Heart rate in heart failure with mid-range ejection fraction

Heart failure is a disease that has high mortality and morbidity rates. However, as a syndrome, different phenotypes have been introduced by the European Society of Cardiology (ESC) 2016 guidelines (1). Heart failure with reduced ejection fraction (HFrEF) is the major phenotype in which evidence-based medicine with ACE inhibitors or angiotensin receptor blockers (or ARNI in place of these agents), beta blockers, mineralocorticoid receptor antagonists, and ivabradine play an important role (1). The ESC 2016 guidelines introduced a novel phenotype, named heart failure with mid-range ejection fraction (HFmrEF), in addition to another major phenotype–heart failure with preserved ejection fraction (HFpEF) (1). Among the two major phenotypes, HFmrEF remains in the "grey" or "transition" zone of diagnosis, with both-sided transitions identified in the literature (2). This little brother (or sister) was initially introduced to behave like HFpEF; hence, the diagnosis simulated HFpEF. However, recent data designate that HFmrEF might be more similar to HFrEF (3).

Heart rate is an integral part of the appropriate function of the cardiovascular system, and high heart rate among patients with HFrEF is related to poor outcomes as high heart rate complicates the calcium current, not only in systole but also in diastole in HF (4). Hence, lowering the heart rate with ivabradine to a certain threshold (<70 bpm) was shown to improve morbidity (5).

In this issue, Xin et al. (6) provided interesting data in a small group of patients with HFmrEF that lower heart rate (<70 bpm) at discharge, among hospitalized HFmrEF patients, particularly among those prescribed with beta blockers, resulted in outcome benefit in the form of combined end-point of HF hospitalization and all-cause mortality. Hence, they provided clue that HFmrEF is more similar to HFrEF than HFpEF with regard to heart rate. Although transitions to HFrEF or HFpEF during follow-up of patients with HFmrEF via echocardiography is not provided in the study, it is likely that the majority of these patients remained in the HFmrEF or HFrEF subcategory during the follow-up. It is also notable that in the absence of beta blockers, such relation was lost. Hence, in patients with HFmrEF, beta blockers seem to provide outcome benefit by also lowering heart rate to <70 bpm in most patients, similar to HFrEF, as shown in a previous study (7). This finding is expected to have some implications in the near future.

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