RESEARCH ARTICLE

Surrogate scale for evaluating respiratory function based on complete blood count parameters

Yang Guang | Zhou Jie | Dong Feng | Liu Hui

College of Medical Laboratory, Dalian Medical University, Dalian, China

Correspondence

Liu Hui, College of Medical Laboratory, Dalian Medical University, Dalian, China.
Emails: immunology@dlmedu.edu.cn or liuhui60@sina.com

Background: In this study, we aimed to identify a simple method for evaluating respiratory function using complete blood count parameters.

Methods: The complete blood count parameters, including red blood cell (RBC) count, hemoglobin (Hb) level, lymphocyte (Lym) and platelet (Plt) count, and partial pressure of oxygen (PO_2) level, were measured using automated analyzers in patients with chronic obstructive pulmonary disease (COPD), aged subjects, and young subjects (control group). The red cell index (RCI) was calculated using the following equation: $(RBC \times Hb) / (Lym \times Plt)$; in theory, the RCI is inversely proportional to the respiratory function.

Results: We observed a significant relationship between the RCI and PCO_2 values, and between the RCI and FEV1/FVC values ($P < .05$). The RCI in the COPD, and aged subject groups were all significantly higher than that in the control group ($P < .05$). The cutoff value for normal respiratory function was 2.3. The positive rates for an abnormal increase in RCI were also considerably higher in each observation group than in the control group ($P < .05$).

Conclusion: The RCI can be considered as a simple and effective tool for evaluating respiratory function.

KEYWORDS

blood count, computer-assisted diagnosis, COPD, respiratory function

1 | INTRODUCTION

Lungs ensure the vital exchange of oxygen and carbon dioxide in the body. In many diseases, particularly during the terminal stage, respiratory failure is the main cause of death. Therefore, it is vital to evaluate respiratory function in clinical practice and during screening for occupational diseases. Physical methods, such as the vital capacity test, have long been used to assess the degree of pulmonary ventilation and evaluate respiratory function.¹⁻³ However, this method is easily influenced by subjective patient factors, and is especially unsuitable for children and bedridden patients. Blood gas analysis can also be used to evaluate respiratory function in bedridden patients. However, it is important to obtain arterial blood samples for this method, which subsequently need to be rapidly analyzed under vacuum conditions, with appropriate pretreatment. Improper pretreatment procedures

affect the reliability of the results,⁴⁻⁶ and it may also not be possible to frequently monitor the respiratory function for certain patients, including those with asthma or obstructive sleep apnea, or those who are athletes. Hence, a convenient and accurate method is needed to objectively evaluate the indices of respiratory function.

The red blood cell (RBC) count and hemoglobin (Hb) level are known to increase to compensate for poor respiratory function.^{7,8} Therefore, these values can be considered as suitable criteria for evaluating respiratory function; however, such measures would have practical significance only when the impact of the changes in blood cell proliferation from other factors on the RBC count and Hb level is excluded. In this study, we used lymphocyte (Lym) and platelet (Plt) counts as the baseline for measuring the general level of blood cell proliferation. The red cell index (RCI: $[RBC \times Hb] / [Lym \times Plt]$) thus obtained could accurately reflect the degree of the compensatory

TABLE 1 Relationship between the RCI and the FEV1/FVC, PO₂, and PCO₂ values

RCI	FEV1/FVC	PO ₂	PCO ₂
<1.6	0.65 ± 0.18	82.13 ± 25.05	42.36 ± 7.90
1.6 ~	0.58 ± 0.18	84.46 ± 19.37	43.98 ± 12.35
>2.6	0.52 ± 0.14	78.42 ± 22.64	53.24 ± 20.21
<i>F</i>	5.127	0.666	5.585
<i>P</i>	.008	.516	.005

RCI: the red cell index [(RBC × Hb)/(Lym × Plt)].

increase in the RBC count and Hb level caused by hypoxia. We included subjects with poor respiratory function (including elderly patients and patients with chronic obstructive pulmonary disease [COPD]) in our study to test the hypothesis that the RCI could be used as an indicator of respiratory function.

