

Notes on patient compensation system suggestion

To the Editor,

We have read with great interest the letter to the editor entitled "An alternative malpractice system suggestion for Turkey: Patient compensation system" by Olcay et al. (1) that was published in *Anatolian J Cardiol* 2015; 15: 775-6. It is our opinion that the patient compensation system (PCS) that was proposed to prevent healthcare staff burnout, defensive medical practices, and increased healthcare expenditures at first appears convenient in general terms. According to our previous study in which judicial issues experienced by emergency physicians were examined, we determined that 57.8% of emergency physicians were complained to patient communication units and 14.2% of them were sued for medical malpractice. Furthermore, we observed that clinical decisions of 41.5% of emergency physicians were affected by previously experienced judicial and administrative inquiries (2). With respect to these studies, we believe that some legal points need to be considered while designing PCS, which is deemed beneficial to conduct healthcare services.

First, PCS cannot alter the physicians' responsibilities within the context of penal law and disciplinary law. It would be useful to mention that such a compensation system cannot concern the physicians' penal and administrative/disciplinary responsibilities but can concern their civil (pecuniary) responsibilities. Moreover, regarding the scope of PCS, it would be appropriate to clarify the compensation matter of "moral damages" alongside "material damages", arising from malpractice.

Besides, it appears that the PCS board would comprise healthcare professionals and is projected to function as part of PCS has been designed as a relatively autonomous "administrative" board. The organization, powers, and activities of such a board should be regulated by the "law" in accordance with the Principle of Legality of the Administration that is provided by Article 123 of the Constitution.

Legislative regulations concerning the compensation board must comply with the constitutional principles and rules. In this context, because the board authorized to pay compensation would not be regarded as a "judicial organ" and its decisions as "judicial decisions"; it would not be legally possible for this board to be organized and authorized in a manner that it would replace "courts"/"judicial review", even for merely a specific field. This system can be expected to form a facultative alternative rather than a compulsory substitution to a judicial review. What needs to be currently stressed is that judicial review cannot be excluded against the board's decisions. Hence, according to Article 125 of the

Constitution stating that "Recourse to judicial review shall be available against all actions and acts of administration.", it will be clearly unconstitutional to enact that decisions of a compensation board, considered to be "administrative", would be definitive and cannot be sued.

Moreover, composing additional regulations should be considered for the time limit to bring actions, such as providing that application to the board shall stop the time limit. Furthermore, Article 129 of the Constitution, which states "Compensation suits concerning damages arising from faults committed by public servants and other public officials while exercising their duties shall be filed only against the administration in accordance with the procedure and conditions prescribed by law, as long as the compensation is resorted to them." should be considered while making legislative regulations with respect to the pecuniary liability of physicians who have a "public official" status.

As it can be observed, an array of legislative regulations and amendments are required to realize PCS. However, in that case, it is clear that such a system would be completely different from the one proposed and would deviate from its original goals when the abovementioned points are to be considered. Moreover, this subject has some other dimensions that may lead to some professional and legal issues that require careful attention. In conclusion, PCS may initially make sense by providing hope of minimizing actions for compensation resulting from malpractice; however, the authors of this study regard it as a proposal that is not so easy to implement in the short term because the "conciliation procedure", with which PCS has some similarities and that had been promulgated in 2011 (3) concerning the compensation for damages arising from the health practices, was abrogated in 2014 (4).

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Author's Reply

To the Editor,

We are very well aware of the fact that the changing current malpractice system in Turkey will be very hard and exhausting when current political, legal, and sociological perspectives are considered. Not assuming any responsibility is a tradition in the Turkish bureaucracy, and this carelessness can only be overcome by interdisciplinary work and education. Fear of penal, administrative, and pecuniary (moral/material) punishment adds a heavy psychological burden on physicians and prevents them from practicing sound clinical medicine. A physician who is held back by the multilayered punishment threat cannot normally function. When an upper respiratory tract infection treatment is in question, a multilayered punishment structure is tolerable by physicians; however, every critically ill patient deserves a fearless doctor's treatment. According to our study, which investigated the defensive medicine practice in 250 Turkish cardiologists, 11.6% were sued for malpractice claims, 6.9% of the sued cardiologists were given financial compensation fines, and 3.4% of the sued cardiologists were given an imprisonment sentence because of negligence. From the surveyed cardiologists, 132 (52.8%) reported that they had revised their practice patterns because of the fear of litigation and 232 (92.8%) reported that they would like to see implementation of our new proposed PCS instead of the current malpractice system (*author's unpublished data*). Legal claims of citizens are universal constitutional rights; however, preliminary results of our study show that a significant percentage of cardiologists unnecessarily appear in courts and change their practice patterns. Current malpractice laws are undermining many citizens with severe diseases from obtaining effective medical treatments.

