challenges, requiring a nuanced approach to treatment. The recent consensus update has elevated catheter ablation to a Class I recommendation for treating patients with AF and Heart Failure (HF), affirming its effectiveness. However, the literature often overlooks patients specifically with DCM, revealing a notable gap and underscoring the critical need for tailored treatment strategies for this subgroup. This review aims to clarify the terms and pathophysiology related to AF and DCM, exploring tailored treatment options for patients dealing with both the conditions. By covering medical therapy, catheter ablation, device implantation, and novel mechanical net therapy, this comprehensive review seeks to offer valuable insights into managing this unique subset of AF patients effectively.

Keywords: Atrial fibrillation; Dilated cardiomyopathy; Catheter ablation; Medical therapy

Introduction

Atrial Fibrillation (AF) and dilated Left Ventricle (LV) dysfunction accompanied by Heart Failure (HF) frequently occur together. The presence of LV dysfunction in patients with AF was identified by Mackenzie et al. a century ago [1]. The prevalence of HF in AF patients ranges from 15% to 27% [2,3]. A recent study disclosed that over one-third (37%) of patients with new-onset Atrial Fibrillation (AF) developed Heart Failure (HF), whereas more than half (57%) of patients with HF developed AF [4]. The prognosis becomes less favorable when HF is diagnosed before AF, as opposed to diagnosing AF before HF [5].

Dilated Cardiomyopathy (DCM) is defined not only by impaired Left Ventricular Ejection Fraction (LVEF) but also by dilation of the left ventricular chamber. DCM is a cardiac disease that leads to severe morbidity and mortality due to arrhythmias and heart failure [6]. The prognosis for DCM was historically poor. However, survival rates have significantly improved, rising from 55% to 87% following the widespread prescription of optimal medication and treatment of underlying diseases [7].

Literature Review

AF begets AF and HF; the presence of these two conditions within a single individual markedly elevates the risk of morbidity and mortality. This mini review article is dedicated to exploring a comprehensive approach to managing this intricate subset of patients suffering from both DCM and AF.

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Terminology and classification

AF is defined as atrial arrhythmia with the absence of discernible P waves and an irregularly irregular ventricular rhythm. Previously, it was classified based on onset and duration as paroxysmal, persistent, long-standing persistent, and permanent [8]. However, in the recent 2023 ACC/AHA/ACCP/HRS guidelines, a new classification was proposed, categorizing AF as follows: At risk for AF, pre-AF, AF (including paroxysmal AF, persistent AF, long-standing persistent AF, and successful AF ablation), and permanent AF [9]. This new proposed classification aims to detect AF in its early stages and tailor treatment strategies accordingly.

DCM is defined as left ventricular or biventricular dilatation and reduced LVEF in the absence of secondary causes such as hypertension, ischemic heart disease, valvular disorders, or congenital heart disease [10,11]. In other words, DCM is an idiopathic disease and a diagnosis of exclusion. The 2016 ESC group proposed a clinical spectrum for DCM, dividing it into pre-clinical and clinical phases [12]. This proposal aimed to facilitate early screening and detection of asymptomatic patients with genetic risk factors to halt disease progression. However, as genetic testing may not be widely available, excluding genetic causes of DCM is becoming increasingly challenging.

Pathophysiology

AF leads to atrial stunning and the loss of atrial transport function, resulting in reduced Left Ventricular (LV) filling and decreased cardiac output [13]. The irregular Left Ventricular (LV) response and contraction, resulting in low cardiac output, can ultimately lead to arrhythmia-induced cardiomyopathy. This condition exacerbates preexisting LV dysfunction and chamber dilatation [14-16]. Elevated LV dysfunction leads to increased Left Atrial (LA) pressure, resulting in LA dilatation [17,18]. Ultimately, LA dilatation is associated with a significant shortening of the LA refractory period and an increased likelihood of developing AF [19].

