

Statins in paroxysmal atrial fibrillation: Beneficial to prevent recurrence but insufficient to stop progression

Atrial fibrillation (AF) is an increasingly prevalent cardiac arrhythmia, currently reaching pandemic proportions with over 33.5 million patients worldwide (1). AF presence independently increases morbidity and mortality, primarily because of thromboembolic stroke, heart failure, and vascular complications (2, 3). AF is characterized by complex electrical and structural remodeling of the atria that is often unrelated to the severity of the underlying cardiac disease (4). Current AF treatment focuses on controlling arrhythmia-related symptoms by antiarrhythmic medications and/or catheter ablation (5). Unfortunately, neither pharmacological nor ablative approach can completely cure AF; both treatment strategies are associated with a risk of complications, and the majority of patients still need life-long anticoagulation (5). Considering that AF pathogenesis is still incompletely understood, it is not surprising that the available treatments are suboptimal; hence, the development of antiarrhythmic therapies, which aim at mechanisms underlying AF occurrence and progression, seem particularly clinically relevant.

Of the possible mechanisms that underlie AF pathogenesis, inflammation and oxidative stress have long been the focus of scientific interest. The strongest evidence linking AF and inflammation is based on acute inflammatory states, such as cardiac or non-cardiac surgery and myo-pericarditis, in which new-onset AF coincides with peak levels of inflammatory biomarkers (6). Similarly, low-grade chronic inflammation and increased oxidative burden have been associated with incident AF (7) and AF recurrence after cardioversion or ablation (8). Increased levels of inflammatory biomarkers have been reported in "lone" AF (9), and inflammation and oxidative stress have been associated with adverse outcomes in AF patients (9, 10).

Theoretically, statins (3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitors) can protect against AF by reducing the burden of vascular disease and by mitigating atrial remodeling via pleiotropic antiinflammatory, antioxidative, and antithrombotic effects; improvement of endothelial function; and neurohormonal regulation. Beneficial effects of intensive statin treatment are most evident for preventing postoperative AF (11). Whether statins are effective for AF prevention in other circumstances (e.g., heart failure, post-cardioversion, and post-ablation) is less clear (11), but current evidence supports their use in stable coronary artery disease (CAD) (12), acute coronary syndromes (13), and renal insufficiency (14).

In this issue of the *Anatolian Journal of Cardiology*, the article "Fluvastatin therapy could not decrease progression of paroxysmal atrial fibrillation" by Qiang et al. (15) has presented the results of a randomized clinical trial including 118 patients with recent-onset paroxysmal AF, without overt CAD, and treated with fluvastatin 80 mg/day or placebo. Although fluvastatin treatment could not effectively prevent the development of permanent AF during the 2-year follow-up, there was a significant reduction in AF recurrence and the occurrence of left-ventricular dysfunction in fluvastatin-treated patients, without increased risk of adverse effects. Fluvastatin treatment also reduced C-reactive protein and homocysteine levels and increased endothelial progenitor cell counts, suggesting that treatment benefits were possibly mediated by pleiotropic actions (15). Although limited by a small number of participants, these findings indicate that high-dose fluvastatin could be an effective and safe addition to antiarrhythmic drug therapy for preventing paroxysmal AF and adverse cardiovascular outcomes in patients without CAD. Further large randomized studies are needed to confirm these observations.

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