Prognostic marker of nonfatal pulmonary thromboembolism: decreased glomerular filtration rate or increased age?

To the Editor,

We read the article titled "Chronic kidney disease: Prognostic marker of nonfatal pulmonary thromboembolism" by Ouatu et al. (1) published in Anatol J Cardiol 2014 Dec 31 with great interest. In this article, the authors aimed to elucidate the relationship between venous thromboembolism-related mortality and renal dysfunction assessed by a regression-based MDRD formula. As a result of their investigation, the authors proposed that GFR is an independent predictor of 2-year mortality in pulmonary embolism besides troponin, dyslipidemia, acceleration time of pulmonary ejection, pericardial effusion, and BNP.

Chronic kidney disease is a well-known prognostic factor, indicating increased morbidity and mortality in various cardiovascular diseases and acute pulmonary embolism. Impairment of renal functions may be related to preexisting chronic kidney disease or deteriorations secondary to hemodynamic failure (2). In clinical practice, renal functions are usually evaluated using creatinine-based formulae, which are based on age and gender. This situation may cause biases even after adjustment for age and gender in statistical analysis when evaluating the data for independence. It may not be cost-effective to evaluate renal functions with inulin or radioisotope-based quantitative determinants of GFR other than regression-based GFR formulae in a relatively large number of cases.

According to the current guidelines (3), various prediction rules have been proposed for the prognostic assessment of patients with acute pulmonary embolism, and the pulmonary embolism severity index is one of the most widely used scores. This scoring system and its simplified form are composed of several variables including "age." Male gender is also a poor prognosis predictor in the original form of the scoring system. In the current article by Ouatu et al. (1), gender difference was not significant between survivors and non-survivors, while age was significantly higher in non-survivors. We wonder if the authors adjusted their findings for age and possibly for gender or if they brought these variables into regression models. Otherwise, it is hard to propose GFR as an independent predictor of mortality owing to the highly possible collinearity between age and GFR. These concerns could be kept in mind while evaluating the results of this study.

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DOI:10.5152/AnatolJCardiol.2015.6413

Author`s Reply

Authors of this mentioned article did not send any reply for this Letter to Editor, in spite of our insistently request.

Analysis of heart rate variability seems to be one step ahead of cardiac reflex tests for investigating cardiovascular autonomic neuropathy

To the Editor,

We read with great interest the paper by Javady et al. (1) entitled "Cardiovascular autonomic neuropathy in rheumatoid arthritis assessed by cardiovascular autonomic function tests: A cross-sectional survey" published as Epub Ahead of print in Anatol J Cardiol 2015; 15: 722-6. They aimed to investigate cardiovascular autonomic neuropathy (CAN) by cardiac reflex tests (CARTs) in patients with rheumatoid arthritis and reported no CAN in these patients.

CAN is defined as an impairment of cardiovascular autonomic control in the absence of other reasons causing dysautonomia. Although CAN has been considered as an important cause of morbidity and mortality in patients with diabetes mellitus since the 1970s, it has recently been shown that CAN has a prognostic importance for some diseases such as myocardial infarction and sudden cardiac death (2, 3).

The Toronto Consensus reported the five most sensitive and specific methods [heart rate variability (HRV), baroreflex sensitivity, muscle sympathetic nerve activity, catecholamine plasma level, and cardiac sympathetic mapping] to diagnose CAN (2, 3). The presence of CAN can be established with two or more abnormal tests. However, these tests except HRV are not easy to perform. These days, cardiovascular autonomic reflex tests (CARTs) demonstrating RR interval variability beat-to-beat which is experimentally induced and HRV parameters (time- and frequency-domain methods showing spontaneous RR variability) are accepted methods in clinical practice (2, 3).

CART's demonstrate HRV alteration during four maneuvers including (I) deep breathing, (II) Valsalva, (III) orthostatic test, and (IV) orthostatic hypotension and indicated in the autoimmune autonomic neuropathy. The first three maneuvers predominantly investigate the parasympathetic activity, and the last one determines the sympathetic tonus in contrast to knowledge given by Javady et al. (1) in the article.

HRV analysis described as RR interval variability beat-to-beat is a valuable non-invasive method for the evaluation of autonomic dysfunction and might be affected by various factors (4, 5). In the study by Javady et al. (1), it is very difficult to state no CAN in patients with rheumatoid arthritis without considering influential factors on HRV such as body weight, body mass index, insulin resistance, and blood

lipid levels. We supposed it is necessary to present the data showing no statistically significant difference between the patients and control subjects with regard to influential factors.

Finally, the international Toronto Consensus supports the spectral analysis of HRV beyond CARTs, which are currently accepted as the gold standard (2). We think that the presence of CAN in patients with rheumatoid arthritis is shown with the spectral analysis of HRV as well as the reflex tests used in the study by Javady et al. (1).

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DOI:10.5152/AnatolJCardiol.2015.6568

Author`s Reply

To the Editor,

We appreciate the precise review and insightful comments by our dear colleagues regarding our recent study entitled "Cardiovascular Autonomic Neuropathy in Rheumatoid Arthritis assessed by Cardiovascular Autonomic Function Tests: A cross-sectional survey" published in Anatol J Cardiol 2015; 15: 722-6.

In our study, we assessed cardiovascular autonomic neuropathy (CAN) in rheumatoid arthritis (RA) patients compared with control subjects by bedside autonomic function tests. Our study failed to show any statistically significant difference between cardiovascular autonomic function tests in RA patients and the control subjects (1).

Although in studies autonomic function tests are considered indices mainly of parasympathetic or sympathetic function, according to Ewing et al. (2), "The autonomic pathways involved in all cardiovascular reflex tests are however extremely complex and include both parasympathetic and sympathetic fibers to a greater or lesser extent. While heart rate responses are primarily mediated via cardiac parasympathetic pathways, additional sympathetic influences, particularly in the Valsalva maneuver, can alter these responses. We and others have previously classified these tests into parasympathetic and sympathetic, depending on whether heart rate alone or both heart rate and blood pressure control was affected. This approach has proved to be extremely useful clinically because it reflects the sequence of damage seen in diabetic subjects and has therefore been widely used. However, we would stress that although clinically useful, such a classification should not be considered physiologically precise because of the complexity of autonomic pathways" (2).

About influential factors of heart rate variability such as body weight, body mass index, insulin resistance, and blood lipid levels (3) that our dear colleagues mentioned, these are not among the variables in our study. We agree these factors can provide complementary information. Therefore, these factors needed to be considered in future studies that will assess the difference between the cardiovascular autonomic function of RA patients and the general population.

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Predictors of successful percutaneous transvenous mitral commissurotomy using the Bonhoeffer Multi-Track system in patients with moderate to severe mitral stenosis: Can we see beyond the Wilkins score?

To the Editor,

We read the original investigation entitled "Predictors of successful percutaneous transvenous mitral commissurotomy using the Bonhoeffer Multi-Track system in patients with moderate to severe mitral stenosis: Can we see beyond the Wilkins score?" by Farman et al. (1) published in the Anatol J Cardiol 2015; 15: 373-9. with great interest. We would like to touch on some points regarding this article.