



## The role of heart rate in the assessment of cardiac autonomic modulation with heart rate variability

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Sirs:

We read with great interest the article by Claudia Arab et al. [1] which found that cardiac autonomic modulation was inversely associated with breast cancer staging before any cancer treatment. However, the study also shows that breast cancer staging is positively associated with a mean heart rate (HR). In fact, heart rate variability is strongly correlated with HR, which is partially determined by mathematical (inverse) relationship between R-R interval and HR [2, 3]. Due to this non-linear relationship, fluctuations of slow HR yield much higher oscillations of R-R intervals than the same fluctuations of fast HR [2] (Fig. 1). Consequently, slow HR usually exhibits higher HRV than fast HR. Therefore, if one compares HRV between patients presenting different HR, one should first correct HRV for the prevailing HR—such an approach enables us to determine if the differences in HRV come from real differences in variability or just from difference in HR [See Sacha et al. [4] for more details in how to correct HRV parameters for HR]. The problem of the HR

impact on HRV could be also solved if the authors included HR as one of the covariates in the multivariate models, however, they did not conduct any of these types of corrections/adjustment for HR in their analyses, which could greatly confuse the results and conclusions of the study. Thus, to draw an objective conclusion if HRV independently differentiates patients with various cancer stages, one should first exclude the HR impact on HRV—otherwise, it is likely that the observed differences in HRV may result from different HR.

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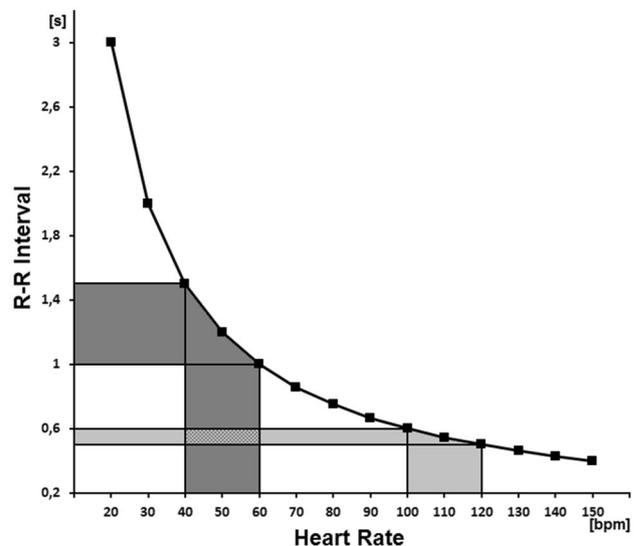
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**Fig. 1** The non-linear (mathematical) relationship between R-R interval and heart rate is depicted. One can see that the oscillations of a slow average heart rate (x-axis, dark gray area) result in much greater oscillations of R-R intervals (y-axis, dark gray area) than the same oscillations of a fast average heart rate (light gray area). As a consequence, the variability of R-R intervals is higher for the slow average heart rate than for the fast one, despite the fact that the variability of heart rate is the same (with permission of Jerzy Sacha [2])

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### Compliance with ethical standards

**Conflict of interest** There are no conflicts of interest to disclose.

### References

1. Arab C, Carlos L, Vanderlei M et al (2018) Cardiac autonomic modulation impairments in advanced breast cancer patients. *Clin Res Cardiol* 107:924–936. <https://doi.org/10.1007/s00392-018-1264-9>
2. Sacha J (2013) Why should one normalize heart rate variability with respect to average heart rate. *Front Physiol* 4:1–2. <https://doi.org/10.3389/fphys.2013.00306>
3. Sacha J, Pluta W (2008) Alterations of an average heart rate change heart rate variability due to mathematical reasons. *Int J Cardiol* 128:444–447. <https://doi.org/10.1016/j.ijcard.2007.06.047>
4. Sacha J, Barabach S, Statkiewicz-Barabach G et al (2013) How to strengthen or weaken the HRV dependence on heart rate—description of the method and its perspectives. *Int J Cardiol* 168:1660–1663. <https://doi.org/10.1016/j.ijcard.2013.03.038>