Author`s Reply

To the Editor,

We thank the authors for the interest they have shown in our article entitled "Successful treatment of a pulmonary embolism with low-dose prolonged infusion of tissue-type plasminogen activator in a 37-year-old female in the early postoperative period," published in Anatolian J Cardiol 2014; 14: 400-2. (1).

Current guidelines suggest using thrombolytic therapy as the first-line treatment modality (2). The approved protocol is 100 mg t-PA during a 2-hour infusion (2). However, it is associated with an increased rate of major bleeding and mobilization of the thrombus. Therefore, many clinicians hesitate in ordering thrombolytic therapy. Recently, Özkan et al. (3) reported that prolonged low-dose prolonged administration t-PA was effective and safe in the treatment of prosthetic valve thrombosis, which significantly decreased major and minor bleeding complications compared to full-dose and accelerated regimens. They suggested that increasing the time of administration and decreasing the thrombolytic dosage provided safety advantages without decreasing the effectiveness (3). Catheter-directed ultrasound-accelerated thrombolysis is a promising treatment alternative, but low-dose ultra-prolonged infusion of t-pa was used in this approach, as well (4). The question is whether low-dose prolonged infusion of t-PA or the ultrasound beam is the key element of the treatment success and safety. Currently, we are conducting research about the effectiveness and safety of low-dose prolonged infusion of t-PA in the treatment of massive pulmonary embolism. This study is registered with Clinical Trials with the number NCT02029456. The initial results of this interventional study were presented in the 2014 ESC Congress (5). In this study, we have also shown that a low-dose prolonged infusion protocol restored right ventricular function in the immediate and medium term, evaluated with echocardiography. Further randomized studies will enlighten us on the safety and efficacy of these protocols.

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Association of mitral annular calcification with fetuin-A levels

To the Editor,

We read the article, entitled "Association of mitral annular calcification with endothelial dysfunction, carotid intima-media thickness, and serum fetuin-A: An observational study," by Ziyrek et al. (1) in Anatolian J Cardiol 2013; 13: 752-8, in which they reported that their findings might reflect a close association between mitral annular calcification and cardiovascular risk factors in patients with coronary artery disease, based on fetuin-A and carotid intima-media thickness evaluation (1). We thank the authors for their valuable contribution to the medical literature. However, we want to point out an important issue about fetuin-A.

Fetuin-A, an acute-phase glycoprotein that is synthesized and secreted by liver, plays a role in bone mineralization and insulin signaling regulation (2). Serum fetuin-A concentration is a good indicator of liver cell function, and it ranges from approximately 450-600 µg/mL in healthy individuals (3). The authors defined mean fetuin-A levels as 2.9±0.1 ng/mL and 3.0±0.2 ng/mL for the MAC group and control group, respectively. In this respect, though lots of previous studies, this study offered approximately 10,000-fold lower mean fetuin-A values, which could not be acceptable. It is already defined in the commercial ELISA kit that the authors used for the fetuin-A measurement that the measured concentration of samples calculated from the standard curve must be multiplied by their respective dilution factor, because the samples were diluted prior to the assay. Most likely, we think that the fetuin-A values of the study are derived from this post-analytical error.

In conclusion, to prevent any misunderstanding, an explanation of this concern will certainly provide clearer information for the readers.

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Author`s Reply

To the Editor,

We would like to thank the authors of the letter for their interest and criticism about our study entitled "Association of mitral annular calcification with endothelial dysfunction, carotid intima-media thickness, and serum fetuin-A: An observational study," published in the December issue of Anatolian J Cardiol 2013; 13: 752-8 (1).

We re-examined our results retrospectively. During the biochemical analysis, the diagnostic range of our spectrophotometry data was not available. For this reason, our blood samples were diluted in a higher percentage.

The differences of the results between our study and some other articles may possibly be the consequence of the dilution ratios of our spectrophotometry values.

We indicated the normal value of fetuin-A in our article. However, the aim of our study was to compare fetuin-A levels between the two groups.

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Cholesterol; is accused for the atherosclerosis proximal to myocardial bridging?

To the Editor,

We excitedly read the article about the close relationship of myocardial bridging (MB) and atherosclerosis at its proximal segment, which was suggested by Hong et al. (1), published in Anatolian J Cardiol 2014; 14: 40-7. They had suggested that the presence of MB on a coronary artery was one of the clinically independent risk factors for atherosclerosis, such as age, diabetes, and dyslipidemia. Duygu et al. (2) previously stated that MB initiated and facilitated the development and progression of atherosclerosis in the Anatolian Journal of Cardiology in 2007 (2). Systolic compression, which is a diagnostic marker for the presence of MB on the coronary angiogram, is generally supposed to account for the hemodynamic and endothelial changes that promote the atherosclerosis. In fact, the hemodynamic abnormalities are induced by MB during the diastolic period, in which the coronary artery flow and the myocardial perfusion are at their maximum (3). Since the MB behaves as an anatomic obstacle that surrounds and limits the coronary artery from its outside, a diastolic flow gradient develops at the proximal part of the bridged arterial segment. So, the diastolic gradient exerts a "seeding effect" that urges the cellular and lipid component of blood to pass into the sub-endothelial layers of the coronary artery. Phagocytic cells, cholesterol, and lipoprotein particles are the main components of an atherosclerotic plaque and also determine the vulnerability of the plaque (4). Moreover, the diastolic gradient at the proximal segment induces an increased shear stress and endothelial dysfunction, which are represented by reduced nitric oxide synthesis, antithrombotic functions, and vasodilation. These are the initial and earliest abnormalities observed in the development of atherosclerotic plaque (AP).

In the preliminary results of our study, we observed that the serum levels of total cholesterol, LDL- and VLDL-cholesterol, and triglyceride were significantly higher in patients with MB and AP (n=7) and AP (n=9) compared to patients with only MB (n=18) (unpublished data). Patients with MB who had a normal lipid profile were free from atherosclerosis, while all patients with MB and coexisting hypercholesterolemia had atherosclerotic plaque in the proximal arterial segment of the MB. It reminded us that the ancient guilty; cholesterol; was again responsible for the atherosclerosis at the proximal coronary segment of the MB. Coexistence of MB and AP in the presence of hyperlipidemia indicates that cholesterol may be a prerequisite for the development of an AP proximal to the MB. MB was surprisingly detected with a high prevalence and was found to be highly associated with atherosclerosis and sudden cardiac deaths in young and young adult subjects (5). Nevertheless, a debate about the criteria of statin therapy, target cholesterol levels, and whether it is an equivalent of atherosclerotic coronary artery disease, as well as diabetes, will develop in the management of those patients with MB. We suggest that MSCT coronary angiography, which has a great capability in the detection of MB and AP, even at the initial stages, may guide the indication of statin therapy by documenting the presence of AP in association with MB.

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