Treatment strategies

Extensive research has historically been devoted to identifying the most effective treatment strategy for managing atrial fibrillation, with a particular focus on the debate between rhythm control and rate control [20-23]. These studies showed neutral results when comparing rhythm control with rate control in managing AF patients. AATAC was one of the first studies to demonstrate the superiority of CA in improving survival in AF patients compared to amiodarone [24]. Subsequent studies, such as CASTLE-AF and CASTLE-HTx, further demonstrated that CA improved mortality outcomes in patients with AF and LV dysfunction compared to medical therapy alone [25,26].

Risk factor modification

Risk modification is essential before proceeding with invasive management in patients with AF and DCM. Obesity has been shown to increase inflammatory infiltration, atrial fibrosis, and shorten the effective refractory period of the pulmonary veins, thereby contributing to the progression into AF substrate in animal models [27,28]. A large cohort study showed that the incidence of AF was among physically active individuals [29]. Smoking and alcohol consumption have been shown to increase the incidence of AF, and cessation of both tobacco and alcohol use is recommended for patients with AF [30,31]. Additionally, blood glucose control lowers the risk of AF incidence [32,33]. Therefore, risk modification is advised for patients with AF, which includes weight loss, engaging in moderate exercise, cessation of smoking, moderation or abstention from alcohol, and controlling blood glucose levels in cases of diabetes mellitus.

Guideline-directed medical therapy

Guideline-Directed Medical Therapy (GDMT), also known as the “four pillars,” remains the mainstay strategy in chronic HF patients. The medications include an angiotensin-converting enzyme inhibitor or angiotensin receptor-neprilysin inhibitor, a beta blocker, a mineralocorticoid receptor antagonist, and a sodium-glucose cotransporter-2 inhibitor [34]. These medications may be initiated simultaneously at low doses as much as the patient is able to tolerate. Alternatively, clinicians may initiate them sequentially and add another medication without achieving target dosing of the previous one.

In clinical practice, patients frequently request the discontinuation of heart failure medications once there is an improvement in LVEF. However, previous studies have documented a deterioration in LVEF following withdrawal, and some patients did not regain their improved status despite resuming GDMT after a worsening of heart failure symptoms [35,36]. Therefore, GDMT should be maintained, and withdrawal is not recommended at any stage of treatment until further studies conclusively address this issue.

Rate control

Heart rate is one of the predictors of Cardiovascular (CV) outcomes in HF patients. The SHIFT trial showed that isolated heart rate reduction led to a substantial reduction in CV mortality and HF hospitalization [37]. This result was consistent with another study in DCM and AF patients, in which heart rate optimization improved long-term CV outcomes [38]. In HF patients with AF, beta-blockers and digoxin are effective in rate control. Particularly, digoxin should be combined with other rate control agents or prescribed as monotherapy if the patient cannot tolerate it [39]. On the other hand, non-dihydropyridine calcium channel blockers

such as diltiazem and verapamil should be avoided in HF patients [40].

Stroke prevention

Prevention of stroke in AF patients is essential not only to improve survival but also quality of life especially in the patients with DCM. Several AF risk scores have been developed such as CHA2DS2-VASc2 [41], ATRIA [42], GARFIELD-AF [43] and mCHA2DS2-VASc [44]. Among these scores, CHA2DS2-VASc2 is the most common, widely used and validated [9]. The current guidelines recommend initiating oral anticoagulants in patients with CHA2DS2-VASc2 ≥ 2 in men and ≥ 3 in women. For AF patients with CHA2DS2-VASc2 of 1 in men and 2 in women, it is reasonable to initiate oral anticoagulant to prevent stroke and systemic thromboembolism [9]. Impaired cardiac function is one of the key indicators in the assessment of stroke risk. In the patients with DCM and AF, the assessment and initiation of stroke prevention is essential.

Vitamin K Antagonists (VKAs) or warfarin's are still widely prescribed due to their lower cost compared to Direct Oral Anticoagulants (DOACs). Warfarin is the preferred option for patients with moderate to severe mitral stenosis or mechanical valve replacement [9]. DOACs, including dabigatran, rivaroxaban, edoxaban, and apixaban, are recommended as first-line therapy due to their lower risk of major bleeding compared to warfarin.

