Prediction of severity of COPD based on red cell distribution width value

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a type of obstructive lung disease characterized by long-term poor airflow. Tobacco smoking is the most common cause of COPD, with a number of other factors such as air pollution and genetics playing a smaller role.

Objectives: The objective of the study is to predict severity of COPD based on RDW value.

Material & Methods: This Retrospective study included total 385 COPD patients. Demographic features, BODE index factors and oxygen saturation were recorded. Survival analysis of all patients was performed. Measured RDW values at the time of the inclusion were evaluated.

Results: Mean age of the patients was 67.2 ± 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.

Conclusions: From our study we would like to conclude that increased level of RDW might be related with increased mortality in COPD patients.

Keywords: COPD; Exacerbation; Hospitalization; RDW.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressively debilitating disease limiting patients' survival. 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 [2].

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. Increased RDW values have been reported to be related with underlying chronic inflammation which promotes red blood cell membrane deformability and changes in erythropoiesis [3].

Material & Methods

This retrospective study was conducted at B.J. Medical College and Civil Hospital, Ahmedabad, India from January 2009 to December 2010 to observe the 9-year survival rate. Study included a total 385 confirmed cases of COPD that was clinically diagnosed by chest physicians.

Exclusion criteria: Patients having any history of autoimmune disorder, history of blood transfusion, malignancy or patients who are taking any type of medication for any systemic illness like DM, hypertension, etc. were excluded from the study. 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 mortality.

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.

Pulmonary function test [4]: PFTs were performed by a single technician between July 2004 and November 2005. The best test among the three consecutive ones was accepted. FEV1 (Forced expiratory volume in 1s), FVC (Forced vital capacity), FEV1/FVC (percentage of FVC expelled in the first second of a forced expiration) were measured.

Blood samples were obtained from all participants for measurement of red cell distribution width (RDW). RDW is measured in 3 part hematology cell counter.

RDW normal range was between 11.6%-13.9% in our laboratory.

Six-minute walk test [5]: 6MWT was performed in a corridor of 35m 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.

BODE index [6]: BODE index was calculated according to body mass index (BMI), FEV1, 6MWT, modified medical research council dyspnea scale (MMRC) at the time of diagnosis.

Oxygen saturation: Oxygen saturation was measured by pulse oxymeter at the time of diagnosis

Statistical analyses: All obtained data were analyzed statistically by using graph pad prism software. Student t-test was calculated for obtaining p-value to see the significance of difference**.** A p-value, <0.05 was considered as a difference 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, FEV1 and 6MWT.

Results

Study included a total 385 COPD patients. Mean age of the study population was 67.2±9.6 years. Demographic characteristic of the participants is mentioned on Table 1. Mean RDW levels were found to be increasing with the severity of COPD (Table 2). RDW was inversely correlated with the 6MWT, pulmonary functional parameters and oxygen saturation.

There was also a mild association with age, GOLD stage and a moderate correlation with BODE index (Table 3).

Pulmonary functional parameters, 6MWT distance and oxygen saturation were lower for patients with an elevated RDW, while age, smoking intensity and BODE index were higher (Table 4).

Table 1: Demographic characteristic of the participants

Characteristic	N (%)
Gender	
Male	338(88)
Female	47(12)
GOLD stages	
Stage 1	64(16)
Stage 2	200(52)
Stage 3	99(26)
Stage 4	22(6)
Smoking status	
Non smoker	50(13)
Smoker	125(32)
Ex-smoker	210(55)
Comorbidity	
Yes	226(59)
CVSD	214(56)
DM	33(9)
Others	122(32)
No	159(41)
Mortality cause	
Cancer	28(9)
COPD	30(8)
Pneumonia	20(5)
CVSD	31(10)
Renal Failure	5(1)
Neurological disorder	2(1)
BODE index (Median/min – max)	1.0(0.0-10.0)

Table 2: RDW levels according to GOLD stages

GOLD stages	Mean RDW (%)
Stage 1	13.5
Stage 2	13.9
Stage 3	14.4
Stage 4	15.7

Table 3: Correlation of RDW with functional and demographic parameters

RDW correlation	r	p
6MWT	-0.279	<0.01
%FEV1	-0.290	<0.01
%FVC	-0.285	<0.01
FEV1/FVC	-0.206	<0.01
%FEF 25-75	-0.303	<0.01
%PEF	-0.227	<0.01
Oxygen saturation	-0.260	0.247
BMI	-0.059	<0.01
Age	0.182	<0.01
BODE index	0.407	<0.01
GOLD stage	0.403	<0.01

