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Comment on: Efficacy of early initiation of ivabradine treatment in patients with acute heart failure: Rationale and design of SHIFT-AHF trial

To the editor:

The reduction in heart failure rehospitalization using heart rate (HR) modulation therapy using ivabradine, a selective I_f channel inhibitor that directly reduces resting HR, has been demonstrated in patients with heart failure with reduced ejection fraction in the SHIFT trial.[1] It is unknown, however, if clinical benefit exists in patients with acute heart failure. Su and colleagues proposed the SFHIT-AHF study, which is a prospective, multicentre, double-blind, randomized, placebo-controlled trial to evaluate safety and efficacy of an early intervention to resting HR using ivabradine in patients with acute heart failure.[2]

In patients with acute heart failure, we should assume that tachycardia likely occurs as compensatory mechanism of clinical decline due to acute congestion or impaired cardiac output. After initial medical optimization, we can infer that inappropriately elevated HR should be a potential therapeutic target to preserve cardiac potential energy and thus improve diastolic filling and overall cardiac function. Thus far, the optimal target HR specifically for HR modulation therapy in the situation of acute heart failure remains unknown. Our group recently proposed a methodology to utilize a trans-mitral Doppler echocardiography for the HR modulation.[3] Cardiac output should be maximized at the HR, for which E-wave and A-wave stand adjacent without any overlap. Our suggestion is to add the measurement of trans-mitral Doppler flow in the scheduled echocardiographic assessments to optimize HR. Averaging consecutive three measurements is recommended particularly for those with occasional arrhythmias. This procedure has a limitation for those with poor acoustic windows.

In the authors' study protocol, chronotropic agents including beta-blockers were not titrated, falling against recommendations regarding implementation of heart failure-specific guideline-directed medical therapies.[4] Without adjusting beta-blocker therapy, HR in the control arm would remain higher compared with the ivabradine arm. The authors in this study are able to assess the implication of early HR modulation (i.e. lower HR vs. higher HR), although some shortcomings remain in understanding the clinical efficacy of ivabradine in the context of incorporating well-validated therapeutics, particularly beta-blocker therapy.

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