However, some major bleeding events with morbidity and mortality still occurred with DOACs. Thus, novel anticoagulant agents, such as factor XI/XIa inhibitors, are being investigated with the aim of achieving more precise anticoagulation and preventing major bleeding. The AZALEA-TIMI 71 trial investigated the injection form of abelacimab versus rivaroxaban in AF patients with moderate to high risk of ischemic stroke. The trial was terminated prematurely due to a significant reduction in bleeding events with abelacimab [45]. On the other hand, the OCEANIC-AF trial investigated oral asundexian versus apixaban for AF patients. However, the study was terminated due to the inferior efficacy of the novel agent [45]. Further studies are warranted to validate these novel agents.

Left atrial appendage occluder

In patients deemed contraindicated for oral anticoagulants, Left Atrial Appendage Occlusion (LAAO) has been proven to be non-inferior to VKAs or DOACs in the prevention of ischemic stroke in AF patients [46]. Alternatively, LAAO may also be offered to those who are not keen on long-term oral anticoagulation.

Rhythm control with medications

Most of the anti-arrhythmic agents are contraindicated in HF patients. Oral amiodarone and dofetilide are the only anti-

arrhythmic agents that may be offered to patients with AF and DCM. Oral dronedarone should be avoided in AF and DCM due to worsening LV function and increased early mortality [47]. Oral flecainide, propafenone, and sotalol are not recommended in AF and HF patients due to possible pro-arrhythmia, worsening HF, and even increased mortality [9].

Rhythm control with catheter ablation

In 2023, the ACC/AHA/ACCP/HRS guidelines classified Catheter Ablation (CA) as a class 1 recommendation for patients with AF and HF [9]. When comparing CA with medical therapy, consistent results were found in reducing mortality [24,25,48], improving LVEF [24,25,49-52], and enhancing quality of life [24,50,52]. The majority of previous studies focused on AF and HF patients. However, subsets such as dilated DCM and AF, particularly those with poor LVEF and dilated chambers, were not addressed.

The CAMERA-MRI study demonstrated that CA of AF improved LVEF in patients with dilated LV chambers, with a more significant improvement observed in AF patients without Late Gadolinium Enhancement (LGE) in cardiac magnetic resonance imaging [51]. LGE may serve as one of the stratification tools for screening candidates for AF and DCM. Ribeiro et al. demonstrated a marked improvement in median LVEF from 40% to 58% and a reduction in Left Ventricular Internal Dimension in diastole (LVIDd) from 6.1 cm to 5.5 cm in patients who underwent CA for AF with dilated LV chambers [53].

Furthermore, Zhao et al. focused on CA for AF in patients with DCM and noticed that a more favorable outcome was observed in the subgroup free of atrial tachyarrhythmia after CA. Specifically, a significant absolute improvement in LVEF of 5.3% was observed after 12 months post-CA, but it was not sustained at the 36-month follow-up [54]. Another study showed that in addition to GDMT, CA of AF in DCM patients was proven to be effective in reducing mortality and HF hospitalizations during a mean follow-up of 7 years. In addition to standard medical therapy, there was an improvement in absolute LVEF, a reduction in LAD, LVIDd, and heart rate in patients after receiving CA [38].

Cardiac implantable electronic devices

For patients who are not eligible for or have failed rhythm control, cardiac resynchronization therapy with Atrioventricular Nodal Ablation (AVNA) has been proven to improve survival rates in advanced heart failure patients with AF [55,56]. Conduction system pacing with AVNA as an alternative improves symptoms, functional class, and LV systolic function [57,58].

Emerging treatments

Novel mechanical therapy with a cardiac supporting net for DCM

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has shown promising results [59]. A modified version of the supporting net, featuring a 3D model and individualized design for each patient, demonstrated a prompt reduction in LVIDD and mitral regurgitation in DCM patients [60]. These mechanical supporting nets might offer new possibilities for patients with DCM and AF.

Conclusion

In conclusion, AF ablation, when combined with standard medical therapy, has been proven effective in enhancing overall survival and facilitating cardiac remodeling in both the LA and LV for patients with DCM and AF over the long term. Alternatively, cardiac implantable electronic devices and AVNA serve as viable options for managing this complex subgroup of patients.

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