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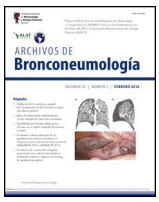

Editorial

New Uses for Old Biomarkers in COPD and Obstructive Sleep Apnea?☆

Viejos biomarcadores, ¿nuevas utilidades en epoc y apnea obstructiva del sueño?

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A key element in personalized medicine in chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD) or obstructive sleep apnea (OSA) has been the hunt for new biomarkers that are easy to obtain and determine, that are reproducible, precise, inexpensive, and associated with the key physiopathological processes involved in disease progression, and that can improve patient risk stratification and provide potential therapeutic benefit.[1,2] Studies in COPD patients have examined the association of analytical parameters obtained from such routine procedures as a complete blood count, including total eosinophil and leukocyte counts or hemoglobin concentration, with therapeutic response or the prediction of complications or disease course.[1,2] Old biomarkers, that we thought were of little use in these diseases, are once again in the limelight. The 2 original studies published in this edition of Archivos de Bronconeumología[3,4] suggest that something similar may be happening with red cell distribution width (RDW). This parameter is determined from a standard blood test and measures variability in the size of circulating erythrocytes. It is calculated from a mathematical formula, so it does not involve any added cost. Although values may vary slightly depending on the laboratory, distribution is generally normal and the range is from 11% to 16%.

RDW, as part of the complete blood count, provides valuable information on anemias, but some recent studies have also shown that high RDW values may reflect underlying chronic inflammatory processes associated with a risk of cardiovascular disease and mortality.[5] A meta-analysis of studies associating RDW and mortality in the elderly revealed that for each 1% increment in RDW, the overall risk of death rose by 14%, and elevated values were consistently associated with the risk of cardiovascular or cancer death (13%).[6] Even in elderly individuals with no underlying disease, RDW is a strong predictor of mortality, although the biological mechanisms that might explain this phenomenon remain unclear.[6]

More and more studies are relating RDW with different diseases. For example, it has been shown to be useful in predicting sepsis, where elevated RDW has been associated with positive blood cultures, or in predicting mortality in patients with community-acquired pneumonia and patients undergoing hemodialysis.[7–9] Patients who suffer panic attacks were found to have higher RDW values than healthy individuals, and the authors of the study proposed RDW as a new marker for this psychiatric disorder.[10] Another study also showed an association between RDW and smoking: RDW values were higher in healthy smokers than in non-smokers, and correlated positively with the number of cigarettes smoked per day and smoking duration.[11] It seems, then, that raised RDW is a good marker of inflammatory activity in smokers, so it may also have an important role in diseases such as COPD and OSA.

In this edition of Archivos de Bronconeumología, Ozgul et al.[3] published a paper in which they analyze RDW values in a large cohort of stable COPD patients and healthy individuals. One of the variables they explore is the presence of cardiovascular disease, determined by an expert cardiologist on the basis of a clinical evaluation, electrocardiogram, and echocardiogram. RDW in these COPD patients was significantly higher than in the group of healthy controls, and showed a weak but significant correlation with C-reactive protein (CRP), right ventricular dysfunction, pulmonary arterial hypertension, cardiovascular disease, and hemoglobin levels. The correlation with serum albumin was negative. In the healthy population, a moderately significant positive correlation was found between RDW and number of cigarettes smoked per day, in line with previously published data.[11] The physiopathological mechanism of this association, in COPD at least, is thought to be associated with the release of inflammatory cytokines that might affect bone marrow function, inhibiting erythropoietin-induced erythrocyte maturation, and as a consequence, increasing RDW.[12] In COPD, RDW is an independent predictive factor for cardiovascular disease. Using an RDW cut off point of 16.9, sensitivity and specificity for the diagnosis of right ventricular dysfunction in this study were 78% and 89%, respectively.[3]

In the second study, León Subías et al.[4] analyzed the utility of RDW as a biomarker for identifying the presence and severity of OSA in subjects with suspected sleep-disordered breathing. In addition to a domiciliary cardiorespiratory polygraphy, they determined RDW from a complete blood count at baseline and after 1 year of follow-up. The most significant results were that RDW was higher in OSA patients than in healthy individuals, and that RDW values in these subjects were independently associated with severity, measured by the apnea–hypopnea index or by time of hypoxemia, although these correlations were weak.[4] However,

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RDW values were curiously unaffected by effective treatment of OSA with CPAP, which would support previous findings on the limited efficacy of CPAP in reducing OSA-related systemic inflammatory status.[13]

The advantage of RDW over other inflammatory markers, such as interleukins or TNF, is that it is already included in the routine complete blood count performed in all patients, it is inexpensive, and may be even more sensitive than CRP for predicting right ventricular dysfunction and cardiovascular disease in COPD patients. Although RDW has been around for many years, it appears to be a promising biomarker. However, more studies will have to be performed in larger patient populations if its real predictive value is to be determined, and if it is to be included in COPD prognostic scores or as a parameter for guiding decision-making in patients with suspected OSA.[14,15]

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