In the current issue of *Circulation Research*, McCrory et al. report on the association of heart rate recovery after simple orthostatic challenge—otherwise known as standing up—with all-cause mortality. The authors measured heart rate changes in the first 110 seconds after standing up in 4475 participants of an Irish population-based, cohort study. Immediately after standing, heart rate, as expected, increased but in most subjects started to fall toward resting levels within 10 seconds. The rate of decline between 10 and 20 seconds post orthostatic challenge—or heart rate recovery (HRR$_{10-20}$)—was lower in older subjects and in subjects with a history of vascular disease. It was also an independent predictor of 4-year mortality: the lower the HRR$_{10-20}$, the greater the mortality.

To put these findings in perspective, we go back 28 years, when Schwartz et al. published a report on a series of experiments that linked baroreceptor function with cardiac response to acute stress. The investigators produced an anterior myocardial infarction (MI) in 301 dogs and compared their baroreceptor sensitivity to 85 controls. They assessed baroreceptor sensitivity by injecting phenylephrine and measuring the regression slope relating fall in heart rate (or more precisely increase in RR intervals) with increase in blood pressure. Among the 192 dogs that survived 4 weeks after MI, baroreceptor sensitivity was markedly decreased compared with controls. The investigators then subjected these 192 dogs to treadmill exercise with acute circumflex artery occlusion during the last minute of exercise. There were 106 dogs that developed ventricular fibrillation with the double whammy of exercise and acute ischemia.

What distinguished the dogs that developed exercise- and ischemia-induced ventricular fibrillation from those that did not? The investigators found a remarkably strong gradient between post-MI baroreceptor sensitivity and risk of ventricular fibrillation—as baroreceptor sensitivity declined, risk of ventricular fibrillation increased. The authors, synthesizing this experiment with previous work, postulated that analysis of heart rate recovery after exercise has painted a picture by which we can understand how decreased baroreceptor sensitivity to 85 controls. They assessed baroreceptor sensitivity by injecting phenylephrine and measuring the regression slope relating fall in heart rate (or more precisely increase in RR intervals) with increase in blood pressure. Among the 192 dogs that survived 4 weeks after MI, baroreceptor sensitivity was markedly decreased compared with controls. The investigators then subjected these 192 dogs to treadmill exercise with acute circumflex artery occlusion during the last minute of exercise. There were 106 dogs that developed ventricular fibrillation with the double whammy of exercise and acute ischemia.

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In the clinical sphere, we cannot routinely inject phenylephrine and measure regression slopes between blood pressure and RR intervals, but it turns out that there is a measure that is largely, if not entirely, influenced by baroreceptor function. That measure is heart rate recovery after exercise. During exercise, heart rate rises in response to vagal inhibition and sympathetic activation, whereas after exercise, heart rate recovery occurs in response to cardiac vagal reactivation and to sympathetic deactivation.

Recent work has demonstrated that events during early exercise and immediate recovery are almost entirely manifestations of vagal function. During early exercise, vagal inhibition reflects changes in central command and responses to muscle mechanoreceptors. However, during immediate recovery—the first 20 or 30 seconds after exercise ends, arguably the mirror image of early exercise—it seems as if neither central command nor mechanoreceptors play a role. Instead, the immediate fall in heart rate, which reflects the immediate increase in cardiac vagal tone, occurs in response to the activity of arterial baroreceptors.

Many clinical investigators and population epidemiologists have demonstrated strong associations between attenuated heart rate recovery and mortality. This association is seen in healthy adults, in patients with suspected coronary disease, and in patients with known coronary disease; the association is also seen with treadmill and bicycle exercise and with different recovery protocols. One large epidemiological study reported that the association between attenuated heart rate recovery and death is largely manifest through sudden cardiac death. The work to date on heart rate recovery after exercise has painted a picture by which we can understand how decreased baroreceptor sensitivity in a post-MI dog model translates into prognostic implications in the clinic.

The report by McCrory et al. adds an important chapter in the growing literature on heart rate recovery by taking us back full circle to the primary physiological event of interest—the baroreceptor reflex. From a mechanistic perspective, the study enables us to isolate the baroreceptor response from the more complex events that occur during moderate to vigorous exercise. It also offers an opportunity for the clinical community to leverage the prognostic properties of heart rate recovery without having to put patients (and the system) through the inconveniences and efforts of formal exercise testing.

If, as it seems, baroreceptor sensitivity is central to cardiovascular health, the obvious question is what interventions might work to improve baroreceptor sensitivity and reduce risks of premature events—especially sudden cardiac death that despite many advances remains a leading cause of mortality. There are several candidates including,
most prominently, physical activity. Although the work of McCrory et al solidifies the strong association between baroreceptor dysfunction, attenuated heart rate recovery, and mortality, we cannot yet jump to the conclusion that routine screening with heart rate recovery is clinically wise—we have learned before that prediction does not equal prevention. At the same time, though, it gives us greater confidence that further research in this area may be well worth the effort.

Disclosures

None.

References


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Heart Rate Recovery: Coming Back Full-Circle to the Baroreceptor Reflex
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