Because of limited space and need for a larger body of experts to implement PCS, we had just discussed the main frame and purpose of PCS in our previous letter. Implementation of our proposed PCS requires an interdisciplinary study between doctors and lawyers and a thorough legal structure that provides patient safety and safeguards physician from unnecessary stress and exaggerated punishments. The authors' suggestions are important to avoid previous mistakes and to design a strong and functional PCS, which will be under the title of "alternative dispute resolution methods." Compared to the developed and most developing countries, it can be reported that it is too late for Turkey to have such functioning bodies to provide alternative dispute resolu-

tions and arbitration services that are alternatives to the court system. We envisage PCS as an "compulsory arbitration board," which is a stronger body than the previously abrogated "conciliation board." A stronger PCS board would regulate penal, administrative/disciplinary, and pecuniary responsibility areas. Moral and material damages will also be resolved under a single entity in PCS. Regarding the patients' right to recourse to judicial review, a strong legal foundation can be established, and jurists who are expert in health law will be required to be part of PCS to provide an independent, impartial, and compulsory arbitration board. The foundation of PCS can be laid from similar compulsory arbitration boards in Turkey, and jurists who are experts in health law need to be educated in the medical law division of law faculties. Patients can leave compulsory arbitration board and follow ordinary court procedures as a basic constitutional right but courts generally accept autonomous arbitration court's decisions.

We believe that PCS is a stronger body than the previously abrogated "conciliation procedure" and its mainframe structure and purpose should not be changed by auxiliary regulations. Although the PCS system includes legal and structural deficits, we believe that discussing this subject will increase awareness, which might be a good start for preventing physicians from discontinuing traditional and solution-targeted medical practice. As distinct from comments of lawyers, the involvement of physicians similar to us who experience this problem in person would help in the development of new systems. We thank the authors for their suggestions, which can help the implementation of our proposed PCS.

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Electrical storm might be the initial presentation of arrhythmogenic right ventricular cardiomyopathy

To the Editor,

We read with great interest the paper by Özcan et al. (1) entitled "Catheter ablation of drug refractory electrical storm in patients with ischemic cardiomyopathy: A single center experience," published as Epub ahead of print in The Anatolian Journal of Cardiology 2015. They aimed to evaluate the safety and efficacy of catheter ablation in a relatively large cohort with the electrical storm. We congratulate the authors for the successful clinical management of these patients.

The electrical storm can be defined as ≥ 3 life-threatening ventricular arrhythmia within a 24-h period and may cause implantable cardioverter defibrillator discharges, resulting in morbidity and mortality. The electrical storm in adults with ischemic heart failure is common. However, the electrical storm might be the initial presentation of arrhythmogenic right ventricular cardiomyopathy (ARVC), although ARVC usually presents with sustained ventricular tachycardia or sudden cardiac death (2). Moreover, some patients with ARVC may have unusual presentations such as acute coronary syndrome or heart failure (3). In clinical practice, if ARVC is not considered as a possible cause of ventricular arrhythmias, the diagnosis might be overlooked because of the requirement of a different diagnostic approach for the diagnosis of ARVC according to the modified criteria (4). In the study by Özcan et al. (1), it would be better to evaluate the patients for cardiomyopathies, including ARVC, in terms of diagnostic and therapeutic management.

Although ventricular tachycardia frequency is reduced after catheter ablation, the incidence of rapid ventricular arrhythmia during long-term follow-up is still common in patients with ARVC. In addition, catheter ablation may not be able to cure ventricular arrhythmia in ARVC, and cardiac transplantation can be the only choice for the treatment of the electrical storm in a patient with ARVC (5). In this large cohort with the electrical storm reported by Özcan et al. (1), it will be valuable to determine whether some patients have undergone cardiac transplantation because of the electrical storm.

