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Assessing cardiac autonomic function via heart rate variability analysis requires monitoring respiration

With great interest we have read the joint position statement about advances in heart rate variability (HRV) signal analysis presented by Dr Sassi *et al.*[1] They present a critical review of newly developed HRV methodologies developed after publication of the initial Task Force HRV overview[2] and their applications in different physiological and clinical studies. These novel approaches improved the technical understanding of the HRV signal; however, their success in clinical applications, such as in the identification of high-risk patients, has been rather limited. Therefore, in this letter, we present one possible explanation for this limited success that merits additional attention: the importance of monitoring respiration for the interpretation of standard HRV analysis and the need to address its complexities using improved signal processing methods.

In a case report of this issue,[3] we introduced a 20-year-old woman who had a non-sustained ventricular tachycardia (VT). Cardiac autonomic function was evaluated via standard HRV analysis which found a remarkably increased power in the low-frequency (LF) band in the resting state. Standard interpretation would suggest an increased sympathetic activity.

In this case report, we additionally looked for respiration. This arose from our experience in this matter that also led to us answering the question raised by Lean Glass 'Is the normal heart rate chaotic?' (Reference 45 in[1]) with another question 'Is the normal heart rate "chaotic" due to respiration?'.[4] There we demonstrated the principal influence of respiration in short-term HRV recordings. In the current case report,[3] the power spectra of both the respiration and HRV showed an almost identical picture; leading to the conclusion that respiration is clearly dominating the HRV. It follows that the 20-year-old woman does not have a sympathetic overactivation, but a situational changed respiratory pattern, shifting the whole spectrum to the LF band.

This letter suggests that respiration has to be considered as a covariate for all HRV analyses. The respiratory signal can be measured very easily, and where the measurement is not possible, the signal can be estimated indirectly from the electrocardiogram with high precision regarding the respiratory rate. This offers the possibility to apply more complex signal processing methods such as cardiorespiratory synchronization or coordination[5] which will very likely improve the success in clinical application. Finally, it avoids mistakes in the interpretation of the cardiac autonomic function of the heart.

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Assessing cardiac autonomic function via heart rate variability analysis requires monitoring respiration: reply

Confounders of heart rate variability

We surely agree with Wessel *et al.* that heart period fluctuations are linked to many physiological oscillations. As already explained in the 1996 heart rate variability (HRV) standards,[1] these oscillations include those of respiration,[2] blood pressure,[3] etc. The shifts in the respiration-related HRV components into the nominal low-frequency band are also known[4] as is the fact that the low-frequency HRV modulations cannot be taken as a single reliable expression of sympathetic activity.[1] It is difficult to consider respiration as an overwhelming determinant of short-term HRV. Adding additional provocations to constant controlled breathing still leads to profound HRV changes.[5] Breathing frequency is also only one and probably a simpler descriptor of respiration. In clinical well-defined populations, the value of respiration assessment[6] also appears somewhat different from that of novel HRV methods.

Moreover, a distinction is needed between the use of HRV in physiological and clinical, e.g. risk stratification, studies. Different confounders including respiration should be controlled in physiological investigations. However, the power of clinical risk assessment studies increases by considering the autonomic homeostatic maintenance comprehensively. Adjusting HRV measurements for confounders that are also under autonomic control might affect their predictive value. Our position statement[7] provided an update on some recent approaches to properly complement previously listed HRV parameters[1] in large clinical studies. We have not aimed at reviewing the vast literature on the interactions between HRV and other signals, but it would certainly be important to clinically validate the multivariate indices in the same way.

We do not see very clearly the association between the somewhat limited clinical applications of the new HRV methods[7] and the respiration–HRV coupling. Multisignal analyses including, among others, electrocardiogram, blood pressure, pulse oximetry, and respiration likely improve physiological quantification of autonomic reflexes, especially under provocations,[8] but the limited spread of novel HRV methods is probably caused by other factors. While the interpretation of the standard, e.g. spectral HRV analyses, reflects well-established physiological models easily comprehended by clinical researchers, such transparent models are not necessarily widely available for the HRV methods that we reviewed[7] and perhaps even less available for novel methods that we excluded since they have not been used in large studies. Applications of the non-standard HRV methods also require tools that are not readily available within commercial electrocardiographic equipment. This limits the new methods to specific laboratories that combine engineering knowledge with clinical experience. Outside such centres, the

contacts between clinical and engineering researchers are sadly limited.[9] On the one hand, collections of clinical data are too frequently either not provided to engineering teams or provided with limited background. On the other hand, engineering groups far too often develop advanced signal processing techniques without a clear vision of clinical problems to which the new concepts might be applied. Naturally, this calls for a more active collaboration between clinical and engineering teams and we can only hope that our position statement would facilitate such research partnerships.

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