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# Finerenone in Atrial Fibrillation: Molecular Mechanisms and Emerging Clinical Evidence

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**Abstract:** ***Atrial fibrillation (AF) is a common tachyarrhythmia characterized by disorganized atrial electrical activity and ineffective contraction. It frequently coexists with various cardiovascular diseases and comorbidities, significantly increasing the risk of stroke, heart failure, and other adverse events. The overactivation of the renin-angiotensin-aldosterone system (RAAS), particularly the upregulation of the mineralocorticoid receptor (MR) signaling pathway, plays a central role in atrial remodeling and AF pathogenesis by driving myocardial inflammation and fibrosis. Finerenone, a novel non-steroidal, highly selective MR antagonist, exerts potent antifibrotic and anti-inflammatory effects by efficiently blocking MR. This review systematically elucidates the potential molecular mechanisms of finerenone in AF treatment and summarizes the emerging clinical evidence regarding its role in AF prevention and management, aiming to provide new insights for its application in the comprehensive management of AF.***

**Keywords:** Atrial fibrillation, Finerenone, Eplerenone, Mineralocorticoid, Mineralocorticoid receptor antagonist**.**

## 1. Introduction

Atrial fibrillation (AF) is characterized by the loss of organized atrial electrical activity, replaced by rapid, chaotic fibrillatory waves. This severe atrial arrhythmia abolishes effective atrial contraction.

Data from the Global Burden of Disease (GBD) 2019 study indicate that the global prevalence of AF reached 59.7 million cases, representing a substantial increase compared with 28.3 million in 1990 and 45.6 million in 2010. Nevertheless, the true prevalence is likely higher, as many individuals remain undiagnosed until symptoms develop or an ischemic stroke occurs. Forecasting studies predict that the number of individuals with AF will rise to 15.9 million in the United States by 2050 and to 17.9 million in Europe by 2060 [1,2]. Beyond its high prevalence and the associated public health burden, AF markedly increases the risk of disabling complications such as stroke and heart failure, and is closely linked to cognitive decline and increased all-cause mortality — thereby constituting a systemic continuum of harm that spans the heart, brain, and multiple organ systems.

According to the 2024 ESC/EACTS guidelines for the management of atrial fibrillation, comprehensive AF care can be summarized within the AF-CARE framework [3]. However, while this strategy is effective in symptom control and complication prevention, it remains limited in its ability to directly target—and ultimately reverse—the key atrial remodeling processes that drive AF initiation and maintenance, particularly atrial fibrosis and inflammation. Therefore, therapies aimed at modifying atrial remodeling represent a critical direction for ongoing research.

Finerenone is a selective, non-steroidal mineralocorticoid receptor antagonist (MRA) and is the first non-steroidal MRA approved worldwide for the treatment of chronic kidney disease associated with type 2 diabetes. By efficiently blocking mineralocorticoid receptor signaling, finerenone can suppress pivotal inflammatory and profibrotic pathways implicated in atrial remodeling, thereby holding promise to fundamentally modify the arrhythmogenic substrate and prevent the onset of AF.

This review aims to systematically summarize the potential mechanisms, available clinical evidence, and future perspectives regarding finerenone in the prevention and treatment of AF, providing a theoretical basis to support the expansion of its clinical applications.

## 2. Pharmacological Mechanisms of Finerenone and Differences from Traditional MRAs

### 2.1 Mechanism of Action of Finerenone

Finerenone is a potent and highly selective antagonist of the mineralocorticoid receptor (MR), with negligible affinity for other steroid hormone receptors. It primarily induces MR conformational changes through its side-chain interactions, resulting in displacement of the C-terminal helix 12 and modulation of the receptor's functional domains. By altering the recruitment of coregulatory factors, finerenone affects MR stability, nuclear translocation, and transcriptional activation [4]. Through these actions, it prevents MR overactivation and attenuates MR-mediated sodium reabsorption in both epithelial tissues (e.g., the kidney) and non-epithelial tissues (e.g., the heart and vasculature). Notably, finerenone shows no relevant binding to androgen, progesterone, estrogen, or glucocorticoid receptors.

MR can be activated by aldosterone and cortisol, thereby regulating gene transcription programs that promote inflammation and fibrosis. In contrast, finerenone exerts robust anti-inflammatory and antifibrotic effects by suppressing the downstream expression of key pro-inflammatory and pro-fibrotic mediators [4].

