To the Editor:

In their article, Monfredi et al.1 addressed the relationship between mean heart rate (HR) and its variability (HRV). In their carefully conducted experiments and with clear reasoning, they demonstrated a universal exponential decay-like relationship between HRV and HR and concluded from this that HRV cannot be used in any simple way to assess autonomic nerve activity to the heart. Like Stauss,2 we tend to agree with this conclusion as it points out a highly relevant and important issue in the field of cardiovascular medicine. However, we note that the complex biophysical model presented is merely an example of a restriction-of-range phenomena, which has been acknowledged in psychophysiological research3,4. These insights were not picked-up and included in the guiding HRV Task Force paper5 and likely, therefore, largely missed.

Ceiling Effect and Restriction of Range

Thirty years ago, Akselrod et al.6 elegantly explained that the nature of the interbeat interval (IBI) time series can explain the relationship between HRV and HR. In short, because IBI is simply an interval between 2 events (viz., the R-peaks in the ECG), R-peaks per definition occur sequentially in time. When IBI values decrease toward a (lower or upper) limit, a ceiling effect will cause a restriction of range for variation and reduce variability of the IBI. To compensate for ceiling effects, the variability for the mean IBI level, the variance coefficient of IBI (VCIBI, 100% multiplied by SD and divided by its mean) is suggested.6,7 To calculate spectral values of HR that include an HR level compensation for variability, Akselrod et al.6 suggested to normalize the power of HR by division by (mean HR).8 She explains, in the footnote (p 869), that this normalization is equivalent to the SD of IBI divided by its mean.

Correction for Mean Level

This correction procedure is applicable for all variables vulnerable for ceiling effects. So not only for frequency domain HRV measures as Akselrod et al.6 proposed but also for time domain measure of HRV like, for example, measures derived with the peak-to-though method, the root mean square value of the successive differences, or SD of normal beat to normal beat intervals (SDNN). For calculation of a VC, neither a mix of IBI and HR variables nor data-based parameter(s) is needed, as is the case in the correction procedure proposed by Monfredi et al.1 when calculating the corrected SDNN index (cSDNN). To support this statement, we give 2 arguments. First, a theoretical argument is given in the Table where we show the mathematical rationale that cSDNN and the VC, for SDNN are statistically equivalent. Second, as an empirical argument, we calculated these 2 HRV measures, viz., the cSDNN and VC, from IBI data of participants in a supine rest condition.8 The relationship between the HRV measures calculated according to the recommendations of Monfredi et al.1 (cSDNN, x-axis) and Akselrod et al.6 (VC, y-axis), respectively, is depicted in Figure 2. As both the slope and the correlation between cSDNN and VC are close to 1.0, the 2 HRV measures should be regarded as interchangeable markers of HRV.

Perspectives

To conclude, we agree with Monfredi et al.1 that the ongoing HR level at which HRV data are assessed should be taken into account to deal with restriction-of-range effects. However, the solution proposed by Monfredi et al.1 although it is well wrought, is not the most parsimonious solution. Instead, we recommend the elegantly simple CV approach to correct the HRV measures of interest, either in the frequency or in the time domain measure, for mean HR level. As was so eloquently put by Goethe: “In der Beschränkung zeigt sich erst der Meister.” (“Less is more” Johann Wolfgang Goethe [1749–1832] from Das Sonett. Erstdruck in “Was wir bringen” Vorspiel bei der Eröffnung des neuen Schauspielhauses zu Lauchstädt [1802].)

Disclosures

None.