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Author's Reply

To the Editor,

We would like to thank the authors of the paper entitled "Electrical storm might be the initial presentation of arrhythmogenic right ventricular cardiomyopathy" for their interest in our article published in *Anatol J Cardiol* 2015 (1). The authors suggested arrhythmogenic right ventricular cardiomyopathy (ARVC) among possible diagnoses for patients who presented with incessant ventricular tachycardia (VT). Firstly, the VT ECG's presented by us highlighted the left ventricle (LV) as the source of arrhythmia and not consistent with epicardial VT. Sinus ECG's did not show the features of ARVC. None of the patients had family history for sudden death. Our patient group was defined as ischemic cardiomyopathy after we performed coronary angiograms at our center or if they had undergone the same at another hospital and was documented to us. If they underwent CABG surgery, they were also included in that group. We also conducted nuclear imaging studies for some patients. Prior to ablation, all of the patients underwent echocardiography, which was performed by experienced physicians, and none of the patients were reported as having abnormalities recalling ARVD. During the electrophysiological study, mapping demonstrated that an abnormal electrogram and scar regions were present in the LV. As known, ARVD-related VT's generally have substrates at the epicardium, and our unipolar recording above 8.27 mV endocardially. We defined LAVA's, late potentials, and diastolic potentials in LV, and all these locations checked with pacing to delineate long stimulus to QRS to define slow conduction zones. Our pace mapping inside LV were also matched with clinical VTs. Procedures that were performed during VT were entrained with concealed fusion, and post-pacing intervals showed that re-entry circuits were present in LV. During follow up, none of our patients underwent cardiac transplantation for incessant VT. However, the issue raised by the authors is important, and one should keep in mind the differential diagnoses for patients presented with the electrical storm.

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Practical considerations on non-vitamin K oral anticoagulants in patients with high body weight

To the Editor,

I have read with keen interest the systematic review by Güler et al. (1) entitled "A review of the fixed dose use of new oral anticoagulants in obese patients: Is it really enough?" published in *Anatol J Cardiol* 2015;1020-9. This review is of importance in everyday practice where patients with high body weights are encountered much more commonly than in clinical trials. The authors summarized the current clinical data based on the efficacy and safety of non-vitamin K oral anticoagulants (NOAC) used in patients with atrial fibrillation (AF) and in the prevention and therapy of venous thromboembolism (VTE) with the emphasis on obesity, which is also a rapidly rising epidemic among subjects requiring long-term anticoagulation. The manufacturers of dabigatran, rivaroxaban, and apixaban currently suggest that no dose adjustments are necessary for patients with high body weights even if the present evidence to support such a recommendation is rather weak (2). Although clinical trials on NOAC showed no weight-associated differences in the outcomes of NOAC in AF or VTE, several reports indicate that clinical outcomes of anticoagulant therapy with NOAC could be unsatisfactory in extremely obese patients in part because of the increased clearance of anticoagulants and distribution volume with largely unaltered drug absorption (2). The authors of the current review (1) highlighted the intriguing concept that compared with factor Xa inhibitors, dabigatran, whose renal elimination is the largest (80%), is more prone to provide insufficient anticoagulation intensity in individuals with high body weights. Although no comprehensive subgroup analysis for rivaroxaban or apixaban administered in obese patients has been published to date, the influence of body weight on the anticoagulant effects of these agents appear small. In our cohort of patients with VTE, subjects with a body mass index (BMI) of $>35 \text{ kg/m}^2$ represent approximately 10% patients, whereas those with BMI below 18 kg/m^2 represent 5%, with the predominance of young women (A. Undas, unpublished data). From our experience, low BMI is associated with a higher risk of bleeding, which is a more consistent feature than similar rate of VTE recurrences in patients with BMI of $>35 \text{ kg/m}^2$ versus those with BMI of $<35 \text{ kg/m}^2$. The choice of appropriate regimens of an NOAC in subjects with high body weights is difficult, particularly if the bleeding risk is increased for example in a form of heavy menstrual bleedings. Therefore, monitoring the anticoagulant effects of NOAC is important in this subset of anticoagulated patients; the need for anticoagulation at high body weights is considered one of the well-established indications to determine the blood concentrations of NOAC (3, 4). However, the association between the blood levels of NOAC measured using

coagulation assays and thrombotic or bleeding complication is uncertain because of a large variability of the results (5).

Taken together, each patient on NOAC who weighs below 50 kg or above 100–120 kg requires regular visits to the outpatient clinic, particularly within the first weeks of the therapy. The appropriate supervision aims to minimize the risk of bleeding or thromboembolic events in particular individuals who at baseline are at a high risk of these complications. As suggested in the current review (1), more common control visits may increase the safety and efficacy of long-term anticoagulation at high body weights regardless of age and sex. In our opinion, laboratory monitoring of trough anticoagulant effects as well as creatinine clearance should be considered in selected patients. Further clinical studies, particularly registries, are needed to determine whether a fixed dose of NOAC is truly efficacious in patients with morbid obesity.

