Atrial remodelling in persistent atrial fibrillation: the potential role of aldosterone

We read with considerable interest the report by Ueng et al.,1 which aimed to demonstrate the beneficial effects of enalapril on maintenance of sinus rhythm after cardioversion of persistent atrial fibrillation. The authors conclude that inhibition of the renin–angiotensin system may favourably affect atrial structural remodelling and thus modify the substrate for atrial fibrillation recurrence.1

Even though aldosterone represents a well-known component of the renin–angiotensin system, its role in atrial fibrillation has not been examined in detail. Goette et al.,2 showed that aldosterone levels are elevated in patients with persistent atrial fibrillation, whereas restoration of sinus rhythm by electrical cardioversion significantly lowers serum aldosterone. Whether atrial fibrillation induces cardiac synthesis of aldosterone in the absence of heart failure or hypertension is not known.3 Regardless its exact source in this setting, aldosterone may exert several deleterious effects provoking cardiac damage independent of its effects on blood pressure.3 In specific, aldosterone induces cell proliferation and myocardial fibrosis possibly due to an increase of AT1-receptors and enhanced local expression of the angiotensin converting enzyme.3 Moreover, it seems to promote inflammation3 and oxidative stress3, processes that have recently been implicated in atrial remodelling.3 Finally, it has been proposed that aldosterone induces baroreceptor dysfunction and thus may facilitate autonomic imbalance during atrial fibrillation.5

It can therefore be hypothesised that aldosterone plays a role in the pathophysiology of atrial fibrillation. Taking into account the aforementioned deleterious effects one can speculate that aldosterone antagonists such as spironolactone may ameliorate atrial remodeling. Undoubtedly, the favourable effects of aldosterone antagonism on ventricular remodeling observed in heart failure do not imply similar actions on atrial myocardium. In conclusion, we believe that the role of aldosterone in atrial fibrillation deserves further study since it may contribute to the development of effective strategies against atrial remodeling.

References

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Atrial remodelling in persistent atrial fibrillation: the potential role of aldosterone: reply

The letter by Dr. Korantzopoulos and co-workers made several good points that are of general interest to the issue of aldosterone in atrial fibrillation (AF). Without a doubt, our findings provide mechanistic support for clinical observations pointing to efficacy against AF-induced structural remodelling of angiotensin converting enzyme (ACE) inhibitors after cardioversion of persistent AF.1 Increased understanding of pathophysiology of AF has shown that activation of the renin–angiotensin–aldosterone (RAA) system has been implicated in the progression of atrial structural remodelling in this setting. Goette et al.,2 has shown that atrial expression of ACE is increased in interstitial tissue of fibrillating human atria. In addition to direct effects of angiotensin II on myocardial tissue, angiotensin II causes the release of aldosterone from the adrenal gland and extra-adrenal tissues. Recently, it has been shown that aldosterone is also produced in the failing human heart. Aldosterone has been shown to stimulate cardiac collagen synthesis and fibroblast proliferation via activation of local mineralocorticoid receptors, or indirectly, interfering with angiotensin II type 1 receptors and enhancing local ACE expression.3

Surprisingly, to date, clinical data directly linking aldosterone with AF are scarce. Systemic aldosterone levels are increased in patients with persistent AF. Thus, it seems likely that elevated systemic levels of aldosterone, perhaps as well as increased local synthesis of aldosterone acting in a paracrine/autocrine fashion, during AF may contribute to atrial remodelling.

The deleterious effect of an activated RAA system has been clearly demonstrated in patients with heart failure. A recent clinical trial4 has shown a marked benefit in patients with chronic heart failure from co-administration of the aldosterone receptor antagonist and ACE-