trometry and high-performance liquid chromatography methods and runs varying in different laboratories (3). As stated by the authors, HPLC coupled to mass spectrometric detection (LC-MS/MS) is not widely available, and the equipment is comparatively expensive (4). So, HPLC was the preferable method for us to detect ADMA.

Intravascular ultrasound is a validated and superior method when compared with coronary angiography to determine neointimal tissue burden, assessment of lesion significance, and stent restenosis (5). But, in our country conditions, it is not feasible to evaluate stent restenosis for every patient because of its cost and low availability.

There are so many relevant biomarkers known for stent restenosis (6), but it is not feasible to evaluate all of them in one study protocol. Our aim was to evaluate if ADMA predicts stent restenosis beyond classic predictors or not. In our study, we concluded that plasma ADMA level may be used as a novel marker for stent restenosis beyond the classic stent restenosis markers. However, as we stated in our study, this result should be confirmed by larger, prospective, and controlled studies.

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Should systemic thrombolytic therapy be considered a first-line treatment in acute pulmonary embolism?

To the Editor,

We read the 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,” by Akyan et al. (1) in Anatolian J Cardiol 2014; 14: 400-2. We believe that it can be a really good idea to administer low-dose thrombolytic agents in pulmonary embolism to minimize possible complications. Of course, randomized controlled trials should be performed to test the reliability of this low-dose regimen. We are curious as to why the authors did not consider using well-proven modalities, like percutaneous ultrasound-accelerated thrombolysis (PUAT) and directed thrombolysis (CDT) (2-4).

There is no clinical study available so far comparing systemic thrombolytic therapy and endovascular thrombolytic therapy, but this kind of study can take considerable time and can also yield major hemorrhagic complications up to 20%; so, it is preferable to go for an endovascular approach, where direct administration of a thrombolytic agent into the thrombus is possible (4, 5). In PUAT therapy, the dose of tissue plasminogen activator (tPA) is 0.5 mg/kg. Engelhardt et al. (4) even showed the efficacy of doses as low as 20 mg tPA for treatment of pulmonary embolism. In our institution, 4 patients with massive/sub-massive pulmonary embolism received PUAT with 0.5 mg/kg tPA infusion for 6 hours. We did not experience any complications or mortality. Remarkable improvement in right ventricular functions was shown in all patients with echocardiography and computed tomography.

Measurements of right ventricle and left ventricle diameters could also be a very useful tool in assessing the efficacy of treatment in massive pulmonary embolism. We would like to hear the authors’ opinions regarding the concerns mentioned above.

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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 prothrombotic 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 Ziyprek 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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