EDITORIAL

Could we improve thromboembolic risk stratification in patients with atrial fibrillation?

Maria Trusz-Gluza[1], Artur Filipecki[2]

1 Medical University of Silesia, Katowice, Poland
2 1st Department of Cardiology, Medical University of Silesia, Katowice, Poland

Atrial fibrillation (AF) is the second most common arrhythmia after premature extrasystolic beats. It is estimated that in Poland AF involves approximately 600 000 to 700 000 patients.[1] AF is not a benign arrhythmia; a substantial number of patients have serious symptoms (especially patients with paroxysmal AF) and significantly worsened quality of life. The thromboembolic consequences of AF, mainly ischemic stroke, are particularly important. About 15% to 20% of strokes are attributed to AF. The course of such stroke is more serious and characterized by a higher 30-day and 1-year mortality. It underlines the great importance of thromboembolic risk assessment in every patient diagnosed with AF before a decision on chronic anticoagulation is made.

In the most common type of AF, namely nonvalvular AF, different scales of thromboembolic risk assessment are used, including $CHADS_2$, ATRIA, and CHA_2DS_2-VASc. Currently, the most frequently used scale is CHA_2DS_2-VASc, endorsed by the European Society of Cardiology, American Heart Association, American College of Cardiology, and Heart Rhythm Society.[2,3] The CHA_2DS_2-VASc scale is simple, easy to remember, and mainly based on data from the patient's medical history and examination. Risk factors include heart failure, hypertension, age ≥75 years (2 points) or 65–74 years (1 point), diabetes, previous stroke / transient ischemia (2 points), vascular disease, and female sex. The scale includes more elements than the previously used $CHADS_2$ scale and thus better identifies low-risk patients. The identification of patients at low thromboembolic risk is recommended by the current guidelines and expert consensuses because these patients do not require anticoagulation.[2] On the contrary, it was previously mandatory to identify patients who are at high risk and require anticoagulation.

However, the CHA_2DS_2-VASc scale is not without limitations. First, it includes mainly general systemic factors of thromboembolic risk. For example, when applied to patients with heart failure, it predicts thromboembolic risk similarly in the population with or without AF.[4] Second, the score does not include numerous clinical, imaging, and biochemical factors, such as the presence of kidney disease, echocardiographic data, blood clotting properties, and other biomarkers. Blood biomarkers, such as von Willebrand factor (vWF), D-dimer, natriuretic peptides, or C-reactive protein (CRP), can provide useful diagnostic and prognostic information in some AF patients.[5,6]

Biomarkers have been intensively studied but without definite conclusions. In the current issue of *Pol Arch Med Wewn*, Rewiuk and Grodzicki[7] have presented data on the correlation of the CHA_2DS_2-VASc score with vWF, high-sensitivity CRP (hs-CRP), and carotid intima-media thickness (IMT). In patients with acute-onset AF lasting less than 48 hours, higher levels of vWF and hs-CRP as well as thicker IMT were found in the group with a CHA_2DS_2-VASc score of 2 points or higher than in the group with a score of less than 2.

The prothrombotic state in AF usually results from a combination of several factors defined as the Virchow triade, which consists of left atrial blood stasis (especially in the left atrial appendage), endocardial or endothelial damage, and abnormal blood constituents. In fact, the relations are much more complicated, including genetic factors, inflammation, and fibrosis as well as the hypercoagulable state. vWF is a marker of endothelial damage or dysfunction; it stimulates platelet adhesion and aggregation, leading to clot formation. Several studies demonstrated an association of vWF with: 1) spontaneous echo contrast or the presence of thrombi in the left appendage; 2) different risk factors of stroke such as diabetes, heart failure, and hypertension; and 3) thromboembolic risk assessed with the $CHADS_2$ or Birmingham

Correspondence to:
Prof. Maria Trusz-Gluza, MD, PhD, Professor Emeritus, Śląski Uniwersytet Medyczny, ul. J. Poniatowskiego 15, 40-055 Katowice, Poland, phone: +48 607 933 944, e-mail truszm@wp.pl
Received: November 16, 2015.
Accepted: November 16, 2015.
Conflict of interest: MT-G gave lectures for Boehringer Ingelheim, Bayer, and Pfizer. AF gave lectures for Bayer.
Pol Arch Med Wewn. 2015; 125 (11): 801-802

scale.[8] As a novel finding, Rewiuk and Grodzicki[7] confirmed the correlation of vWF with the currently used CHA_2DS_2-VASc scale.

