Heart Rate Variability
Just a Surrogate for Mean Heart Rate?

Harald M. Stauss

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In this issue of Hypertension, Monfredi et al1 address a phenomenon that has been repeatedly described in the literature2–5 but, nevertheless, went largely unnoticed by the scientific community using heart rate variability (HRV) to assess cardiac autonomic control or to predict cardiovascular health. The phenomenon studied by Monfredi et al1 is that most HRV parameters are inversely related to the actual level of HR, such that HRV is usually lower if HR is high and vice versa. The importance of the work by Monfredi et al1 is that it explores the physiological mechanisms underlying the relationship between HR and RR-interval using mathematical and biophysical models applied to data from various species and even in vitro preparations with differing levels of mean HR. Furthermore, using the standard deviation (SD) of normal to normal intervals6 as an example of one of the more frequently used HRV parameters; they provide a simple equation that can be used to normalize this HRV parameter so that it is independent of the actual level of HR.

By convention, HRV is typically calculated from RR-interval and not from HR time series.6 As pointed out in a recent review article by Sacha,7 the relationship between HRV (calculated from RR-intervals) and HR is partly because of the inverse relationship between HR and RR-interval (eg, if HR fluctuates by ±10 bpm, the corresponding fluctuations in RR-intervals are ±250 ms at an average HR of 50 bpm but only ±60 ms at an average HR of 100 bpm). Thus, if HRV is calculated from RR-intervals, a high HR is associated with low HRV and vice versa. Therefore, one may ask if the relation between HR and RR-interval (illustrated in Figure 1) because a given perturbing current acting on the diastolic depolarization of the sinoatrial pacemaker cells affects both the HR and cardiac cycle length (eg, +15 bpm and −200 ms at a heart rate of 60 bpm in Figure 2, top) than at higher heart rates (Figure 2, bottom) when the intrinsic ion currents driving the diastolic depolarization are already large (eg, +6 bpm and −60 ms at a heart rate of 75 bpm in Figure 2, bottom). Importantly, this phenomenon is independent of the inverse relationship between HR and RR-interval (illustrated in Figure 1) because a given perturbing current acting on the diastolic depolarization of the sinoatrial pacemaker cells affects both the HR and the RR-interval more at low (Figure 2, top) when compared with high heart rates (Figure 2, bottom).

Because of the established relationship between HR and HRV, interpretation of HRV parameters obtained from groups of subjects with differing HR seems difficult. For example, numerous studies have reported reduced HRV in patients with heart failure9–11 and in experimental animal models of heart failure.12,13 Because heart failure is often associated with tachycardia, one would expect HRV to be reduced in heart failure simply because of the established relationship between HR and RR-interval. However, it has been demonstrated that aerobic exercise training increases HRV in patients with heart failure,14 which has been interpreted as improved cardiovascular health. However, because aerobic exercise training is associated with a reduction in heart rate, the increased HRV in patients with heart failure after an aerobic exercise training intervention is to be expected simply because of the lower heart rate. Even though the relationship between mean HR and HRV in heart failure has been described >20 years ago,15 the majority of more recent studies have largely ignored this relationship and, thus, are difficult to interpret.
On the basis of aforementioned considerations, one may ask the question whether HRV is just a surrogate for mean HR. However, such a notion would be an oversimplification and not give credit to many studies in which investigators used HRV parameters that are less dependent on HR, such as the coefficient of variation of the SD of RR-intervals and the low frequency/high frequency ratio of HRV or used other means to correct for the relationship between mean HR and HRV. These and many other studies have indeed demonstrated that HRV has prognostic power in patients with cardiovascular diseases that is independent of HR and provides information on cardiac autonomic regulation beyond the information that can be gained simply by the mean level of HR. However, the study by Monfredi et al published in this issue of Hypertension clearly demonstrates that to interpret HRV parameters correctly, it is essential that the relationship between mean HR and HRV is taken into account. To deal with this issue, Monfredi et al have derived 2 useful equations (Equations 8 and 9 in their article) that can be applied to correct SD of normal to normal intervals (a commonly used time domain HRV parameter) for HR. Potentially, another way to deal with this issue would be to calculate HRV parameters from HR time series rather than from RR-interval time series as illustrated in Figure 1. However, this approach is not yet established and would require further testing.

In conclusion, HRV is not just a surrogate of mean HR. HRV is still an independent predictor of cardiovascular risk and can provide useful information on autonomic cardiac control. However, using HRV parameters without considering the mean level of HR can lead to serious misinterpretation of experimental data. The hope is that the study by Monfredi et al will increase the awareness of this important issue and, thus, improve the quality and interpretation of future studies using HRV.

**Disclosures**

None.

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In this Hypertension, Monfretti et al. [1] applied 3-4 heart rate variability (HRV) to assess cardiac autonomic control in patients with essential hypertension. HRV is known to be a predictor of cardiovascular events, including mortality. In this study, Monfretti et al. [1] reported that HRV was lower in patients with hypertension compared to controls. The authors concluded that HRV may be a useful tool for the early detection of cardiovascular risk in patients with hypertension.


In this Hypertension, Monfretti et al. [1] measured HRV in a group of patients with essential hypertension and compared it to a group of healthy controls. The authors found that HRV was significantly lower in the patient group compared to the control group. The authors concluded that HRV may be a useful tool for the early detection of cardiovascular risk in patients with hypertension.


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Figure 2. The same perturbing current (eg, caused by the application of experimental data. The hope is that the study by Monfredi et al will increase the awareness of this important issue and, in conclusion, HRV is not just a surrogate of mean HR. However, the study by Monfredi et al 1 demonstrates that to interpret HRV parameters correctly, it is essential that the relationship between mean HR and HRV is still an independent predictor of cardiovascular risk and provides useful information on autonomic cardiac control. However, using HRV parameters without considering this relationship between mean HR and HRV would require further testing.

References


