Letter to the Editor

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, Harriëtte Riese

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 research[3,4]. These insights were not picked-up and included in the guiding HRV Task Force paper[5] 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 variation coefficient of IBI ($VC_{IBI,}$ 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).[6] She explains, in the footnote (p 869[6]), 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_{IBI} for SDNN are statistically equivalent.

Second, as an empirical argument, we calculated these 2 HRV measures, viz., the cSDNN and VC_{IBI}, 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_{IBI}, *y*-axis), respectively, is depicted in Figure 2. As both the slope and the correlation between cSDNN and VC_{IBI} 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

1. Monfredi O, Lyashkov AE, Johnsen AB, Inada S, Schneider H, Wang R, Nirmalan M, Wisloff U, Maltsev VA, Lakatta EG, Zhang H, Boyett MR. Biophysical characterization of the underappreciated and important relationship between heart rate variability and heart rate. *Hypertension*. 2014;64:1334–1343. doi: 10.1161/HYPERTENSIONAHA.114.03782.
2. Stauss HM. Heart rate variability: just a surrogate for mean heart rate? *Hypertension*. 2014;64:1184–1186. doi: 10.1161/HYPERTENSIONAHA.114.03949.
3. Mulder LJ. Measurement and analysis methods of heart rate and respiration for use in applied environments. *Biol Psychol*. 1992;34:205–236.
4. Althaus M, Van Roon AM, Mulder LJ, Mulder G, Aarnoudse CC, Minderaa RB. Autonomic response patterns observed during the performance of an attention-demanding task in two groups of children with autistic-type difficulties in social adjustment. *Psychophysiology*. 2004;41:893–904. doi: 10.1111/j.1469-8986.2004.00252.x.
5. Task Force of the European Society of Cardiology and the North American Society of pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation*. 1996;93:1043–1065.
6. Akselrod S, Gordon D, Madwed JB, Snidman NC, Shannon DC, Cohen RJ. Hemodynamic regulation: investigation by spectral analysis. *Am J Physiol*. 1985;249(4 pt 2):H867–H875.
7. Bayly EJ. Spectral analysis of pulse frequency modulation in the nervous systems. *IEEE Trans Biomed Eng*. 1968;15:257–265.
8. Munoz ML, van Roon A, Riese H, Thio C, Oostenbroek E, Westrik I, de Geus EJ, Gansevoort R, Lefrandt J, Nolte IM, Snieder H. Validity of (Ultra-)Short recordings for heart rate variability measurements. *PLoS One*. 2015;10:e0138921. doi: 10.1371/journal.pone.0138921.

From the Department of Vascular Medicine (A.M.v.R., J.D.L.), Department of Epidemiology (H.S.), and Interdisciplinary Center Psychopathology and Emotion regulation (ICPE), Department of Psychiatry (H.R.), University of Groningen, University Medical Center Groningen, The Netherlands; and Department of Biological Psychology, VU University Amsterdam and Institute for Health and Care Research (EMGO+), VU Medical Center, The Netherlands (E.J.C.d.G.).

Correspondence to Arie M. van Roon, Department of Internal Medicine, Division of Vascular Medicine, University of Groningen, University Medical Center Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands. E-mail a.m.van.roon@umcg.nl

(*Hypertension*. 2016;68:e63-e65. DOI: 10.1161/HYPERTENSIONAHA.116.08053.)

