

Soluble suppression of tumorigenicity-2 for risk stratification in outpatients with heart failure

To the Editor,

I have read the article by Gül et al. (1) entitled "Prognostic role of soluble suppression of tumorigenicity-2 on cardiovascular mortality in outpatients with heart failure," which was published in *Anatol J Cardiol* 2017; 18: 200-5, with great interest. In their study, the authors reported that baseline levels of soluble suppression of tumorigenicity-2 (sST2) are an independent predictor of mortality in outpatients with heart failure (HF) with a high sensitivity of 87%. They concluded that patients who died during follow-up had higher sST2 levels than patients who survived (1). I would like to emphasize some important points about this well-written study.

It has been demonstrated that sST2 is associated with inflammatory and immune process in several diseases including cardiovascular disorders. sST2 is released into the circulation in HF patients as a response to cardiac stress as well as inflammation (2). Therefore, the authors should state if there was any difference between the two groups in terms of inflammatory states. Measuring inflammatory marker levels could provide insights into the cardiovascular role of sST2 in HF patients, as non-myocardial sources of sST2 are well-known (3).

A strong association between NYHA functional class, heart rate, body mass index, and outcomes in patients with systolic HF has been demonstrated in previous studies. Also, it has been shown that there is a correlation between NYHA functional class and sST2 levels (4, 5). So, I was wondering if there was any difference between the two groups in terms of these parameters? I think that the abovementioned factors should be taken into consideration to verify the prognostic value of sST2 on cardiovascular mortality in outpatients with HF.

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DOI:10.14744/AnatolJCardiol.2018.05914



Author's Reply

To the Editor,

First, we would like to thank you for your interest in our paper entitled "Prognostic role of soluble suppression of tumorigenicity-2 on cardiovascular mortality in outpatients with heart failure" (1).

We had pointed out in the paper that soluble suppression of tumorigenicity-2 (sST2) levels increased in collagen tissue diseases, cancer, sepsis, and ulcerative colitis, indicating that it is also associated with inflammation and immunological processes (2). However, cancer, sepsis, and ongoing systemic inflammatory conditions including autoimmune diseases were among our exclusion criteria, although our patients were HF outpatients and inflammatory markers such as CRP levels were not routinely tested.

The association between sST2 level and the functional capacity of patients with chronic heart failure had been previously evaluated in a smaller case-control study from our cohort with an available double-checked NYHA Class data, although survival data had not been considered (3). We herein reiterate the results designating that sST2 levels were higher in patients with NYHA functional classes III and IV than in patients with NYHA functional classes I and II ($p < 0.001$). However, we also declare that in both of our works, body mass index and heart rate were not thoroughly considered and that these chronic HF outpatients were well-treated with beta blockers, and the relation between ST2 level and heart rate is not well-validated in the presence of chronic beta blocker therapy.

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Interleukin-1 gene cluster polymorphisms associated with coronary slow flow phenomenon

To the Editor,

We found the publication "Association of Interleukin-1 Gene cluster polymorphisms with coronary slow flow phenomenon (CSFP)" (1) very interesting. Mutluer et al. (1) concluded that "IL-1 β +3954 SNP mutations are significantly more common in patients with CSFP" and "It may suggest that the tendency for inflammation may contribute to the presence of this phenomenon." In fact, based on the present study, a conclusion can be made only regarding genetic frequency. It is not possible to propose any pathophysiology regarding the inflammation process since no inflammatory parameter was assessed. In fact, if there is a direct pathological process as a result of the polymorphism, similar findings should be observed for both IL-1 β +3954 SNP and IL-1 β +3954 SNP. Finally, other SNPs of IL-1 β , which were not investigated by Mutluer et al. (1), such as IL-1 β -634SNP (2), can also have the same effect on CSFP.

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at www.anatoljcardiol.com

DOI:10.14744/AnatolJCardiol.2018.26429



Author's Reply

To the Editor,

We would like to thank authors for their valuable comments on our recently published study titled "Association of Interleukin-1 Gene cluster polymorphisms with coronary slow flow phenomenon (CSFP)" (1). We cannot disagree on their comment on the association between inflammation tendency and IL-1 gene polymorphisms. We would like to clarify that there is a thin line between drawing conclusions and suggesting hypotheses, and we stay on the side of just suggesting hypotheses. The main weakness of small-sized genetic case-control studies is their lack of power to draw conclusions from the results. This is the reason why the methodology of genetic studies is moving toward genome-wide association studies (2). It would have been better if serum interleukin-1 β and interleukin-1RA levels were evaluated in our study. This is among the limitations of our study. However, it should be noted that the effects of mutations on inflammatory mechanisms might as well be simply beyond increasing and decreasing the synthesis of the gene product. Conflicting results testing the same hypothesis that these mutations have effects on the course of diseases associated with inflammation also underline this complexity. Additionally, we should emphasize that the co-occurrence of single nucleotide polymorphisms is not a rule. Associations might vary between different polymorphisms in the same gene as a result (3). Finally, screening for all defined mutations and even describing new mutations is possible with next-generation sequencing. However, with conventional methodologies, how many different mutations can be studied is a matter of time and resources (4).

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