### 2.2 Differences Between Finerenone and Traditional Mineralocorticoid Receptor Antagonists (MRAs)

Although traditional MRAs (e.g., spironolactone and eplerenone) provide well-established cardiovascular benefits, their clinical use remains constrained by safety and pharmacological limitations. Compared with these

conventional agents, finerenone is generally considered to offer a more favorable balance between efficacy and tolerability.

First, finerenone represents a key optimization in both potency and selectivity. As a first-generation MRA, spironolactone is highly potent but lacks receptor selectivity, predisposing patients to adverse effects such as hyperkalemia and antiandrogenic reactions (e.g., gynecomastia). Eplerenone, a second-generation agent, improves selectivity but has relatively limited potency. Finerenone, as a third-generation non-steroidal MRA, combines a potency comparable to spironolactone with a higher selectivity than eplerenone, thereby maintaining therapeutic efficacy while reducing the risk of MRA-related adverse events. In the ARTS (Mineralocorticoid Receptor Antagonist Tolerability Study), patients with heart failure with reduced ejection fraction (HFrEF) and chronic kidney disease treated with finerenone (5 mg/day or 10 mg/day) achieved reductions in BNP, NT-proBNP, and albuminuria that were at least comparable to those observed with spironolactone (25 mg/day or 50 mg/day). Importantly, compared with spironolactone, finerenone was associated with smaller increases in serum potassium, a lower incidence of hyperkalemia, and fewer cases of worsening renal function [5,6].

Second, a distinctive pharmacokinetic feature of finerenone is its more balanced tissue distribution between the kidney and the heart. This relatively even distribution may reduce the risk of adverse effects related to preferential renal accumulation. In contrast, spironolactone and eplerenone tend to accumulate predominantly in the kidney [7]. Such a distribution profile suggests potential advantages for finerenone in cardiorenal protection, enabling concurrent benefits in both organs while minimizing electrolyte disturbances. In hypertension-driven models of heart failure, finerenone has demonstrated protective effects on target organs including the heart and kidney. Notably, when diuretic-equivalent doses are used in chronic models, steroidal MRAs such as eplerenone may require 10–100-fold higher doses to achieve comparable target-organ protection [8].

In addition, non-steroidal MRAs appear to exert more pronounced anti-inflammatory and antifibrotic effects than steroidal MRAs. In a short-term murine model of cardiac fibrosis induced by isoproterenol, finerenone effectively prevented isoproterenol-triggered myocardial fibrosis and macrophage infiltration, whereas eplerenone showed no significant effect [9]. In a transverse aortic constriction (TAC) mouse model, finerenone demonstrated a stronger antihypertrophic effect than eplerenone [10]. Consistently, preclinical studies indicate that at diuretic-equivalent doses, finerenone exhibits more robust anti-remodeling activity than eplerenone [8].

## 3. Pathogenesis and Disease Progression of Atrial Fibrillation

The initiation and maintenance of atrial fibrillation (AF) are closely associated with a “vicious triad” comprising myocardial fibrosis, inflammation, and oxidative stress. An initial insult activates relevant signaling pathways, triggering oxidative stress and inflammatory responses, which subsequently promote fibrotic remodeling. Fibrosis disrupts the structural substrate of atrial conduction, thereby directly facilitating AF onset and perpetuation. Conversely, AF itself can serve as a new injurious stimulus that further amplifies oxidative stress and inflammation, creating a self-reinforcing cycle—often summarized as “AF begets AF.”

## 4. Increased Risk of Atrial Fibrillation Across Multiple Disease States

### 4.1 Chronic Kidney Disease (CKD)

Chronic kidney disease (CKD) is an independent risk factor for the onset and progression of atrial fibrillation (AF). Its arrhythmogenic effects are closely linked to atrial structural remodeling, driven by specific molecular signaling pathways.

#### 4.1.1 CKD-Induced Atrial Fibrosis

CKD promotes pronounced atrial fibrosis, with activation of the transforming growth factor-β1 (TGF-β1)/Smad2/3 pathway recognized as a central mechanism [11]. TGF-β1 is a key regulator coordinating atrial structural remodeling (ASR) and the development of atrial fibrosis across diverse pathological contexts. Through downstream Smad signaling and the pivotal profibrotic mediator connective tissue growth factor (CTGF), this pathway accelerates excessive deposition of extracellular matrix (ECM) components, including type I collagen and α-smooth muscle actin (α-SMA) [12]. Such ECM accumulation disrupts the normal spatial architecture of myocardial fiber bundles, creating a structural substrate that facilitates AF initiation and perpetuation.

