Resting Heart Rate Predicts Risk of Adverse Cardiovascular Outcome

Written by Brian Hoyle

Analysis of pooled data from 2 placebo-controlled studies has revealed an association between resting heart rate in patients with systolic dysfunction and subsequent cardiovascular events and death. This risk persists with repeated measurements of resting heart rate, despite adjustment for baseline or prior heart rate measurement. Prior analysis of a third study indicated that these risks persist with time if the elevated heart rate is maintained. The findings of an international consortium of researchers were presented by Karl Swedberg, MD, University of Gothenburg, Gothenburg, Sweden.

Resting heart rate in sinus rhythm is linked with increased morbidity and death in patients with systolic heart failure (HF). Data suggest that reducing the resting heart rate can be beneficial for patient outcomes [Swedberg K et al. *Lancet* 2010]. But whether the association between resting heart rate and cardiovascular risk persists in the long term and whether continued monitoring of heart rate is associated with further reductions in risk remain unknown.

To clarify, the researchers analyzed pooled data from the placebo-treated patients in 2 studies. The Effects of Ivabradine on Cardiovascular Events in Patients With Stable Coronary Artery Disease and Left Ventricular Systolic Dysfunction [BEAUTIFUL; NCT00143507] was a randomized, double-blind, placebo-controlled, parallel-group trial that involved almost 11,000 patients with coronary arterial disease with left ventricular ejection fractions <40%. In BEAUTIFUL, patients were randomly selected to receive either ivabradine 5 mg or placebo in addition to appropriate cardiac medications [Fox K et al. *Lancet* 2008]. The Systolic Heart Failure Treatment With the If Inhibitor Ivabradine Trial [SHIFT] was a randomized, placebo-controlled study that involved 6558 patients with symptomatic HF and left ventricular ejection fractions ≥35%. In SHIFT, patients were randomly selected to receive either ivabradine or matching placebo [Swedberg K et al. *Lancet* 2010].

For the present study, patients were pooled to assess the impact of repeated electrocardiographic measurements of heart rate on the rate of cardiovascular disease or hospitalizations for HF, the primary end point. Additional endpoints included cardiovascular disease or hospitalization for myocardial infarction, hospitalization for myocardial infarction only, hospitalization for HF only, and cardiovascular disease.

Compared with the reference heart rate group, patients with heart rates ≥85 beats/minute had significantly elevated risk compared with those with heart rates of <60, 60 to 64, 70 to 74, 75 to 79, and 80 to 84 beats/minute in all categories except hospitalization for myocardial infarction.

The risk was maintained with repeated measurements of resting rate, even after adjusting for baseline or the immediately preceding heart rate determination.

To determine if increased heart rate at baseline was predictive of adverse events during a 6-month to 1-year follow-up, the researchers analyzed data from the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity program [Pfeffer MA et al. *Lancet* 2003] to assess the association between the heart rate at each clinic visit and the subsequent outcome. The results, which were first presented by Vazir A et al. at the 2014 American College of Cardiology annual meeting, revealed an increased risk both for subsequent hospitalization for HF and for cardiovascular-related death, with increasing heart rate measured at any time during follow-up for 3.5 years.

Dr. Swedberg and colleagues concluded that resting heart rate in patients with systolic dysfunction is associated with subsequent cardiovascular outcomes and with death. The risk is maintained with repeated measurements, even after adjustment for baseline or previous measurements. The repeated heart rate measurements strengthen the evidence indicating that a resting heart rate <70 beats/minute is desirable in terms of cardiovascular risk.

Characterization of Poor Diuretic Response in AHF and the Impact of Serelaxin

Written by Maria Vinall

The primary reason for hospitalization among patients with acute heart failure (AHF) is congestion, for which the most common treatment is intravenous loop diuretics [Mentz RJ et al. *Eur J Heart Fail* 2014]. However, many patients fail to respond or have an inadequate response to this treatment and are discharged without weight loss and with continued signs of congestion. Adriaan Voors, MD, PhD, University Medical Center, Groningen, the Netherlands, presented the results of a sub-analysis of data from the Relaxin for the Treatment of Acute Heart Failure trial [RELAX-AHF; Teerlink JR et al. *Lancet* 2013], which showed that poor diuretic response was independently associated with residence in a Western-like region, lower diastolic blood pressure (DBP), lower levels of aspartate aminotransferase (AST) and potassium, higher blood urea nitrogen (BUN), and an absence of edema. Serelaxin use was associated with lower doses of intravenous loop diuretics and slightly less weight loss, resulting in a neutral effect on diuretic response.