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The possibility of using spectral indices of heart rate variability to improve the diagnostic value of cardiovascular autonomic function tests in rheumatoid arthritis patients

To the Editor,

Our comment is related the paper by Javady Nejad et al. (1) where they reported cardiovascular autonomic control in 44 rheumatoid arthritis (RA) patients and 44 healthy subjects. Until now, the involvement of the autonomic nervous system in chronic systemic inflammatory disorders is disputable. Several authors reported significant differences in cardiovascular autonomic control in RA patients and healthy subjects: Refs. 3, 7, and 10-14 in the paper by Javady Nejad et al. (1).

The strong point of the cross-sectional study performed by Javady Nejad et al. (1) is the employment of a variety of cardiovascular autonomic function tests, namely, deep breathing with a frequency of 6 breaths per minute, active tilt test, Valsalva maneuver, and sustained handgrip. On the contrary to previous results, the authors found no difference between the RA patients and control subjects in their responses to the autonomic function tests. This important result requires an additional analysis. The ECG recording was performed by Nejad et al. (1) during all tests. Therefore, it is advisable to further explore the indicators of heart rate variability (HRV) (2) that may complement the classical interpretation of the cardiovascular autonomic function test results.

The response of heart autonomic control, which is studied by HRV, to external periodic disturbances (such as controlled breathing, controlled eye opening, etc.) is determined by a frequency-dependent phenomenon (3, 4). The external 0.1-Hz disturbance at a rate of six actions per minute is a powerful factor for baroreflex control that shows itself in healthy subjects as a resonance response in the low-frequency heart rate variations (3, 4). Moreover, a 0.1-Hz controlled breathing is potentially the main external factor for the study of baroreflex gain and its dysfunction. Thus, spectral analysis of HRV can supplement the results of the study conducted by Javady Nejad et al. (1). The controlled breathing can also be combined with a tilt test (3) to obtain useful additional information in the further study of cardiovascular autonomic control in RA patients.

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Author's Reply

To the Editor,

We appreciate the careful review and insightful comments by our colleagues regarding our recent study entitled "Cardiovascular autonomic neuropathy in rheumatoid arthritis assessed by cardiovascular autonomic function tests: A cross-sectional survey," which was published in *Anatol J Cardiol* on Nov 11, 2014. (1)

In our study, we assessed cardiovascular autonomic neuropathy (CAN) in rheumatoid arthritis (RA) patients compared with that in control subjects by bedside autonomic function tests (1).

These tests include the following: 1) beat-to-beat heart rate variation during deep breathing, 2) heart rate response to standing up, 3) heart rate response to the Valsalva maneuver, 4) blood pressure

response to standing up, and 5) blood pressure response to a sustained handgrip.

There are other approaches for evaluating the autonomic nervous system by heart rate variability (HRV) parameters from short- or long-term monitoring (2). We agree that HRV and bedside autonomic function tests for evaluating the autonomic nervous system provide complementary information regarding autonomic regulatory mechanisms in health and disease. However, the bedside autonomic function tests were more feasible for us during the study.

We also considered that spectrum bias may account for differences in the reported results between the investigations.

Therefore, in order to point out the difference between the cardiovascular autonomic function of RA patients and general population, we will design another prospective cohort study with complementary and more sensitive tests.

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Restless leg syndrome and slow coronary flow. Is it inflammation or autonomic nervous system?

To the Editor,

Erden et al. (1) recently published a very interesting paper in the *Anatolian Journal of Cardiology* 2014; 14: 612-6 entitled "Association between restless leg syndrome and slow coronary flow," which suggests an association between the coronary slow flow (CSF) phenomenon and restless leg syndrome. The article showed that patients with the CSF phenomenon were more likely to suffer from restless leg syndrome compared to subjects with normal coronary flow. Although, I appreciate the authors for their work, there are some issues that need to be clarified in order to glean more data from the article. The definition of CSF relies upon TIMI frame count (TFC), which varies depending on the image acquisition rate. The authors chose a recording speed of 25 frames/s. Still, they defined CSF according to the criteria based on the reference values of Gibson et al. (2). "a TFC greater than two standard deviations from the normal range for a particular coronary artery."

Gibson used a frame rate of 30/s. Thus, the authors could have underestimated TFC. I believe that they need to multiply their corrected TFC with a factor of 1.2 in order to find the real corrected TFC, which may render some of their normal patients into a group of CSF (2, 3). It would be appropriate to know the mean cTFC values of patients with the CSF phenomenon and those of the normal patients in this regard. Even though the authors reported the overall prevalence of restless leg syndrome, it would be useful to know how many patients with and without the CSF phenomenon had restless leg syndrome. In our current practice, we do not come across patients having both the CSF phenomenon and restless leg syndrome, thus, they may have mild symptoms. Was there any association with symptom severity and TFC? We previously showed that patients with the CSF phenomenon had attenuated heart rate recovery, suggesting impaired vagal activation of the cardiovascular system (4). Therefore, we agree with the authors that the common link between the CSF phenomenon and restless leg syndrome is the probably autonomic nervous system.

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Author's Reply

To the Editor,

We thank to Tekin for her interest in our investigation entitled "Association between restless leg syndrome and slow coronary flow" published in *Anatol J Cardiol* 2014; 14: 612-6 (1).

Some standard recommendations are made for the quantitative analysis of epicardial blood flow. Pérez de Prado et al. (2) reported that imaging speed should ideally be 25 frames/s. Nevertheless, the corrected TIMI frame count (cTFC) can be calculated at any recording speed, and subsequently it can be expressed in seconds or adjusted to the recommended speed. The images obtained by cineangiography in