

Comparison of Assessment Methods of Cardiac Vagal Modulation

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The theme “heart rate variability” (HRV) deserves to be continually studied by the scientific community, being one of our research lines. Regarding the article published in volume 97 (6), “Comparison of assessment methods of cardiac vagal modulation¹”, the following is worth noting: A) the samples were very different: older patients with coronary heart disease on beta-blockers *versus* healthy youngsters not treated with beta-blockade. Although the aim was to compare patients with coronary heart disease and healthy individuals, would the considerable age difference between

groups (approximately 40 years) not act as a confounding variable in the HRV values²? B) the use of beta-blockers was observed in 100% of the patients with coronary heart disease, as expected, considering the current guidelines, and in 0% of the healthy group. Autonomic modulation depends on a complex regulatory mechanism involving interaction between the sympathetic and parasympathetic pathways^{3,4}. However, after beta-blockade, the “modulatory” behavior of the vagus nerve is no longer spontaneous. Thus, would avoiding beta-blockers not provide more accurate results? C) time domain variables tend to be more precise in long-lasting registries⁵. D) Of the variables selected to measure “vagal action”, would SDNN (standard deviation of normal RR intervals) not be better for studying the sympathetic nervous system? Finally, we congratulate the authors and thank the opportunity to shed some light into those questions.

Keywords:

Heart rate; assessment; autonomic nervous system.

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Response letter

Dear Editor,

The interest in our recently published article¹ brought us great satisfaction. We appreciate the opportunity to respond to the editor's considerations. It is worth emphasizing that our research group has been investigating that theme for over two decades², with publications on the *Arquivos Brasileiros de Cardiologia*, and that the scientific community has not reached a consensus yet (over 10 thousand publications on MedLine). First, it is worth noting that the selection of

groups with different clinical conditions and age brackets was intentional, aiming at selecting individuals with distinct cardiac vagal function. That selection was correct, because the differences in the characteristics of the groups reflect a greater cardiac vagal modulation (CVM) in the healthy group as compared with that in the group of patients with coronary heart disease with the three methods studied [Heart Rate Variability (HRV), Respiratory Sinus Arrhythmia (RSA) and Four-second Exercise Test (4sET)].

However, by analyzing the effect size and ROC curves, we observed that the RSA and 4sET methods, as compared with the HRV, were more precise to discriminate CVM among

healthy individuals and patients with coronary heart disease. In that context, it is unlikely that the use of beta-blockers has influenced only the results obtained with the HRV. There is consistent evidence that beta-blockers increase CVM through both a direct effect on the central nervous system³ and a peripheral effect, due to a reduction in heart rate, which increases the probability that acetylcholine acts on the slow diastolic depolarization of sinoatrial node cells⁴, and due to a reduction in the pre-synaptic inhibition of the release of acetylcholine mediated by sympathetic activity⁵.

Thus, the beta-blocker-mediated increase in CVM is likely to have influenced the three methods assessed in the study and not only HRV, reducing the difference in the cardiac vagal function between the groups. It is worth noting that the assessment of patients on medications has increased not only the external validity of the results but the study applicability as well, since it is a similar situation to that found in clinical practice. Finally, the RR intervals were registered for ten minutes in a calm environment, with the individuals in the supine position and with controlled respiratory frequency.

In such conditions, the HRV results are more dependent on CVM, including the SDNN variable (standard deviation of normal RR intervals), and not on intervening variables⁶, thus generating more reproducible results⁶. Differently, on long-lasting registries, there is an influence of non-autonomic variables on the HRV results (ex.: temperature variations, hormonal variations), hindering the interpretation of the autonomic contribution.

Sincerely,

Vagner Clayton de Paiva

Kelen Rabelo Santana

Bruno Moreira Silva

Plínio Santos Ramos

Júlio César Moraes Lovisi

Claudio Gil Soares de Araújo

Djalma Rabelo Ricardo

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