Revista Portuguesa de
Cardiologia
Portuguese Journal of **Cardiology**

www.revportcardiol.org

LETTER TO THE EDITOR

Red cell distribution width is a predictor of mortality in patients with major bleeding☆

A largura de distribuição dos eritrócitos é um preditor de mortalidade em pacientes com hemorragia grave

Dear Editor,

We have read with great enthusiasm the recently published article entitled ''Impact of red blood cell distribution width on risk for bleeding events in patients with non-ST elevation acute coronary syndromes'' by Gonçalves et al.[1] In this well-presented article they aimed to determine the prognostic value of red blood cell distribution width (RDW) in patients with non-ST segment elevation acute coronary syndromes (NSTE-ACS), particularly regarding the risk of major bleeding. They concluded that RDW was an independent predictor of major bleeding in patients with non-ST segment elevation myocardial infarction (NSTEMI). They suggested that higher RDW values were associated with greater in-hospital mortality and were an independent predictor of in-hospital major bleeding in patients with NSTE-ACS. The ready availability of this parameter at no additional cost may encourage its wider use in clinical practice in the future. We thank the authors for their contribution.

It is known that anemia is an important predictor of short- and medium-term mortality after ACS.[2] In the present study, there were significant differences between the third tertile of RDW compared to the other groups. Anemia can be an independent risk factor of ACS patients with major bleeding in the present study. RDW is a standard laboratory parameter that shows variation in red blood cell size on a standard hemogram and is usually used in assessing blood diseases. It has recently been reported as an independent predictor of all-cause long-term mortality in patients with coronary artery disease.[3] However, conditions in the differential diagnosis of anemias can affect RDW and so this parameter might change in the presence of abnormalities such as thyroid disease, renal or hepatic dysfunction (creatinine >1.5 mg/dl or aspartate aminotransferase and alanine transaminase more than twice the upper limit of normal,

respectively), inflammatory diseases, and use of medications which could influence RDW. On the other hand, it is also reported that an increased RDW is associated with nutritional deficiency (of iron, vitamin B_{12}, and folic acid) and ethnicity.[4]

Recent clinical studies have considered the importance of bleeding events in the prognosis in patients with ACS. In fact, the risk for cardiovascular complications associated with bleeding is similar to that of a myocardial infarction (MI). Some bleeding risk scores are now available that dependably quantify the likelihood of an ACS patient experiencing a bleeding complication. There is a strong relationship between bleeding and some conditions including older age,[5] renal impairment, female gender, and an invasive management approach. Although patients who tend to bleed frequently have more comorbidities than their non-bleeding counterparts, several lines of experimental and clinical evidence suggest an independent causal pathway for bleeding-associated cardiovascular risk. When possible, bleeding should be avoided, and strategies such as use of risk scores, novel antithrombotics (such as bivalirudin and fondaparinux), vascular closure devices and radial access may decrease major bleeding.[6]

Reduced glomerular filtration rate (GFR) may be also associated with adverse outcomes in patients with cardiovascular disease. The authors used the Cockcroft-Gault (CG) equation for GFR. However, compared to the Modification of Diet in Renal Disease (MDRD) formula, the CG equation can give lower GFR measurements in younger age groups but higher GFR measurements in older individuals. The value of GFR in predicting various cardiovascular endpoints in patients with MI is established. Compared to the CG formula, the MDRD formula is significantly more accurate in predicting the severity of coronary artery disease and two-year cardiovascular risk in patients admitted to the intensive care unit with MI.[7] For this reason, it can be useful, and the results of the study might have been different if the authors had also used the MDRD formula.

In a previous study it was found that elevated levels of inflammatory molecules are markers of in-hospital major bleeding and also indicate an increased risk for the progression of NSTEMI. These molecules can be reduced by medications including antihypertensive therapy[8] and aspirin. Additionally, as well as RDW, neutrophil/lymphocyte ratio, gamma-glutamyltransferase, C-reactive protein, mean platelet volume and uric acid are also easy methods to assess patients' cardiovascular disease.[9] Moreover,

---

☆ At the time of publication, the authors of the article had not responded to requests for a response.

hypoalbuminemia on admission is also a strong independent predictor of long-term mortality and development of advanced HF in patients with STEMI undergoing percutaneous coronary intervention.[10] These markers might be useful in clinical practice.[11] Finally, it would have been better if the authors had defined how much time they specified for measuring RDW levels, since delaying blood sampling can cause abnormal results in RDW measurements.

In conclusion, we strongly believe that the findings of the current study will lead to further large-scale studies examining the relationship between RDW and in-hospital major bleeding in patients presenting with ACS. However, one should keep in mind that RDW alone, without other inflammatory markers, may not give precise information to clinicians about their patients' inflammatory condition and prognostic indication. So, on this basis we think that it should be evaluated together with other serum inflammatory markers.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Gonçalves S, Ferreira Santos J, Amador P, et al. Impact of red blood cell distribution width on risk for bleeding events in patients with non-ST elevation acute coronary syndromes. Rev Port Cardiol. 2013;32:27–33.
2. Timóteo AT, Hamad H, Miranda F, et al. Can the presence of anemia on admission improve the predictive value of the GRACE risk score for short- and medium-term mortality after acute coronary syndrome? Rev Port Cardiol. 2012;31:279–85.
3. Tonelli M, Sacks F, Arnold M, et al. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. Circulation. 2008;117:163–8.
4. Grant BJB, Kudalkar DP, Muti P, et al. Relation between lung function and RBC distribution width in a population-based study. Chest. 2003;124:494–500.
5. Timóteo AT, Ramos R, Toste A, et al. Impact of age on treatment and outcomes after acute myocardial infarction, particularly in very elderly patients. Rev Port Cardiol. 2011;30: 897–903.
6. Rao SV, Dai D, Subherwal S, et al. Association between periprocedural bleeding and long-term outcomes following percutaneous coronary intervention in older patients. JACC Cardiovasc Interv. 2012;5:958–65.
7. Barra S, Providência R, Silva J, et al. Glomerular filtration rate: which formula should be used in patients with myocardial infarction? Rev Port Cardiol. 2012;31:493–502.
8. Karaman M, Balta S, Ay SA, et al. The comparative effects of valsartan and amlodipine on vWF levels and N/L ratio in patients with newly diagnosed hypertension. Clin Exp Hypertens. 2013;35:516–22.
9. Demirkol S, Balta S, Unlu M, et al. Evaluation of the mean platelet volume in patients with cardiac syndrome X. Clinics (São Paulo, Brazil). 2012;67:1019–22.
10. Oduncu V, Erkol A, Karabay CY, et al. The prognostic value of serum albumin levels on admission in patients with acute ST-segment elevation myocardial infarction undergoing a primary percutaneous coronary intervention. Coron Artery Dis. 2013;24:88–94.
11. Demirkol S, Balta S, Unlu M, et al. Neutrophils/lymphocytes ratio in patients with cardiac syndrome X and its association with carotid intima-media thickness. Clin Appl Thromb Hemost. 2012 Nov 26. [Epub ahead of print], http://dx.doi.org/10.1177/1076029612467227.

Sevket Balta*, Sait Demirkol, Murat Unlu, Turgay Celik

Department of Cardiology, Gulhane Medical Academy, Ankara, Turkey

* Corresponding author.
E-mail address: drsevketb@gmail.com (S. Balta).