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Author's Reply

To the Editor,

We would like to thank the authors for their interest in our paper and their comments regarding our study entitled "A review of

the fixed dose use of new oral anticoagulants in obese patients: Is it really enough?" published in *Anatol J Cardiol* 2015; 15: 1020-9 (1).

Under-representation of obese patients in the subgroups of relevant studies raises concerns about the efficacy and safety of new oral anticoagulants (NOACs). The number of patients with high body weights is quite low in studies investigating the pharmacodynamics and pharmacokinetics of NOACs. In the context of data obtained from these studies, a fixed dose use of NOACs is recommended for obese or morbidly obese patients with no distinction from other patients. However, various recent case reports of pulmonary embolism or stroke under NOAC therapy have led to questions about the efficacy of fixed dose in this patient population. Increased creatinine clearance seems to be the most likely responsible mechanism. To overcome this problem, it is advisable to use drugs with less renal excretion in patients with increased creatinine clearance. Nevertheless, this hypothesis needs to be confirmed with randomized studies.

We would like to thank the authors for sharing their unpublished data about their patients with high body weights. Apart from the inefficiency problem with fixed dose use of NOACs in obese patients, concerns about bleeding risk in patients with a low body mass index or weight <50 kg are noteworthy as the authors stated. Similarly, rivaroxaban 15 mg was used in the J-ROCKET AF trial unlike the global ROCKET-AF trial, and this dose was recommended for the Japanese population (2). Routine monitorization of the plasma levels of NOACs in morbidly obese patients to decrease complications might be an alternative option. Although determination of activated partial thromboplastin time for dabigatran and factor Xa level for rivaroxaban was suggested for urgent conditions (3), methodological uncertainty prevents the recommendation of an ideal treatment dose in clinical practice as emphasized by the authors (4). Approval and marketing of unavailable antidotes for NOACs could be useful to some extent in patients suffering from bleeding complications.

Furthermore, frequent follow-up visits of patients under NOAC therapy might help the earlier detection of bleeding or embolic complications; however, it may not always prove useful because of the lack of instruments for monitorization of drug efficacy. Further studies are warranted for the determination of an ideal dose of NOACs in morbidly obese patients.

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The atrial conduction time in patients with normal atrial size

To the Editor,

We have read with great interest the manuscript by Housseinsabet (1) entitled "Assessment of atrial conduction times in patients with mild diastolic dysfunction and normal atrial size," published in the *Anatolian Journal of Cardiology* 2015; 15: 925-31. In this study, Hosseinsabet (1) clearly demonstrated that there were no differences in atrial conduction times (ACTs) and atrial electro-mechanical delays (EMDs) in patients with mild diastolic dysfunction and normal left atrial volume compared with normal subjects.

We want to share further comments about the findings of the study. The evaluation of atrial EMD with tissue Doppler echocardiography fundamentally shows the time during the propagation of cardiac impulse through atria. If the atrial size increases, the pathway of the cardiac impulse and the required time for the propagation of the impulse will also increase. This situation has already been supported with the findings of recent studies that include patients of different diseases with atrial enlargement such as mitral stenosis or atrial septal defect (2, 3). These studies also revealed the association of increased atrial size and increased EMD (2, 3). On the other hand, a condition without atrial enlargement can be expected with similar EMD values as a normal control group. The findings of the study by Hosseinsabet supported this expectation (1). It seems that when the enlargement of the atria reaches a critical size, then the increase in atrial EMD can be appreciable. However, in the literature, there are conflicting findings of various studies evaluating the susceptibility for atrial fibrillation (AF) in many medical conditions without the enlargement of atria, such as atrial septal aneurysm or familial Mediterranean fever (4, 5). These studies documented the increase in EMD and ACT in patients with a similar size of atria compared with control groups by using the same method of tissue Doppler echocardiography as Hosseinsabet. It can be speculated that the underlying mecha-

nism of AF is multiple, and the damage of the atrial tissue, presence of inflammation, or decrease in the mechanical function of atria can influence the homogeneity of atrial conduction without atrial enlargement. However, using this echocardiographic technique to measure atrial EMD may be doubtful for patients with normal size of atria because atrial dilatation is the major cause for the increase in ACT. The gold standard measure for atrial EMD is direct measurement with electrophysiological study (EPS). If it is possible to demonstrate the increase of EMD in different conditions with EPS findings, it may be helpful in clarifying the issue.

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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 "Assessment of atrial conduction times in patients with mild diastolic dysfunction and normal atrial size" published in November issue of The Anatolian Journal of Cardiology 2015; 15: 925-31 (1).

