

that continuing the search for the best therapy for PVT is no longer necessary. Two therapeutic alternatives exist for managing these severe patients (thrombolytic therapy and surgery), but they are complementary. We propose thrombolysis as the initial treatment if no contraindications are present (e.g., thrombi + 10 mm). Surgery is reserved for patients with contraindications to thrombolysis, those in whom this therapy is unsuccessful, and per se, who present with stroke and left atrial thrombus (2).

The main related limitation with the thrombolytic treatment is when the cerebral embolism occurs. An interesting option to treat this complication during the thrombolytic treatment in the PVT is the thrombolysis continuity as it has reported in this case for Özkan et al. (1).

In the year 2004, Lengyel et al. (3) indicated that twenty cases of non-hemorrhagic stroke or transient ischemic attack have been treated with thrombolysis, with only one hemorrhagic transformation.

In the year 2005 were published the guidelines of the Society of Heart Valves Disease for the management of PVT and recommend as an indication Class III the thrombolysis in presence of ischemic stroke documented for cerebral CT scan before the 4 hours that initiate the symptoms (4).

We suggest that the thrombolytic therapy in the ischemic stroke can be effective in the first 3 hours of the beginning of symptoms if the cerebral scan do not show signs of hemorrhages. It is generally recommended to interrupt thrombolysis for PHVT if there is clinical evidence of a cerebrovascular accident during treatment, and to perform an urgent cranial CT scan to differentiate between a hemorrhagic and ischemic origin. If there is no evidence of brain hemorrhage on CT scan, thrombolytic therapy can be restarted (5).

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## Author Reply

Dear Author,

Thank you very much for your comprehensive and encouraging comments on our article published in "letter to editor" section of *Anatolian Journal of Cardiology* that I was entirely agree and feel nothing to add on top of it.

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## Influence of gender, C- reactive protein and triglycerides in risk prediction of coronary heart disease

*Koroner arter hastalığı riskini öngörmeye cinsiyet, C-reaktif protein ve trigliseridin etkisi*

Dear Editor,

Having read the article entitled "Clinical biomarkers of high-density lipoprotein dysfunction among middle-aged Turks" by Onat et al. (1), where the mentioned author studied some clinical biomarkers of high-density lipoprotein dysfunction in a stratified adult Turkish population. We would like to join the discussion about the influence of gender, and C-reactive protein (CRP) and triglycerides (TG) levels in risk prediction of coronary heart disease (CHD). For this purpose, we show the results of our small-sample study of schizophrenic patients on long-term clozapine, a drug that consistently raises CRP levels, where we evidenced that women had lower CRP increases than men (about a half) in response to a constant stimulus as clozapine long-term treatment. Also, we found that elevated CRP levels were associated with high levels of cholesterol, low-density lipoprotein and body mass index (2).

Cholesterol and TG, rise CRP levels through the activation of toll-like receptor 4 (TLR4) and subsequently liberation of proinflammatory cytokines such as tumor necrosis factor and interleukin -6, among others. This CRP-release, in turn, can activate TLR4 and lead, under certain circumstances and/or stimuli to a self-perpetuating cholesterol/TG-CRP loop (3, 4).

Moreover, TLR4 constitutes a link between nutrition, lipids and proinflammatory cytokines, being TG and cholesterol from any source, including diet, the most common metabolic-triggers for TLR4 (5). This TLR4 activation is also gender-dependent, with an LPS-stimulated accumulation of proinflammatory cytokines, significantly decreased in women (6), where its production would be facilitated by the presence of elevated levels of TG.

Putting it all together, we can conclude that women, whose innate immune response TLR4-mediated as mentioned also by Imahara (6) is

more decreased than men, requires higher levels of TG than men to stimulate production of CRP, TLR4 mediated, and that TG constitutes a clinical biomarker of impaired antiinflammatory or atheroprotective function in women, while in men it would be CRP, whose release would not depend on TG; in agreement with the findings of Onat et al. (1), about the usefulness of CRP and TG, among others, as clinical biomarkers of impaired or atheroprotective high-density lipoprotein antiinflammatory function for men and women, respectively.

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## Author Reply

**Sex divergence in rise of serum CRP to pro-inflammatory mediators  
Proinflamatuvar mediyatörlerin serum CRP artışında cinsiyet farkı**

Dear Author,

Regarding prediction of coronary heart disease, for which we tried to identify clinical biomarkers in the population at large in our recently published study (1), Lozano et al. (2) commented on the influence of gender on circulating C-reactive protein (CRP), representing the inflammatory response of the organism. Concurring with our conclusion that, added to fasting triglyceride concentrations, elevated CRP was proposed to mark high-density lipoprotein (HDL) dysfunction in cardiometabolic diseases among men but not in women (in whom elevated complement C3 was identified as independent marker), the author pointed out that, in the long-term treatment of schizophrenic patients with clozapine, a drug that consistently raises CRP levels, women respond with about half as great a rise in CRP as men.

We have reached the opinion since our study was concluded, that this sex difference on CRP is related to the association of circulating

lipoprotein [Lp] (a) with triglycerides and the possible concomitant existence of autoimmune activation, a slow process which comprises aggregation between certain damaged proteins and protective serum proteins, and predominates in females (3). HDL dysfunction in males is usually, though not exclusively, due to simple pro-inflammatory state whereas it is associated in women commonly with inflammation-induced autoimmune process as well which often involves Lp(a) and apolipoprotein A-I. The immune complex formation is associated with complement C3 elevation (4) and with less independence from other clinical markers of systemic inflammation (including fasting triglycerides) and a lesser degree of rise in CRP levels. Hence, the divergence between sexes in rise of CRP levels to certain pro-inflammatory mediators. One may speculate whether clozapine, beyond stimulating CRP release, affects in women the induction of autoimmune processes.

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## Can isolated ST elevation in aVR lead be a sign of acute pulmonary embolism?

*aVR'de izole ST yükselmesi akut pulmoner emboli belirtisi olabilir mi?*

Dear Editor,

Pulmonary embolism (PE) remains the major challenge of acute chest disease. The clinical and electrocardiographic manifestations may deviate to a diagnosis of acute coronary syndrome and even myocardial infarction. The current report documents the case of a 42-year-old woman who presented to the emergency department with chest pain and dyspnea. She had no known history of ischemic heart disease, cardiomyopathy, arrhythmia, or central nervous system disease. She had a 6-year history of minimal tobacco use. On examination, the patient's blood pressure was 100/60 mm Hg in the supine position; oxygen saturation, 96%; and heart rate, 123 beats per minute and regular. Her electrocardiogram showed interestingly isolated ST elevation in aVR lead and