final diagnosis of high-risk unstable angina or non-ST segment elevation myocardial infarction.

The authors measured RDW values only at admission and did not collect data on bleeding events or stent thrombosis during hospitalization. Increased RDW levels are also associated with aging, sex, genetic factors, thyroid diseases, renal or hepatic dysfunction, inflammatory disease, nutritional deficiency, and medications.\textsuperscript{7}

Sánchez-Martínez et al\textsuperscript{6} grouped anemic and nonanemic patients together in the analysis. However, in patients with acute coronary syndrome, functional iron deficiency anemia can be seen as a result of increased synthesis of hepcidin in the liver.\textsuperscript{2} Hepcidin, a peptide hormone, is also found in the heart and its expression is regulated by hypoxia and inflammation. An increased level of hepcidin inhibits the absorption of iron from the intestinal epithelium and blocks iron release from macrophages.\textsuperscript{8,9} As iron has detrimental effects in arteriosclerosis and ischemia/reperfusion,\textsuperscript{10} an elevated RDW value in patients with coronary artery disease possibly indicates functional iron deficiency anemia rather than worse clinical outcomes. It can be speculated that elevated RDW values are a reflection of reduced iron-toxicity in the infarcted myocardium.

In addition, a recent study by Meroño et al\textsuperscript{11} showed that nosocomial anemia without apparent bleeding in patients with acute coronary syndrome was a frequent complication (25%) and a predictor of mortality and cardiovascular complications during the first year of follow-up. Nosocomial anemia was associated with a marked inflammatory state, indicated by increased C-reactive protein levels.

Finally, the authors suggest that future research should assess the potential role of including RDW values in bleeding risk scales to improve the stratification of non-ST-segment elevation acute coronary syndrome patients, especially after hospital discharge. Should physicians be alerted to a higher risk of major bleeding by the presence of a higher RDW without a universally accepted cut-off value and a single measurement of RDW alone without taking into consideration other inflammatory indicators? If so, while the imprecision values are not defined, is it useful to follow RDW as a surrogate marker of subsequent adverse outcomes, much as a diabetologist follows glycated hemoglobin? More importantly, how can we manipulate the RDW to improve outcomes? Thus, when a mechanism explaining the association of RDW with adverse outcome is developed and definitive interventions to reduce RDW are identified, it will become a member of the standard evaluation test panel for our patients. Currently, the only clear thing about RDW is its ability to predict adverse outcomes.

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Red Cell Distribution Width and Coronary Artery Disease. Response

Amplitud de distribución eritrocitaria y enfermedad coronaria. Respuesta

To the Editor,

We appreciate the interest expressed by Dr Yavuzer Koza in our recently published article.\textsuperscript{1} Acute coronary syndrome is one of the major causes of mortality, morbidity, and health care costs.\textsuperscript{2} In our study, we demonstrate the value of red cell distribution width (RDW) as a predictor of major bleeding after hospital discharge in patients with non-ST-segment elevation acute coronary syndrome.

As we point out in the article, all of the bleeding events were recorded, including in-hospital episodes (27% of the total number). As in other studies,\textsuperscript{3,4} the patients with the highest RDW values at admission were older and had a higher prevalence of comorbidities. They also had lower hemoglobin concentrations and mean corpuscular volume. However, when baseline hematocrit was included in the multivariate analysis, RDW continued to be an independent predictor of major bleeding. Moreover, our findings demonstrate that RDW improves the prognostic accuracy of the CRUSADE bleeding score, which also includes the hematocrit level as a variable. These results, in agreement previously reported results demonstrating that the predictive value of RDW is independent of the hemoglobin concentration or anemia,\textsuperscript{5} indicate that its ability to predict major bleeding goes beyond its pathophysiological relationship to anemia.\textsuperscript{6} As has been pointed out, given the relationship between RDW and ferrokinetics, an analysis of absolute or functional iron deficiency would have enabled a study of the pathophysiological relationship between RDW and major bleeding. Unfortunately,
such analyses are rarely available at admission. We also completely agree that serial sampling would permit evaluation of changes in the RDW value and their relationship to major bleeding over time. These samples are now available and this study is in the process of being analyzed.

It is true that the exact cutoff point of the RDW value to be considered in the risk stratification of these patients is still unknown. Future studies will need to establish a universally accepted cutoff, although, in light of the available results, it would be reasonable to consider reference values ranging between 14.5% and 15.5%.1,3,4

In short, we consider RDW to be a promising marker in the management of non–ST-segment elevation acute coronary syndrome as it is inexpensive, readily available, and improves the widely validated CRUSADE bleeding score.

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