I conducted my study on the basis of the hypothesis that electrical remodeling can occur before structural remodeling in diastolic left ventricular dysfunction (2), and I adopted the evaluation of atrial conduction times as a marker for atrial electrical remodeling (3).

Since then, I have received comments from my dear colleagues. According to these comments, an increase in atrial electromechanical delays (EMDs) occurs when left atrial enlargement reaches a certain level. There is some evidence supporting this hypothesis. Tsang et al. (4) demonstrated that when left atrial size reaches $>27 \text{ mL/m}^2$, the probability for the first episode of atrial fibrillation increases in the presence of left ventricular diastolic dysfunction. However, the question remains as to what is the critical point in left atrial size. To my knowledge, it has yet to be defined through new research. On the other hand, several pathological processes such as structural and electrical remodeling with multiple etiologies underlie the occurrence of atrial fibrillation. It has been suggested that atrial size is an index of structural remodeling and that atrial conduction times are markers of structural and electrical remodeling (3). In another part of these comments, it was cited that tissue Doppler echocardiography is not a reliable method for the evaluation of atrial EMDs in subjects with a normal atrial size. There is one study (5) that compared atrial conduction times as evaluated by tissue Doppler echocardiography and electrophysiological studies, and this study showed a weak association between the two methods regarding inter-atrial EMD, a moderate association with respect to left intra-atrial EMD, and no association in terms of right intra-atrial EMD. Left atrial size in that study was normal. Nevertheless, it should be considered that in that study, a high right atrial signal was used instead of a tricuspid annulus signal. It can be cause of these weak associations found in that study. Consequently, although there are some doubts with respect to the measurement of atrial EMDs by tissue Doppler echocardiography, the existing literature lacks a well-designed study that compares results between electrophysiological study and tissue Doppler echocardiography. Moreover, there is no evidence for the shortcomings of tissue Doppler echocardiography in the evaluation of atrial EMDs in a normal atrial size. These are, therefore, queries that merit future research on the feasibility of tissue Doppler echocardiography in the evaluation of atrial EMDs.

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Obstructive sleep apnea and cardiovascular disease: Is mean platelet volume one of the links?

To the Editor,

We read with great interest the excellent review entitled "Obstructive sleep apnea and its effects on cardiovascular diseases: a narrative review" by Rivas et al. (1) on the cardiovascular comorbidities of patients with obstructive sleep apnea (OSA) published. Indeed, it is increasingly being appreciated that patients with OSA are at a higher risk of coronary artery disease, congestive heart failure, stroke, and atrial fibrillation. Treatment with continuous positive airway pressure (CPAP) reduces these comorbidities (1).

A novel important, though less widely used, marker of the severity of OSA is mean platelet volume (MPV), as shown by Varol et al. (2, 3) and us (4). Again, CPAP treatment has been reported to reduce MPV (3). Given its role as a marker of vascular disease and a predictor of acute vascular events (5), it appears that MPV also links OSA with cardiovascular disease. Specifically, in patients with OSA, MPV is also associated with atrial fibrillation (5).

In conclusion, it is now established that OSA poses patients at an increased risk of cardiovascular disease (1). MPV may prove useful as a marker of the latter in patients with OSA (4, 5); therefore, it should be more widely utilized for this purpose.

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Author's Reply

To the Editor,

We appreciate Dr. Nena's comments about our review article entitled "Obstructive sleep apnea and its effects on cardiovascular diseases: a narrative review," published in *Anatol J Cardiol* 2015; 15: 944-50, and her suggestion that mean platelet volume (MPV) may have prognostic importance as a risk factor for cardiovascular events and therapeutic importance as an indicator of a response to CPAP management in patients with obstructive sleep apnea (OSA) (1). MPV is a marker for thrombocyte activation. Larger platelets contain more granules and thromboxane A₂ and express more glycoprotein receptors. Therefore, these platelets aggregate more quickly and adhere more strongly to collagen, and this potentially leads to either an increased frequency or severity of thromboembolic events. Because patients with OSA have an increased frequency of atrial fibrillation and stroke and because OSA has adverse effects on outcomes in patients with other cardiovascular disorders, measuring MPV may help classify patients into risk categories and identify patients who might need additional therapy.