In addition, CKD has been associated with increased expression of non-phosphorylated connexin 43 (np-Cx43), reduced expression of Cx40 and phosphorylated Cx43 (p-Cx43), and lateralization of Cx43/Cx40 distribution within the atria—features consistent with connexin (gap junction) remodeling and impaired intercellular electrical coupling [13,14]. Connexins Cx40 and Cx43 are the predominant atrial gap junction isoforms; their orderly localization at the intercalated discs is essential for rapid impulse propagation and the maintenance of sinus rhythm. Any abnormalities in their expression levels, phosphorylation status, or spatial distribution are considered highly proarrhythmic.

#### 4.1.2 CKD-Induced Inflammatory Responses

Upon activation, the NLRP3 inflammasome** catalyzes the cleavage of pro-caspase-1 into active caspase-1, which subsequently processes the precursor cytokines pro–IL-1β and pro–IL-18 into their mature, pro-inflammatory forms, IL-1β and IL-18 [15,16]. In the setting of CKD, this inflammatory axis is markedly upregulated.

Experimental evidence indicates that the pro-inflammatory milieu induced by CKD enhances NLRP3 inflammasome activity within atrial tissue, leading to elevated circulating IL-1β levels. This, in turn, promotes atrial electrical remodeling and fibrosis, thereby increasing susceptibility to AF. Conversely, neutralization of circulating IL-1β using an anti–IL-1β antibody suppresses atrial fibrosis and hypertrophy and effectively prevents AF in CKD models. The

clinical relevance of this mechanism is further supported by observations in dialysis-dependent CKD patients, in whom IL-1β production is significantly higher in those with AF than in those maintaining sinus rhythm [17].

Beyond the NLRP3 inflammasome pathway, angiotensin II (Ang II) represents another pivotal mediator linking inflammation to atrial remodeling. Inflammatory signaling can stimulate Ang II generation, whereas Ang II not only acts as a potent profibrotic factor but also feeds back to amplify inflammatory pathways, thereby establishing a self-perpetuating pro-inflammatory – pro-fibrotic loop. Elevated Ang II activates downstream signaling cascades — including Rac1, CTGF, and NADPH oxidase—and alters the expression and function of connexin 43 (Cx43). Collectively, these mechanisms accelerate atrial structural remodeling and provide a permissive substrate for AF initiation and maintenance.

### 4.2 Heart Failure (HF)

In pathological states such as heart failure (HF), activation of the renin–angiotensin–aldosterone system (RAAS) and the consequent rise in aldosterone levels represent a major mechanistic link to the increased risk of atrial fibrillation (AF).

RAAS contributes to AF development primarily by promoting oxidative stress and profibrotic remodeling. Both angiotensin II (Ang II) and aldosterone generated during RAAS activation facilitate atrial fibrosis, although aldosterone appears to exert a particularly potent profibrotic effect. Aldosterone promotes fibrosis through at least two complementary mechanisms: it triggers inflammatory responses and upregulates connective tissue growth factor (CTGF) in cardiomyocytes. Upon binding to the mineralocorticoid receptor (MR), aldosterone can directly activate profibrotic signaling pathways, and fibrotic remodeling itself is tightly associated with heightened AF susceptibility [18–21].

In addition, aldosterone can enhance renal potassium excretion, lowering serum potassium toward the low-normal range. Hypokalemia reduces the resting membrane potential, thereby increasing cardiomyocyte automaticity; it also prolongs repolarization and facilitates the occurrence of early afterdepolarizations (EADs). These electrophysiological perturbations can act as triggers for AF and re-entrant atrial tachyarrhythmias [22].

Clinical studies provide direct evidence supporting these links. In a long-term follow-up study by Dixen et al. (2006) involving 158 patients with a history of AF who had restored sinus rhythm, higher aldosterone levels were significantly associated with AF recurrence [23]. Moreover, multiple studies have reported that successful cardioversion markedly reduces plasma aldosterone levels in patients with persistent AF [24]. Similarly, in a prospective single-center study of 45 consecutive patients with non-valvular persistent AF and preserved left ventricular systolic function, the magnitude of aldosterone reduction at 24 hours after cardioversion correlated positively with short-term maintenance of sinus rhythm [25]. From a mechanistic perspective, a rat model study by Jan-Christian Reil et al. (2012) demonstrated that exogenous aldosterone exposure prolonged atrial conduction time and aggravated fibrosis and structural remodeling, leading to inducible atrial arrhythmias in all treated animals — significantly more than in controls [22].

