

Letter by Lin et al Regarding Article, “Dabigatran and Thrombin Modulate Electrophysiological Characteristics of Pulmonary Vein and Left Atrium” by Chang et al

To the Editor:

Dr Chang et al¹ experimentally reported that thrombin and a blood clot solution regulated pulmonary vein and left atrium arrhythmogenesis through electric and mechanical modifications by nitric oxide production and protease-activated receptor type 1 activation. Dabigatran has electrophysiological effects and attenuated the effects of thrombin and a blood clot solution on pulmonary vein and left atrium electric and mechanical modulation.¹ As is known, thrombin is also a vital regulator involving in some inflammatory pathways. For instance, thrombin is a potent inducer of fibrogenic cytokines, such as transforming growth factor- β , connective tissue growth factor, and platelet-derived growth factor-AA. In addition, thrombin can increase expression of proinflammatory chemokines, extracellular matrix proteins in various cells, and activation of complement system. To date, inhibition of thrombin using the oral direct thrombin inhibitor dabigatran has been found with marked anti-inflammatory and antifibrotic effects to attenuate lung injury in a murine model of interstitial lung disease.² Therefore, the antiarrhythmic properties of dabigatran may be partly associated with the anti-inflammatory and antifibrotic effects on pulmonary vein and left atrium by blocking plasma thrombin. However, the evidence of dabigatran to reduce the incidence of atrial fibrillation (AF) is still lacking clinically.

In this respect, warfarin has been considered as the standard anticoagulant therapy to prevent thromboembolic events in high-risk patients for decades and inevitably used in comparison with dabigatran in clinical trials. Pharmacologically, warfarin can also decrease inflammation and thrombin generation by reducing plasma factor VII, an important thrombin precursor in the coagulation cascade. Previously, we had proposed that warfarin has a protective trend to reduce risk of stroke by preventing the development of AF aside from the anticoagulation effect for patients with systolic heart failure and sinus rhythm.³ In the Warfarin and Antiplatelet Therapy in Chronic Heart failure (WATCH) trial, the incidence of paroxysmal AF was marginally higher in the aspirin group than in the warfarin group if patients who discontinued drug therapy during the study period were taken into account (13.2% for aspirin vs 9.6% for warfarin, respectively; $P=0.08$).⁴ Similarly, in the Warfarin versus Aspirin in Reduced Cardiac Ejection Fraction (WARCEF) trial, the incidence of AF/supraventricular tachycardia was significantly higher in the aspirin group than that in the warfarin group at the end of study (4.8% for aspirin vs 3.1% for warfarin, respectively; $P=0.032$).⁵ According to this finding, we may expect that

the antiarrhythmic effect of dabigatran on pulmonary vein and left atrium in experimental findings by Chang et al can be successfully translated to the suppression of AF occurrence in high-risk patients clinically in the following studies as well.

Disclosures

None.

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