Table 4: Functional and demographic parameters of the participants according to upper limit of RDW value

	All patients	RDW <14.3	RDW >14.3	p
Age	65.6	64.4	68	
FEV1(L)	1.66	1.80	1.34	<0.01
%FEV1	60.2	64.6	50.5	<0.01
FVC(L)	2.86	3.04	2.45	<0.01
%FVC	80.8	85.1	71.2	<0.01
FEV1/FVC	57.2	58.7	53.9	<0.01
PEF(L)	4.79	5.1	4.1	<0.01
%FEF 25/75	26.1	28.7	20.3	<0.01
Smoking (pack year)	56	52.5	63.3	>0.01

Smoking beginning age	17.8	18.2	16.8	>0.01
BMI	25.4	25.6	24.9	<0.01
6MWT (In meters)	435	453	393	<0.01
O_2%	96	96.4	95.1	<0.01
BODE index	1.83	1.32	2.98	<0.01

Table 5: Impact of RDW and potential confounders on survival

	Odds ratio	95% Confidence limit	P-value
FEV1	0.529	0.375-0.747	<0.01
RDW	1.222	1.153-1.295	<0.01
6MWT	0.998	0.997-1.000	>0.01
Age	1.055	1.033-1.077	<0.01
Comorbidities	1.430	1.004-2.036	<0.01

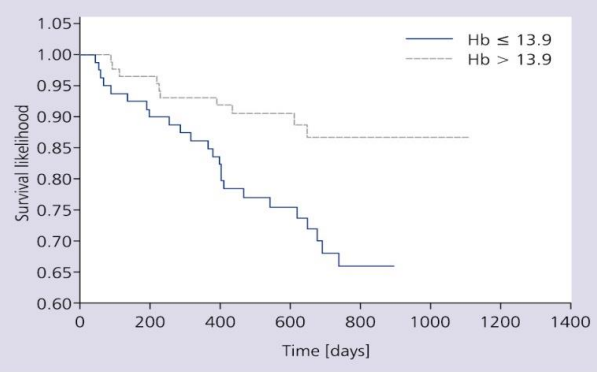

Fig 1: Showing likelihood of survival rate

The overall 9-year survival rate of the study population was 61%. When the patients were divided into 2 groups according to RDW the 9-year survival rate was 75% for patients with normal RDW (≤13.9%) and 31% for patients with an elevated RDW (>13.9%) ($p < 0.001$) (Fig. 1). On multivariate analysis, when adjusted for potential confounders, age and 6MWT were found to be associated with survival (Table 5).

Discussion

COPD is a chronic respiratory disease with significant mortality and morbidity. Elevated levels of RDW have been reported to be related with cardiovascular mortality. Considering RDW as a mortality predictor, in this study we investigated the relationship between RDW and air-flow limitation severity stages, BODE index and survival in COPD patients. We found increased RDW levels associated with COPD severity and also observed a higher mortality in patients with increased RDW levels.

However, in another study, smokers RDW levels were found to be higher than the ones associated with non-smokers [7,8]. In another study investigating the prognostic usefulness of RDW in idiopathic pulmonary fibrosis, the authors found that the patients with lower FEV1 and lower diffusing capacity had higher RDW and concluded that RDW was an independent prognostic information at baseline and follow-up. The results of our study also demonstrated that pulmonary function test parameters were negatively associated with RDW. This finding was concordant with the high RDW levels we observed in severe COPD stages, especially in the very severe group. We also detected a relationship between smoking intensity and RDW levels, which might be due to hypoxemia related erythropoiesis. The correlation of the oxygen saturation and RDW levels also supports this hypothesis. BODE index, which has been found to be related with mortality in COPD, was associated with RDW in our study.

In a recent study investigating the prognostic value of RDW in COPD, cardiac, respiratory, and hematological status were evaluated and RDW was found to be correlated with C reactive protein, pulmonary arterial hypertension and right ventricular dysfunction [9]. As we found increased RDW levels in severe COPD similarly, we think that RDW could also be considered as a prognostic systemic inflammatory marker in COPD. The independent association between RDW and survival has been described for a broad spectrum of cardiovascular and pulmonary disease such as pulmonary hypertension, acute pulmonary embolism, and idiopathic pulmonary fibrosis and even for COPD [10].

Conclusions

From our study we would like to conclude that increased level of RDW might be related with increased mortality in COPD cases and simple and non-invasive tests might be used as preliminary biomarker in the evaluation of diseases severity.

Conflicts of interest: None

Acknowledgements: None

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