### 4.3 Diabetes Mellitus

Diabetes mellitus markedly increases the risk of atrial fibrillation (AF) by inducing both atrial electrical remodeling and structural remodeling, with the synergistic interplay between reactive oxygen species (ROS) and advanced glycation end products (AGEs) serving as central mechanistic drivers.

With respect to electrical remodeling, Zheng and colleagues reported that in diabetic mouse models, atrial myocytes exhibit significant reductions in the L-type calcium current (I_Ca, L), transient outward potassium current (I_to), and ultra-rapid delayed rectifier potassium current (I_Kur). These changes prolong action potential duration and impair atrial conduction, thereby increasing AF vulnerability. Mechanistically, binding of AGEs to their receptor (RAGE) activates the p16/Rb signaling pathway, which in turn modulates ion-channel expression [26]. Complementing these findings, Yi et al. demonstrated that a high-glucose milieu prolongs atrial action potential duration, in association with downregulation of small-conductance $Ca^{2+}$-activated $K^{+}$ channels, collectively promoting an arrhythmogenic substrate [27].

At the level of structural remodeling, hyperglycemia and AGEs promote myocardial interstitial fibrosis. AGEs can form cross-links with extracellular matrix components such as collagen, altering their structure and biomechanical properties and thereby accelerating fibrotic progression. In a diabetic rabbit model, Liu et al. (2012) observed that hyperglycemia-induced atrial dilation, interstitial fibrosis, and interatrial conduction delay jointly constitute the structural basis for AF initiation and maintenance [28].

## 5. Current Evidence on MRAs for Atrial Fibrillation: From Conventional Agents to Finerenone

### 5.1 Conventional MRAs and Atrial Fibrillation

The role of conventional mineralocorticoid receptor antagonists (MRAs) in atrial fibrillation (AF) has been explored in multiple preclinical and clinical studies.

From a mechanistic standpoint, a series of animal experiments has highlighted the potential of conventional MRAs to prevent AF by attenuating structural remodeling. In a canine model of long-term rapid atrial pacing, spironolactone was shown to mitigate atrial structural remodeling—by suppressing apoptosis, myolysis, and atrial fibrosis—and thereby effectively prevented AF onset [29]. Similarly, in a rat model of AF induced by hypertension and a high-salt diet, eplerenone improved atrial myocyte hypertrophy and interstitial fibrosis, significantly reduced the expression of pro-inflammatory mediators, and completely prevented AF inducibility [30]. Collectively, these findings suggest that the

major benefits of MRAs may derive from their favorable modulation of the atrial substrate.

Clinical evidence has been mixed but is overall supportive. In patients with heart failure, eplerenone demonstrated a substantial benefit in the EMPHASIS-HF trial, reducing the risk of new-onset AF by 42% in patients with mild heart failure [31]. This signal has been reinforced by several meta-analyses. For example, a 2024 analysis reported that MRAs reduced the overall risk of AF by 32%, with more pronounced effects observed with longer-term therapy and among patients with left ventricular dysfunction and recurrent AF [32]. A 2019 systematic review similarly found a significantly lower incidence of AF in the MRA group than in controls (15.0% vs 32.2%), with a particularly clear benefit in reducing AF recurrence [33]. A 2017 meta-analysis reached comparable conclusions, confirming that MRAs significantly lower the risk of new-onset or recurrent AF, although no significant effect was observed for postoperative AF (POAF) [34].

In addition, MRAs have shown promise as adjunctive therapy after catheter ablation. In a clinical study of 161 patients with persistent AF, post-ablation use of eplerenone increased the 24-month freedom from AF recurrence from 40% to 60%, significantly improving maintenance of sinus rhythm [35]. Real-world evidence also suggests that spironolactone use is associated with a reduced AF burden and fewer hospitalizations for direct-current cardioversion [36].