References

Table. Mathematical Rationale for the Relationship Between VC and cSDNN

Measured values of mean IBI and SDNN of subject, are used to calculate VCIBI (\(v_i\)) as described by Akselrod:

\[ v_i = 100 \frac{SDNN}{IBI} \]

And the corrected SDNN, cSDNN (\(c_i\)), as described by Monfredi et al:

\[ c_i = \frac{SDNN}{IBI} e^{-\frac{60000}{IBI}} = SDNN e^{60000/a} \]

\(a=58.8\) bpm

We can write the IBI of each subject \(i\) as the group mean IBI (\(\bar{IBI}\)) and a relative deviation \(\delta\) of that mean:

\[ IBI_i = \bar{IBI} (1 + \delta_i) \]

Under the common assumption that the \(\delta_i\)'s are <1, we can use the first-order Taylor expansion as approximations:

\[ \frac{1}{1+\delta} = 1 - \delta \]

\[ e^\delta = 1 + \delta \]

\[ \delta^2 = 0 \]

For the ratio of VCIBI and cSDNN, we find now:

\[ \frac{v_i}{c_i} = 100 \frac{IBI}{IBI(1+\delta)} e^{-\frac{60000}{IBI}} = 100 e^{-\frac{60000}{IBI}} (1 - \delta) \left( 1 + \frac{60000}{a IBI} \delta \right) \]

\[ \frac{v_i}{c_i} = 100 e^{-\frac{60000}{IBI}} (1 + \frac{60000}{a IBI} - 1) \delta \]

When the group mean IBI is close 1020 ms and/or \(\delta\) is small, the value of the last part of the equation is close to zero, so

\[ \frac{v_i}{c_i} = 100 e^{-\frac{60000}{IBI}} (1 + 0) \]

The relationship between variables VCIBI and cSDNN is

\[ v_i = 100 \frac{IBI}{c_i} e^{-\frac{60000}{IBI}} \]

And after log-transformation, it is linear:

\[ \ln(v_i) = \ln(c_i) + \ln \left( \frac{100}{IBI} e^{-\frac{60000}{IBI}} \right) \]

with slope 1, highly correlated and constant difference of

\[ Const = \ln \left( \frac{100}{IBI} e^{-\frac{60000}{IBI}} \right) = \ln(100) + \ln \left( \frac{1}{IBI} \right) - \frac{60000}{a} \frac{1}{IBI} \]

In case of the group shown in Figure 1, \(\bar{IBI}=896.1\) ms, the estimated constant is \(-3.33\), which is close to the estimated empirical value of \(-3.38\) shown in Figure 2. The maximum value, \(-3.32\) is present at \(\bar{IBI} = 60000/a = 1020.4\) ms.

Note: calculation rules for logarithms are \(\ln(ab) = \ln(a) + \ln(b)\), \(\ln(e^x) = x\). IBI indicates interbeat interval; cSDNN, corrected SD of normal beat to normal beat intervals; VCIBI, variation coefficient of IBI.
Figure 1. Estimated constant as function of group mean interbeat interval IBI. The constant varies only over a small interval of −3.5 to −3.3. Group mean of used data is 896.1 ms, maximum of the estimate is at 1020.4 ms.

Figure 2. Graphical representation of the relationship between heart rate variability (HRV) measures calculated in 4976 human subjects (group mean interbeat interval [IBI]=896.1 ms) following 2 different procedures to correct for the relationship between HRV and HR: On the x-axis, the logarithmic transformed corrected SD of normal beat to normal beat intervals (cSDNN), ln(cSDNN), as proposed by Monfredi et al (Equation 8); on the y-axis, the logarithmic transformed variation coefficient (ln(VC)), proposed by Akselrod et al. Logarithmic transformation is commonly used to achieve a normal distribution before statistical analyses. The relationship approaches a perfect correlation ($R^2=0.995$; slope in the regression equation=1.01) and the constant (intercept) in the regression equation is −3.38.
Parsimonious Correction of Heart Rate Variability for Its Dependency on Heart Rate
Arie M. van Roon, Harold Snieder, Joop D. Lefrandt, Eco J.C. de Geus and Harriëtte Riese

Hypertension. 2016;68:e63-e65; originally published online September 26, 2016;
doi: 10.1161/HYPERTENSIONAHA.116.08053

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2016 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/68/5/e63

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/