

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We would like to thank the authors for sharing their unpublished data about their patients with high body weights.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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 at www.anatoljcardiol.com
 DOI:10.14744/AnatolJCardiol.2016.6972



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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