### 5.2 Finerenone and Atrial Fibrillation

At present, the potential role of finerenone in the prevention and treatment of atrial fibrillation (AF) has not been evaluated as a primary endpoint in large-scale randomized trials; however, clinically meaningful evidence has emerged from prespecified and post hoc analyses. In 2021, Filippatos and colleagues reported that among patients without a history of AF or atrial flutter at baseline, the incidence of new-onset AF was significantly lower in the finerenone group than in the placebo group (82/2593, 3.2% vs 117/2620, 4.5%). In the overall population, AF event rates were likewise lower with finerenone than with placebo (3.7% vs 4.8%) [37]. These findings strongly suggest that in patients with type 2 diabetes and chronic kidney disease—a population at particularly high risk of AF—finerenone may confer protection against incident AF.

Mechanistically, this clinical signal is consistent with experimental observations. As early as 2005, Milliez et al. demonstrated in a rat model of post–myocardial infarction heart failure that blockade of aldosterone signaling markedly attenuated atrial fibrosis and suppressed the occurrence of spontaneous AF [38]. As a potent MR antagonist, finerenone may therefore reduce AF susceptibility by inhibiting MR-driven profibrotic pathways, thereby slowing—and potentially partially reversing—atrial structural remodeling.

Taken together, finerenone may offer a distinct value proposition in AF prevention and management. It represents not merely an incremental optimization of conventional MRAs, but also a potential strategy to shift the therapeutic window upstream toward the mechanisms of atrial remodeling. The preventive signal observed in high-risk populations supports a paradigm transition from largely symptom- and complication-oriented care to substrate-directed, disease-modifying intervention, thereby opening new avenues for integrated AF management.

## 6. Potential Mechanisms of Finerenone in the Treatment of Atrial Fibrillation

### 6.1 Inhibition of MR Overactivation

Excessive activation of the mineralocorticoid receptor (MR) is closely associated with cardiac interstitial fibrosis, inflammation, hypertrophy, and enhanced generation of superoxide anions [39–41], all of which contribute to the structural substrate underlying atrial fibrillation (AF). As the principal ligand of MR, elevated aldosterone levels promote sodium and water retention and sodium overload, while increasing the production of reactive oxygen species (ROS). This triggers inflammatory responses, accelerates fibrotic progression, and exacerbates oxidative stress. Collectively, these pathological processes drive cardiac remodeling and heighten vulnerability to arrhythmias. Accordingly, therapeutic strategies that target MR overactivation may attenuate MR-mediated inflammatory and profibrotic injury [4].

Evidence indicates that both MR mRNA and protein expression are increased in atrial tissue from patients with AF, with MR predominantly localized to the cytoplasm of cardiomyocytes. Concomitantly, expression of 11β-hydroxysteroid dehydrogenase type 2 (11βHSD2) at both the mRNA and protein levels is also upregulated [42]. In humans, aldosterone and the glucocorticoid cortisol bind to MR with comparable affinity. By converting glucocorticoids to their inactive metabolites, 11βHSD2 finely regulates MR activation, thereby allowing aldosterone to preferentially occupy and activate MR—further amplifying MR signaling in patients with AF.

Finerenone can effectively inhibit aldosterone-induced MR nuclear translocation (i.e., reducing the nuclear-to-cytoplasmic ratio of MR), thereby preventing receptor overactivation. By selectively binding MR and competitively antagonizing aldosterone–MR interactions, finerenone suppresses downstream signaling activation. Consequently, the protective effect of finerenone against incident AF may, at least in part, be attributable to its capacity to blunt aldosterone-driven MR signaling.

### 6.2 Suppression of Fibrosis

Finerenone appears to exert stronger anti–atrial fibrotic effects than conventional steroidal MRAs (e.g., spironolactone). Following aldosterone binding, MR translocates to the nucleus, recruits coregulatory factors, and orchestrates the transcription of fibrosis-related genes. Although spironolactone can partially interfere with this process, its receptor engagement is relatively limited and its binding affinity is lower. In contrast, owing to its unique non-steroidal structure, finerenone establishes broader and more specific interactions with MR, thereby more effectively preventing coregulator recruitment and downstream

transcriptional activation of profibrotic gene programs.

At the molecular level, finerenone substantially suppresses the expression of multiple profibrotic mediators. Experimental data indicate that finerenone attenuates TGF-β upregulation induced by activation of the Rac1 GTPase pathway [43]. By antagonizing MR signaling, finerenone reduces macrophage expression of TGF-β1 and plasminogen activator inhibitor-1 (PAI-1), while concomitantly upregulating antifibrotic gene expression [44–46]. In addition, finerenone inhibits CTGF expression and completely prevents the upregulation of lysyl oxidase (LOX) and fibronectin. Notably, LOX, fibronectin, and miR-21 are MR-dependent and have been identified as important downstream profibrotic effectors within the CTGF axis.

