

of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2014; 35: 2541619.

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## Author's Reply

To the Editor,

We thank Zhou et al. (1) for their interest in our previous editorial entitled "Impact of high on-treatment platelet reactivity on long-term clinical events in AMI patients: a fact or mirage?" published in *Anatol J Cardiol* 2016 Nov 16. Epub ahead of print.

Based on their recent meta-analysis (2), Zhou et al. (1) have pointed clinical usefulness of phenotype (platelet function test)-guided antiplatelet therapy to maximize clinical efficacy and safety following percutaneous coronary intervention (PCI). Understandably, our group generally agrees with the concept of therapeutic window between high and low platelet reactivity (HPR and LPR, respectively) during P2Y12 inhibitor administration. For the past 10 years, we also have performed numerous clinical studies to reveal strategies against the imminent risks related with platelet reactivity.

In 2012, Jeong et al. (3) firstly suggested the concept of "East Asian Paradox." Despite low response to clopidogrel in East Asians (mainly due to high prevalence of the cytochrome P450 2C19 loss-of-function allele), East Asian patients have a similar or lower rate of ischemic events after PCI compared with that in Caucasian patients, suggesting the different therapeutic window of platelet reactivity in East Asian patients. More importantly, active metabolite concentration during potent P2Y12 inhibitor (e.g., ticagrelor and prasugrel) appeared greater in East Asian vs. Caucasian population (~40%) (4), suggesting that their reduced-dose regimen could be more optimal for East Asian patients. Therefore, we need to be cautious in applying the clinical data and guideline originated from Western patients for East Asian subjects.

How can we understand this mystery? Maybe the concept of platelet reactivity itself could not explain the whole spectrum of this unique phenomenon. Our group has confidence in the concept of "vulnerable blood," including the whole blood components related to thrombogenicity. Although we believe that platelets are the main factors for arterial thrombosis, there is much evidence to support clinical importance of other blood components (e.g., cholesterol, hormone, inflammation, coagulation, and fibrinolytic system). Inflammation and thrombin cascades may

play crucial roles in the development of atherosclerosis and thrombosis. Intriguingly, the levels of these biomarkers in East Asian population seem lower than those in Caucasian population (5). When a patient has less corrupt "vulnerable blood," the impact of HPR may be limited and the hazard of LPR would be prominent after PCI.

Life is beautiful because it is not an open book. In the same manner, in vivo blood is mostly safe because it is very complicated and interactive. Although the concept of platelet reactivity was a big step forward, we now need to have more prudent and comprehensive approach to cover the real aspect of "vulnerable blood."

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## Usefulness of left atrial speckle-tracking echocardiography in patients with atrial fibrillation

To the Editor,

We read the article entitled "Association between left atrial function assessed by speckle-tracking echocardiography and the presence of left atrial appendage thrombus in patients with

atrial fibrillation" published in *Anatol J Cardiol* 2017;18:15-22, by Kupczynska et al. (1) with great earnest and wish to commend the authors for their interesting work on this new and potentially impactful subject. The study investigated the link between trans-thoracic echocardiographic markers of left atrial function, including novel ones obtained through speckle-tracking echocardiography, and the presence of left atrial appendage thrombus on transoesophageal echocardiography.

Speckle-tracking echocardiography is a novel technique, which uses dedicated software that analyses the motion of specific segments of the myocardium to determine their fractional shortening, but it is fraught with technical issues. One of them is related to heart rate variability because strain and strain rate values are directly influenced by the length of diastole, and as such, this technique is designed for patients with regular heart rhythms (2). In this regard, the authors' approach of using speckle-tracking echocardiography in patients with atrial fibrillation is brave and their solution of using an indexed beat with the smallest R-R variability compared with previous beats could be a very practical solution.

A specific limitation of atrial strain is the dependence of atrial function on left ventricular function, and in this regard, the study groups are markedly different. The patients with left atrial appendage thrombi had a reduced left ventricular ejection fraction compared with those without a thrombus, with 53% of them having a severely reduced ejection fraction, perhaps owing to the increased prevalence of coronary artery disease. Although this is somewhat expected, it translates into increased ventricular filling pressures and increased atrial filling pressures, a fact demonstrated by the significantly increased mean indexed left atrial area and volume of the thrombus group compared with those in the no thrombus group (12 vs. 14 cm<sup>2</sup>/m<sup>2</sup> and 28 vs. 34 mL/m<sup>2</sup>, respectively). For evaluating this interdependence, the evaluation of left ventricular diastolic function would be useful, but the authors did not present this data.

However, the results of the study are very interesting because they identify left atrial longitudinal strain rate as a better predictor of left atrial appendage thrombus than the CH2ADS2-VASc score in this study population. Although this score is not used for predicting a left atrial appendage thrombus, it uses clinical variables known to be associated with thrombus formation and can be a good indicator of its presence (3). In this sense, speckle-tracking echocardiography cannot replace clinical evaluation, but it can provide additional information to improve risk assessment, as demonstrated by the improvement in predictive power of the model that uses both the score and atrial strain developed by the authors.

The added value of atrial longitudinal strain measurements brought to the CH2ADS2-VASc score in thrombus prediction proves that it is a valuable tool, and this study lays the groundwork for future prospective studies that can provide more proof of its usefulness in these patients.

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## Author's Reply

To the Editor,

We would like to thank Nistor (1) for his interest in our recent article entitled "Association between left atrial function assessed by speckle-tracking echocardiography and the presence of left atrial appendage thrombus in patients with atrial fibrillation." published in *Anatol J Cardiol* 2017; 18: 15-22. regarding the association between left atrial function assessed by speckle-tracking echocardiography and the presence of left atrial appendage thrombus in patients with atrial fibrillation and for his insightful comments concerning our study.

Indeed, the heart rate variability poses a problem for reliable speckle-tracking echocardiography analysis during atrial fibrillation, and to handle this concern we have implemented the previously proposed method and have validated it for the assessment of left ventricular strain during atrial fibrillation (2).

With regard to the difference in left ventricular function between patients with and without left atrial appendage thrombi, we agree that it could have influenced the difference in atrial function, but at the same time, we would like to emphasize that left atrial function parameters (average left atrial longitudinal early diastolic strain rate, average left atrial longitudinal systolic strain rate, and average peak positive longitudinal systolic atrial strain) were independently associated with the presence of left atrial thrombi in the multivariate analysis.

We greatly appreciate Nistor's comment regarding the need for further prospective clinical studies. We fully agree that additional data are essential to clarify the diagnostic role of the left