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The Epidemiology of the Clinical and Health Effects Associated With Cocaine. Response



Epidemiología de los efectos clínico-asistenciales asociados al consumo de cocaína. Respuesta

To the Editor,

Gironés-Bredy et al have carried out an extremely interesting analysis of the impact of cocaine-related disorders in patients treated in hospital emergency departments. We agree with these authors that the costs of the care of these patients are higher than those calculated for inpatients, due to both the out-of-hospital circumstances and the emergency department setting, as the authors point out in their article, and to other factors such as worker absenteeism (number of absences and their duration), loss of productivity, drug dependence treatments, social assistance, and others. The application of a minimum data set for emergencies treated in hospitals is imminent in some Spanish autonomous communities, which will help to more accurately assess the true impact of these disorders on patient prognosis and on the cost overruns associated with their care.

Gironés-Bredy et al suggest the possibility that our series may have included readmitted patients. As we explain in the methods section,¹ a first episode of acute myocardial infarction was defined as that in which the code appeared in the primary diagnosis (ICD-9 code 410 with a fifth digit = 1). We excluded other cases of acute myocardial infarction with codes not indicating a first episode in the primary diagnosis, as well as those cases in which the 410.x1 code corresponded to a secondary diagnosis. These criteria, recommended by the Agency for Healthcare Research and Quality of the United States,² were designed to ensure that readmissions for acute myocardial infarction not be recorded as first episodes.

Gironés-Bredy et al stress the importance of investigating drug consumption in all patients and of undertaking interventions to provide information and to treat dependence for primary and secondary prevention of the problems associated with substance

use. We agree with these authors that this course of action is an exercise in professionalism and should not be limited to emergency departments and inpatients, but should be extended systematically to all health care settings.

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Red Cell Distribution Width and Coronary Artery Disease



Amplitud de distribución eritrocitaria y enfermedad coronaria

To the Editor,

Red cell distribution width (RDW) has traditionally been considered useful in the differential diagnosis of anemia. RDW, which is routinely reported in complete blood counts as a statistical concept, is a measure of the variation in red blood cell volume.¹

In recent years, interest has significantly increased in RDW as a risk marker in cardiovascular research. Several studies have shown that high RDW levels are associated with higher mortality among patients with heart failure,² coronary artery disease,³ or myocardial infarction,⁴ and in those undergoing percutaneous coronary intervention.⁵

In a recent study published in *Revista Española de Cardiología*, Sánchez-Martínez et al⁶ showed that in non-ST-segment elevation acute coronary syndrome patients, elevated RDW values were predictive of increased major bleeding risk and provided additional information to the CRUSADE scale. The authors studied 293 consecutive patients with an established

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.⁷

Sánchez-Martínez et al⁶ 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.⁸ 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.^{8,9} As iron has detrimental effects in arteriosclerosis and ischemia/reperfusion,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 al¹¹ 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.¹ Acute coronary syndrome is one of the major causes of mortality, morbidity, and health care costs.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,^{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,⁴ indicate that its ability to predict major bleeding goes beyond its pathophysiological relationship to anemia.⁵

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,