Multiple animal studies further support the antifibrotic advantages of finerenone. In a canine AF model, Yasir Parviz and colleagues demonstrated that conventional MRAs (spironolactone and eplerenone) can prevent fibrotic remodeling and suppress inducible AF [47]. In 2018, Grune et al. reported that in a murine model of cardiac fibrosis induced by isoproterenol, finerenone potently blocked fibrosis and macrophage infiltration, whereas eplerenone did not show significant effects—suggesting that non-steroidal MRAs may provide superior antifibrotic and anti-inflammatory activity compared with steroidal agents [9]. Mechanistically, this may relate to finerenone's differential modulation of MR coregulator interactions and suppression of the profibrotic gene TNX (tenascin-X). TNX is an extracellular matrix protein that serves as a critical regulator of collagen deposition and degradation. In this model, finerenone markedly reversed isoproterenol-induced TNX upregulation in the heart, while spironolactone and eplerenone failed to do so [9].

Comparable antifibrotic effects have also been observed in fibrotic models of other organs. In 2017, Lattenist et al. showed in a rat renal ischemia–reperfusion injury model that finerenone prevented the upregulation of fibrotic markers such as TGF-β and collagen I [48]. In 2019, Lavall et al. used Sirius Red staining in RacET mice—a model of myocardial fibrosis—to demonstrate that finerenone significantly reduced the extent of left atrial fibrosis [43].

### 6.3 Suppression of Inflammation and Attenuation of Oxidative Stress

The dual anti-inflammatory and anti–oxidative stress properties of finerenone underpin its therapeutic potential in reducing the incidence and recurrence of atrial fibrillation (AF).

A growing body of evidence across diverse disease models has demonstrated the anti-inflammatory actions of finerenone. In 2018, Barrera-Chimal et al. reported in a murine renal ischemia–reperfusion injury (IRI) model that expression of the pro-inflammatory cytokines IL-6 and IL-1β was markedly increased 24 hours after reperfusion, whereas finerenone effectively suppressed this response—supporting an MR antagonist–mediated anti-inflammatory effect [45]. In a rat model of hypertension, the expression of multiple pro-inflammatory mediators (including osteopontin [OPN], MCP-1, IL-1β, and IL-6) was elevated; both spironolactone and the non-steroidal MRA BR-4628 reduced the mRNA and protein levels of inflammatory markers such as IL-1β, MCP-1, and CXCL1 [49]. Moreover, in KK-Ay diabetic mice, treatment with eplerenone or spironolactone significantly attenuated inflammatory responses and downregulated mRNA expression of mediators including MCP-1 and plasminogen activator inhibitor-1 (PAI-1) [50].

Finerenone also confers clear benefits with respect to oxidative stress. In 2023, Lan Yao and colleagues showed that in human proximal tubular epithelial cells cultured under high-glucose conditions, both mitochondrial and intracellular ROS levels were substantially increased, whereas finerenone markedly reduced ROS signals measured using the MitoSOX and H2-DCFDA probes [51]. In Zucker fa/fa rats, a metabolic syndrome model, short-term finerenone treatment likewise decreased ROS generation in myocardial tissue [52]. Mechanistically, MR activation may induce mitochondrial dysfunction via the PI3K/Akt/eNOS pathway, thereby promoting ROS production; by blocking MR signaling, finerenone can reverse this cascade and ultimately ameliorate oxidative stress [51].

## 7. Conclusion

Finerenone, a novel non-steroidal mineralocorticoid receptor antagonist (MRA), may intervene in atrial remodeling by inhibiting MR overactivation, suppressing fibrosis, and exerting anti-inflammatory and anti–oxidative stress effects. In high-risk populations with cardiorenal–metabolic disease, finerenone has shown potential to reduce the likelihood of incident atrial fibrillation (AF). In this context, finerenone may represent a strategic shift in AF management—from "downstream" control of symptoms and complications toward "upstream" disease-modifying therapy—thereby offering a new option within integrated AF care. Although the current evidence is largely derived from post hoc analyses and requires prospective validation, it nevertheless opens a promising avenue for AF prevention and treatment.

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