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ORIGINAL ARTICLE

Could ''red cell distribution width'' predict COPD severity?☆

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Abstract
Background and objectives: Erythrocyte morphology changes not only by primary hematological diseases but also by systemic inflammation, ineffective erythropoiesis and nutritional deficiencies. Red blood cell distribution width (RDW) is a parameter reflecting erythrocyte morphology. We aimed to investigate the relationship of RDW with chronic obstructive pulmonary disease (COPD) stages, BODE index and survival in COPD patients.
Methods: Medical records of 385 COPD patients between July 2004 and November 2005 were studied retrospectively. Demographic features, BODE index factors and oxygen saturation were recorded. Survival analysis of all patients by 2014 was performed. Measured RDW values at the time of the inclusion were evaluated.
Results: Mean age of the patients was 65.6 ± 9.6 years. Distribution of the COPD stages of the patients were stage 1: 16%, stage 2: 52%, stage 3: 26%, stage 4: 6%. RDW was found significantly different between stages. The highest RDW was observed in the very severe stage ($p < 0.001$). Median of BODE index was 1 (0–3). As the BODE index increased RDW also increased ($p < 0.001$). When the patients were grouped according to the laboratory upper limit of RDW, survival rate was 31% in the RDW >14.3% group and 75% in the RDW <14.3% group.
Conclusion: The variability in the size of circulating erythrocytes increases as the COPD severity progresses. Therefore, a simple and noninvasive test, such as RDW, might be used as a biomarker in the evaluation of the severity of COPD. At the same time, there seems to be a correlation between the survival of COPD patients and RDW.

☆ All coauthors declare that Dr. Kemal Can Tertemiz is responsible for editorial correspondence. This manuscript, including related data, figures and tables has not been published previously and is not under consideration elsewhere.

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Introduction

Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease characterized by usually progressive persistent airflow limitation that is associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases.[1] However, it is still the fifth leading cause of death and estimated to be the third in 2030 worldwide.[2] Currently, COPD has been accepted as a component of systemic inflammatory syndrome and the mortality mostly depends on cardiovascular diseases rather than respiratory failure.[3] Possible explanations for the high cardiovascular morbidity and mortality observed in COPD patients are high smoking prevalence, diet and sedentary life style as well as systemic inflammation due to oxidative stress and chronic hypoxia.[4,5]

The red cell distribution width (RDW) is a routine laboratory parameter that indicates the variability in the size of circulating erythrocytes. The main area which the RDW is used is the differential diagnosis of microcytic anemia. It has been defined as a prognostic tool in different clinical settings such as pulmonary arterial hypertension, congestive heart failure and coronary heart disease.[6–8] It has also been reported as a powerful predictor of mortality in general population and older adults.[9,10] Increased RDW values have been reported to be related with underlying chronic inflammation which promotes red blood cell membrane deformability and changes in erythropoiesis.[11]

Accordingly, we hypothesized that systemic inflammation may be the common link between increased RDW values and mortality in patients with COPD. Therefore we aimed to study the relationship between RDW and airflow limitation severity stages, BODE index and survival in COPD patients.

Methods

We conducted a retrospective cohort study in patients diagnosed as COPD by global initiative for chronic obstructive lung disease (GOLD) criteria between July 2004 and November 2005 to observe the 9-year survival rate.[1] The inclusion criteria was: being on stable state (no history of hospitalization or admission to an emergency department for at least 8 weeks), absence of cancer history, connective tissue disorders, inflammatory bowel disease, hematological system diseases, blood transfusion and anti-inflammatory drug (systemic steroids, immunosuppressive drugs) usage in the last 2 months. In January 2014 we searched for the survival of these patients in the registry to evaluate 9-year survival rate. We used the hospital automation software which was integrated with the national population system to determine the deaths.

Demographic features and medical history including comorbid diseases such as hypertension, diabetes mellitus, cardiovascular disease and smoking status of the study population were recorded. Six-minute walk test (6MWT), pulmonary function tests (PFT), BODE index and complete blood count results at the time of the inclusion (July 2004 and November 2005) were also collected from the medical records of the patients.

It would be better to use the composite COPD assessment index recommended by GOLD since 2011. That was not possible because at the time of the study, dyspnea scores and the number of exacerbations in the previous year were not accessible.

Pulmonary function tests

PFTs were performed with Jaeger Master Screen Pneumo V452i device by a single technician between July 2004 and November 2005. The best test among the three consecutive ones was accepted. FEV_1 (Forced expiratory volume in 1 s), FVC (Forced vital capacity), FEV_1/FVC (percentage of FVC expelled in the first second of a forced expiration) were measured according to American Thoracic Society criteria.[12] The airflow limitation severity staging was done according to GOLD 2015.[1]

Laboratory measurements

Blood samples obtained between July 2004 and November 2005 were evaluated. RDW normal range was between 11.8% and 14.3% in our laboratory.

Six-minute walk test

6MWT was performed in a corridor of 35 m at the time of diagnosis. Patients were motivated to walk as fast as they could. Oxygen saturation was measured before and after the test and the distance walked was recorded.[13]

BODE index

BODE index was calculated according to body mass index (BMI), FEV_1, 6MWT, modified medical research council dyspnea scale (MMRC) at the time of diagnosis.[14]

Oxygen saturation

Oxygen saturation was measured by pulse oxymeter at the time of diagnosis (Plusmed).

Statistical analyses

Data were analyzed by SPSS 15.0 package program. The frequencies of the results were expressed according to the dispersion properties of data. Variables were compared by unpaired *t* tests for continuous data and Mann Whitney *U*-test for nonparametric data. Chi-square analysis was used for categorical data. Spearman and Pearson correlation tests were used for correlation analysis. A p value, <0.05 was considered significant.

Survival analysis was performed thereafter grouping patients according to the laboratory upper limit of RDW. The patients' inclusion date in the study was considered as the first day. The last check date or the discharge date was considered as the last day on survival analysis. Kaplan–Meier survival analysis was performed for univariate survival analysis. Multivariate analysis for survival rates were further performed by Cox proportional hazards regression to adjust for age, comorbid diseases, FEV_1 and 6MWT.