

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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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