Table. Mathematical Rationale for the Relationship Between VC and cSDNN

Measured values of mean IBI and SDNN of subject *i* are used to calculate VC_{IBI} (v_i) as described by Akselrod[6]
$v_i = 100\frac{SDNN_i}{IBI_i}$
And the corrected SDNN, cSDNN (c_i), as described by Monfredi et al[1]
$c_i = \frac{SDNN_i}{e^{-\frac{HR_i}{a}}} = SDNN_i e^{60000/(a IBI_i)}$ a=58.8 bpm
We can write the IBI of each subject *i* as the group mean IBI ($\overline{IBI}$) and a relative deviation δ_i of that mean:
$IBI_i = \overline{IBI}(1+\delta_i)$
Under the common assumption that the δ's are <1, we can use the first-order Taylor expansion as approximations:
$\frac{1}{1+\delta_i} \approx 1-\delta_i \quad e^{\delta_i} \approx 1+\delta_i \quad \delta_i^2 \approx 0$
For the ratio of VC_{IBI} and cSDNN, we find now:
$\frac{v_i}{c_i} = \frac{100}{\overline{IBI}(1+\delta_i)} e^{-\frac{60000}{a\overline{IBI}(1+\delta_i)}} \approx \frac{100}{\overline{IBI}} e^{-\frac{60000}{a\overline{IBI}}}(1-\delta_i)\left(1+\frac{60000}{a\overline{IBI}}\delta\right)_i$
$\frac{v_i}{c_i} \approx \frac{100}{\overline{IBI}} e^{-\frac{60000}{a\overline{IBI}}}\left(1+\left(\frac{60000}{a\overline{IBI}}-1\right)\delta_i\right)$
When the group mean IBI is close 1020 ms and/or δ_i is small, the value of the last part of the equation is close to zero, so
$\frac{v_i}{c_i} \approx \frac{100}{\overline{IBI}} e^{-\frac{60000}{a\overline{IBI}}}(1+0)$
The relationship between variables VC_{IBI} and cSDNN is
$v_i \approx \frac{100}{\overline{IBI}} e^{-\frac{60000}{a\overline{IBI}}} c_i$
And after log-transformation, it is linear:
$\ln(v_i) \approx \ln(c_i) + \ln\left(\frac{100}{\overline{IBI}} e^{-\frac{60000}{a\overline{IBI}}}\right)$
with slope 1, highly correlated and constant difference of
$Const \approx \ln\left(\frac{100}{\overline{IBI}} e^{-\frac{60000}{a\overline{IBI}}}\right) = \ln(100) + \ln\left(\frac{1}{\overline{IBI}}\right) - \frac{60000}{a}\frac{1}{\overline{IBI}}$
In case of the group shown in Figure 1, $\overline{IBI}$=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 $\overline{IBI} = 60000/a = 1020.4$ ms.

Note: calculation rules for logarithms are ln(*ab*)=ln(*a*)+ln(*b*), ln(e^x)=^{e}log(e^x)=*x*. IBI indicates interbeat interval; cSDNN, corrected SD of normal beat to normal beat intervals; and VC_{IBI}, variation coefficient of IBI.

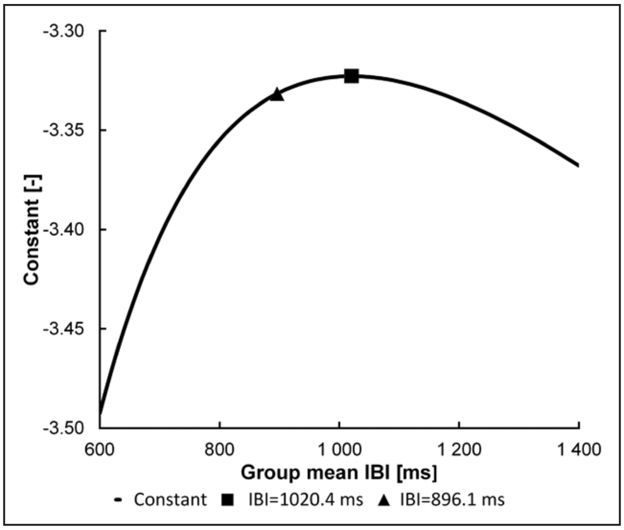

Figure 1. Estimated constant as function of group mean interbeat interval IBI. The constant varies only over a small interval of −3.5 to −3.3. Group mean of used data is 896.1 ms, maximum of the estimate is at 1020.4 ms.

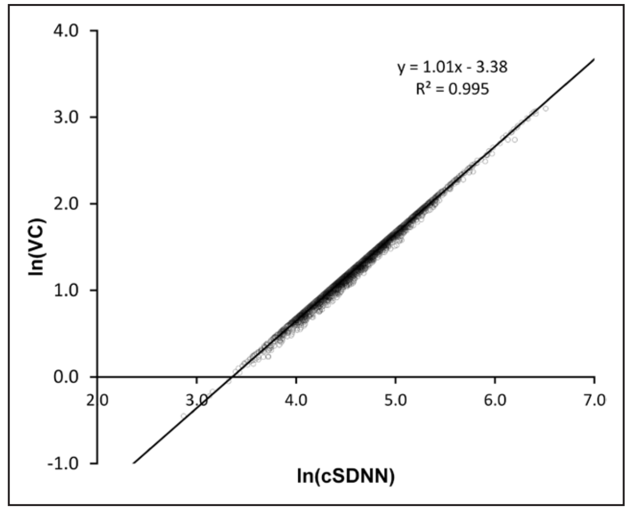

Figure 2. Graphical representation of the relationship between heart rate variability (HRV) measures calculated in 4976 human subjects (group mean interbeat interval [IBI]=896.1 ms) following 2 different procedures to correct for the relationship between HRV and HR: On the *x*-axis, the logarithmic transformed corrected SD of normal beat to normal beat intervals (cSDNN), ln(cSDNN), as proposed by Monfredi et al (Equation 8)[1]; on the *y*-axis, the logarithmic transformed variation coefficient (ln(VC)), proposed by Akselrod et al.[6] 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.

Hypertension
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

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

Print ISSN: 0194-911X. Online ISSN: 1524-4563