One important issue in studies using MPV as an indicator of vascular events is whether to consider MPV as a continuous variable or as a categorical variable, which is of interest only if it is above the upper limit of normal or some other critical value based on outcome studies. Another important issue is the study population. Is it more important to study patients with underlying risk factors for cardiovascular disease or to study patients without any obvious evidence of cardiovascular disease? Karakaş et al. (2) analyzed MPV in controls and in patients with OSA with mild, moderate, and severe increases in apnea-hypopnea index (AHI). They found that it was significantly higher in patients with severe OSA than in control subjects. However, the reported values appeared to be within the normal range, and absolute differences were small (8.6 versus 7.8 femtoliters). They did find significant correlations

between MPV and AHI and minimum O₂ saturation. Nena et al. (3) studied 610 non-diabetic subjects with suspected OSA. MPV (12.1 femtoliters) was significantly higher in patients with severe OSA defined by an AHI greater than 30 events per hour than in controls (9.8 femtoliters). They found significant correlations between MPV and AHI and between MPV and the percent of time the O₂ saturations were below 90%. This study suggested that there are significant correlations between MPV and important variables in patients with severe OSA. Varol et al. (4) studied 31 patients with severe OSA and measured MPV before and after treatment with CPAP for 6 months. The median MPV was significantly higher in patients with severe OSA than in control subjects, and there was a significant reduction in this volume after 6 months of CPAP therapy.

In our view, MPV is an easily available laboratory test that may identify patients with an increased risk for cardiovascular events and may represent a response parameter to monitor during treatment of these patients. It seems important to develop large prospective studies on its utility in patients with OSA.

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The role of platelet-lymphocyte ratio in the severity of coronary artery disease assessed by the angiographic Gensini score

To the Editor,

I am grateful to have read with great interest the article entitled "The association between platelet-lymphocyte ratio and coronary artery disease severity" by Yüksel et al. (1), published

in *Anatol J Cardiol* 2015; 15: 640-7. In this well-presented study, the authors aimed that the platelet-lymphocyte ratio (PLR) was associated with the severity of coronary artery disease, assessed by the Gensini score, because a high PLR was shown to be closely related with inflammation and atherosclerosis. They found that a high PLR was significantly and independently related with the severity of coronary artery disease.

Prior studies investigated that PLR, a combination of both platelet and lymphocyte counts, is a novel inflammatory marker and predictor of adverse cardiovascular outcomes (2-6). Yüksel et al. (1) showed that PLR was significantly higher in the group of severe atherosclerosis than in the other control and mild atherosclerosis groups. As known, the mild atherosclerosis group has a more severe inflammation than the control group; however, there was no difference between the mild atherosclerosis and control groups (p=0.729).

In conclusion, according to these results, it was not clear to highlight the pathogenesis role of PLR in the severity of coronary artery disease. According to me, further larger studies are needed to show and clarify this situation.

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Author's Reply

To the Editor,

We are grateful for the kind comments to our manuscript entitled "The association between platelet-lymphocyte ratio and coronary artery disease severity," published in *Anatol J Cardiol* 2015; 15: 640-7 (1). In their Letter to the Editor, the authors emphasize the importance of the recently emerged inflammatory marker, platelet-to-lymphocyte ratio (PLR), in atherosclerotic pathogenesis and request for the comparable PLR values of the mild atherosclerosis and control groups in our study.

There may be a few reasons to find similar PLR values between the mild atherosclerosis and control groups. Firstly, as we mentioned, our study sample size is not large enough to statistically demonstrate the significance of such a minor difference in PLR values of these two groups. Secondly, atherosclerotic plaques develop and progress within the arterial wall long before to protrude into the lumen, which cannot be detected by conventional angiography (lumenography). Because of the nature of the atherosclerotic process, we might misdiagnose patients with positive remodelling as normal coronary arteries, which could only be diagnosed by intravascular ultrasound. Finally, although statistically insignificant, there were more smokers in the control group than in the mild atherosclerosis group, which might affect our results.

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The role of platelet-to-lymphocyte ratio in saphenous vein graft disease

To the Editor,

I read with great interest the article by Kundi et al. (1) entitled "Association between platelet-to-lymphocyte ratio and saphenous vein graft disease in patients with stable angina pectoris," published online in *Anatol J Cardiol* 2015 May 5. In their study, authors reported that there was a significant association of platelet-to-lymphocyte ratio (PLR) with saphenous vein graft dis-

ease (SVG) and suggested that PLR could be used as a marker of SVG. I have the following comments and concerns.