So far, studies addressing the correlation between hs-CRP levels and AF confirmed the important role of inflammation in the progression from paroxysmal to chronic AF. Negi et al[9] proved a positive correlation of inflammatory index (hs-CRP) and oxidative stress (derivates of reactive oxygen metabolites) with the $CHADS_2$ score in patients with chronic AF. They suggested that these biomarkers could be useful in clinical practice in patients with moderate risk of ischemic stroke. In the current paper, Rewiuk and Grodzicki[7] proved the correlation of hs-CRP levels also with the CHA_2Ds-VASc scale.

According to our best knowledge, the correlation between the CHA_2DS_2-VASc and IMT has been reported by Rewiuk and Grodzicki[7] for the first time and therefore cannot be discussed in the context of other studies.

We hope that all the findings reported by Rewiuk and Grodzicki will be further investigated in a prospective large-scale study with the assessment of such endpoints as thromboembolic event, death, and others. It could be also interesting to analyze the presented data in different subgroups (eg, CHA_2DS_2-VASc of 0 vs that of ≥1; CHA_2DS_2-VASc of 0 in males and of 1 in females vs of 1 in males and of 2 in females).

Some interesting questions could be also raised analyzing Figure 1 in the paper by Rewiuk and Grodzicki.[7] We paid special attention to the relation between the vWF level and hypertension: vWF was significantly higher in patients with AF and hypertension. Perhaps we could speculate that good control of blood pressure will result in lower levels of vWF. If well-controlled hypertension will cease to be a risk factor, than the vWF assessment could become a test of practical value. It will be especially interesting for patients who score 1 point for hypertension.

Ischemic stroke due to AF is associated with worse prognosis. If there are no contraindications, it is obvious that patients with a CHA_2DS_2-VASc score of 2 or higher should be anticoagulated. The decision should take into account the lifelong length of treatment and possible complications, some of which may be severe. Thus, in patients with a CHA_2DS_2-VASc score of 1 in males and of 2 in females, the decision should be balanced and depend not only on the patient's informed consent. Males with a score of 0 and females with a score of 1 are assumed to be a low-risk population and they should not be anticoagulated.[2] However, even in these patients some controversies exist. We suggest that in such situations additional tests should be performed to make a correct decision, including detailed assessment of renal function, imaging studies (transthoracic and transesophageal echocardiography, computed tomography, and magnetic resonance imaging for the assessment of the left appendage or IMT), and measurement of the levels of classical cardiovascular risk factors or biomarkers (hs-CRP, vWF, D-dimer, pro-B-type natriuretic peptide [BNP], N-terminal BNP, and others).[5,6] The choice of additional tests should depend on individual characteristics of the patient.

REFERENCES

1 Trusz-Gluza M. Atrial fibrillation: epidemiology and consequences. 2015; 2: 24-30.

2 Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J. 2012; 33: 2719-2747.

3 January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation. 2014; 130: 2071-2104.

4 Melgaard L, Gorst-Rasmussen A, Lane DA, et al. Assessment of the CHA_2DS_2-VASc score in predicting ischemic stroke, thromboembolism, and death in patients with heart failure with and without atrial fibrillation. JAMA. 2015; 314: 1030-1038.

5 Kornej J, Apostolakis S, Bollmann A, Lip GY. The emerging role of biomarkers in atrial fibrillation. Can J Cardiol. 2013; 29: 1181-1193.

6 Szymanski FM, Lip GY, Filipiak KJ, et al. Stroke risk factors beyond the CHA_2DS_2-VASc score: Can we improve our identification of "high stroke risk" patients with fibrillation? Am J Cardiol. doi: 10.1016/j.amjcard.2015

7 Rewiuk K, Grodzicki T. Correlations of C-reactive protein, von Willebrand factor, and carotid artery intima-media thickness with CHA_2DS_2-VASc in patients with acute atrial fibrillation. Pol Arch Med Wewn. 2015; 125: 835-844.

8 Lip GY, Lane D, Van Walraven C, Hart RG. Additive role of plasma von Willebrand factor levels to clinical factors for risk stratification of patients with atrial fibrillation. Stroke. 2006; 37: 2294-2300.

9 Negi SI, Greener I, Anand A, Dudley SC Jr. A circulating biomarker risk-prediction model correlates with CHADS-2 risk score in chronic atrial fibrillation. IJC Metab Endocr. 2015; 6: 24-26.