Numerous clinical trials showed the relation between PLR and poor cardiovascular outcomes in cardiovascular disease. Because most of the stenosis and occlusion of saphenous vein grafts after the first year is caused by atherosclerosis, is there any difference in the meantime from coronary artery bypass grafting to the last coronary angiogram between the two groups? Also, the patency of bypass grafts on functionally significant lesions is higher than that on nonsignificant lesions (2). Yüksel et al. (3) reported that high PLR appears to be additive to conventional risk factors and commonly used biomarkers in predicting severe atherosclerosis. I was wondering if there was any difference between patients with or without SVG in terms of severity of coronary artery disease.

Finally, obesity is a chronic inflammatory disease characterized by an increase in the levels of inflammatory cytokines (4). It has been shown that metabolic disorders such as obesity and insulin resistance are related to the progression of coronary atherosclerosis and increased incidence of cardiovascular events such as saphenous vein graft occlusion and acute coronary syndrome (5). Because PLR is a novel biomarker showing inflammation in cardiac and non-cardiac patients, authors should state the body mass index for each group.

In my opinion, the findings from this study could be related to the abovementioned limitations.

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Author's Reply

To the Editor,

We thank the author(s) for their great interest in our work entitled "Association between platelet-to-lymphocyte ratio and saphenous vein graft disease in patients with stable angina pectoris," which was published in the *Anatolian Journal of Cardiology* 2015 May 5 (1).

As we mentioned in the limitation section of our paper, we included patients who had CABG surgery >1 year ago to minimize graft failure factors related to the surgery itself. We completely agree with the author(s), but we do not have sufficient data about the mean time from coronary artery bypass grafting to the last coronary angiograms because it was a retrospective study. Also, we do not have the patient's body mass indexes because of the same reason.

We believe that further prospective trials, including data on body mass index measurements and the duration between coronary artery bypass surgery and saphenous vein graft disease, would better clarify the relationship between the platelet-to-lymphocyte ratio with saphenous vein graft disease.

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Effects of pentoxifylline on blood transfusion

To the Editor,

We congratulate the authors for their study entitled "Pre-operative oral pentoxifylline in case of coronary artery bypass grafting with left ventricular dysfunction (ejection fraction equal to/less than 30%)," published in *Anatol J Cardiol* 2015; 15: 1014-9. This study evaluated the feasibility of pentoxifylline when patients with low ejection fraction are considered (1). Systemic inflammatory response is one of the basic parameters that affect the postoperative results of coronary bypass surgery. In this context, pentoxifylline may have posi-

tive effects through the inhibition of some of the inflammatory cytokines (2-4). However, the study of Mansourian et al. (1) reveals another interesting result, i.e., a statistical decrease of blood transfusion in the pentoxifylline group. None of the similar studies have obtained this result. How do the authors explain that?

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Author's Reply

Authors of this mentioned article did not send any reply for this Letter to the Editor despite our persistent request.

Bonsai-induced coronary artery spasm

To the Editor,

I have read the article by İnci et al. (1) entitled "Bonsai-induced Kounis Syndrome in a young male patient" with great interest, which was published in *Anatol J Cardiol* 2015, 15: 952-3. The authors presented an unusual form of acute coronary syndrome, which developed following the synthetic cannabinoid "Bonsai" use. I would like highlight some points regarding this article.

Although there are no definite diagnostic criteria to differentiate Prinzmetal angina from Kounis syndrome, systemic allergic reactions associated with acute myocardial ischemia in a patient should suggest that the patient has Kounis syndrome (2). Are there any signs and symptoms of systemic allergic reactions such as generalized erythema or urticarial rashes in the patient? Also, after clinical stabilization, additional allergy tests, including skin prick test, may be helpful for diagnosis.

I also would like to highlight a specific point in the treatment of the abovementioned patient. In the cases where type 1 Kounis syndrome progresses to acute myocardial infarction with increased cardiac enzymes and troponins, anti-allergic treatment, including administration of H1 and H2 blockers together with corticosteroids combined with classical treatment of acute coronary syndromes, is recommended (3). Also, in patients with non-ST-elevation acute coronary syndromes, dual antiplatelet therapy with aspirin and clopidogrel has been recommended for 1 year over aspirin alone, irrespective of the revascularization strategy and stent type according to the current guidelines (4). However, the utilization of aspirin is controversial because of the underlying anaphylactic reaction in Kounis syndrome. Acetylsalicylic acid can cause allergic reactions and induce anaphylaxis; therefore, the safety of aspirin use in patients with Kounis syndrome is unknown (5). I would like to kindly ask the authors whether there is any specific reason for the treatment of aspirin in this case?

In conclusion, because the use of synthetic cannabinoid is gradually increasing in our country, rapid diagnosis and appropriate treatment in these patients has great importance because of the complex and complicated course of acute coronary syndromes associated with allergic reactions.

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Author's Reply

To the Editor,

We thank you for the interest in and positive reviews for our case report published in the *Anatolian Journal of Cardiology* entitled "Bonsai-induced Kounis Syndrome in a young male patient" (1).

The most important step of the diagnosis of Kounis syndrome is determining the presence of allergic symptoms accompanying chest pain. Systemic allergic reaction is manifest with skin, mucosa, respiratory system, cardiovascular system, or gastrointestinal system signs in minutes/hours after exposure to the allergen. The clinical picture is variable in a wide spectrum from mild skin lesions that might be unnoticed to anaphylactic shock. The course of the allergic reaction occurring in this case was chest pain without skin involvement. No skin lesion was encountered in this patient. However, skin lesions may be absent in majority of the cases (2). The patient was questioned and examined for skin lesions; nevertheless, the mild nature of the skin lesions should be considered so that they may be unnoticeable (3). Leukocytosis, eosinophilia, and increased IgE levels were detected in this case, and other tests could not be performed because of technical unavailability. The skin prick test may be helpful in diagnosis; however, its rate of usage is found to be low in the literature (4).

Primary treatment of Kounis syndrome is AKS management and suppression of the allergic reaction. Because the primary mechanism is coronary vasospasm in young and otherwise healthy patients who have no risk factors for coronary artery disease and are considered to have Type I variant Kounis syndrome, the first-line treatment is nitrates and calcium channel blockers. Suppression of allergy by steroids and antihistamines alone may even alleviate coronary vasospasm. AKS management in those patients, on the other hand, is unclear. Debatable applications have been reported, particularly on the antiaggregants. Because aspirin is a basic building block treatment in the management of AKS, we started aspirin (5). However, as you have mentioned, aspirin has the potential to increase the continuing allergic reaction in patients with Kounis syndrome. It may be more suitable to prefer clopidogrel in patients with hypersensitivity to aspirin.

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Is Turkey a prothrombin gene mutation region similar to the Mediterranean countries?

To the Editor,

Myocardial infarction (MI) is a leading cause of morbidity and mortality worldwide (1). Acute MI generally develops following a critical narrowing of the coronary artery or a narrowing or complete occlusion of the coronary vessel by an acute plaque rupture (2). MI in young adults may be categorized into two groups as normal coronary artery anatomy and coronary artery disease (CAD) accompanied by various etiologies; moreover, conditions associated with hypercoagulopathy play a significant role in the pathophysiology of both groups (3).

We examined 68 patients (aged <45 years) with ACS and 69 healthy controls for hypercoagulable states in our institution between January 2008 and June 2010. We found a statistically significant difference between the groups for factor V Leiden (FVL), whereas there was no statistically significant difference for prothrombin gene mutation (P G20210A).

The two most common reasons of familial thrombophilia are P G20210A and FVL. P G20210A is frequently observed in Southern European countries and most notably in countries that have coast to the Mediterranean (4). Despite conflicting results, some studies have demonstrated that the combination of known risk factors and P G20210A is a risk factor for the development of arterial thrombus and ACS (5). In our study, there was no statistically significant difference between the patient and control groups (2.9% vs. 1.4%, $p=0.551$). P G20210A was found to be heterozygotic in three (2.2%) among a total of 137 cases. However, in the study by Akar et al. (6), P G20210A prevalence rate in Tur-

key was reported to be 6.2%, which is similar to the rate in Mediterranean countries; however, this finding is contradictory to our study findings. Despite being a Mediterranean country, Turkey is located right in the middle of three continents and has a distinctive geography. Therefore, FVL mutation prevalence rather than P G20210A may be more frequent, particularly in the Central Anatolian, Eastern Anatolian, and Black Sea Regions, which is similar to that observed in the Northern European countries.

Data regarding the association of FVL mutation with the development of CAD and ACS are conflicting. However, large studies investigating young patients with ACS have reported that FVL mutation was found to be statistically significant (7). Similarly, we found in our study that FVL mutation was statistically significant in the patient group compared with that in the control group (22.1% vs. 5.8%, $p=0.006$).

In conclusion, patients with ACS carrying FVL mutation might have a role in the pathophysiology of developing ACS. Furthermore, Turkey appears as a FVL mutation region rather than a P G20210A mutation region, which is similar to the Northern European countries, thereby opposing the known current literature. However, further prospective controlled studies in larger patient populations with careful analysis of other risk factors and mutations are required to understand the pathophysiological process of ACS.

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