2 | METHODS

2.1 | Subjects

For the analysis of blood gas measurements, we randomly selected patients from among those who underwent blood gas analysis for different reasons; a total of 228 patients (115 men and 113 women; mean age, 66.9 ± 12.8 years) were selected.

Moreover, for the determination of respiratory function, we randomly selected patients from among those who underwent respiratory function examination for different causes; a total of 101 patients (49 men and 52 women; mean age, 65.6 ± 13.8 years) were selected.

The COPD group comprised 45 inpatients (23 men and 22 women; mean age, 75.7 ± 11.4 years) who were admitted to the Dalian Municipal Friendship Hospital, Affiliated Hospital of Chifeng College, and the Affiliated Hospital of Dalian University in China. We defined COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.⁹ The patients were evaluated by 2-4 respiratory physicians. The FEV1/FVC (where FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity) was <0.7 for all the patients in this group. The exclusion criteria included mental disorders, or death within 1 week after sampling.

The aged group comprised 85 residents (40 men and 45 women; mean age, 84.7 ± 3.2 years) of Dalian city, China. Individuals were eligible to participate if they were >80 years of age. The exclusion criteria included the presence of obstructive sleep apnea or hypoventilation-obesity syndrome, the exacerbation of various chronic diseases 4 weeks prior to the study, or the long-term use of medications.

A total of 239 reference adults (120 men and 119 women; mean age, 29.1 ± 5.0 years) were selected from a random population of the same city as the control group in our study. All the reference adults underwent medical checkups and were deemed to be healthy.

All the included subjects were of Northern Han Chinese ethnicity. The experiments were conducted in accordance with the Declaration of Helsinki. The blood samples taken were part of the usual care of

the subjects, rather than for research purposes alone. The Institutional Ethics Committee of Dalian Medical University approved the study and waived the need for written informed consent from the participants due to the observational nature of the study.

2.2 | Blood sampling and blood analyses

Blood samples were drawn from the antecubital vein of the participants at 07:00 AM, and anticoagulation with ethylene diamine tetraacetic acid was performed. The complete blood count parameters, including RBC count (10¹²/L), hemoglobin level (g/L), Lym count (10⁹/L), and Plt count (10⁹/L), were measured using an automated hematology analyzer (Sysmex SF-3000, Japan) with standard commercial reagent kits.

Arterial blood samples were obtained from the radial artery by direct puncture for blood gas analysis. All the samples were immediately sent to the laboratory and analyzed with a Blood Gas Analyzer at 37 ± 0.1°C within 5 minutes. The blood gas parameters included partial pressure of oxygen (PO₂; reference range, 83-108 mmHg) and partial pressure of carbon dioxide (PCO₂; reference range, 35-48 mmHg).

2.3 | Statistical analysis

The RCI was estimated using the following equation: RCI = (RBC × Hb)/(Lym × Plt). In theory, the RCI is inversely proportional to respiratory function.

The relationship between RBC × Hb and Lym × Plt was assessed using Spearman's correlation analysis in subjects with normal PO₂ and PCO₂ from the blood gas analysis group.

Analysis of variance (measurement data) and the chi-squared test (enumeration data) were used to analyze the differences among the various groups. Data were considered to be statistically significant when the probability of a type I error was <0.05.

Receiver operating characteristic (ROC) curves were plotted using the data of patients with COPD and the control group to determine the optimal cutoff value.¹⁰ Calculations were performed using SPSS software for Windows.

3 | RESULTS

We observed a significant relationship between RBC × Hb and Lym × Plt in subjects with both normal PO₂ and normal PCO₂ ($r = .300$; $P < .001$).

The FEV1/FVC and PCO₂ values were significantly different among groups divided based on the RCI values. However, the PO₂ value did not exhibit significant differences among these groups, as shown in Table 1.

Table 2 describes the original data in the various groups. All the measurements, including RCI, exhibited significant differences among the 4 groups.

ROC analysis (Figure 1) showed that the cutoff of the RCI was 2.3. The positive rates of an abnormal increase in the RCI were considerably higher in each observed group than in the control group ($P < 0.05$). The detailed results are shown in Table 3.

TABLE 2 Original data of blood cell counts in the different groups (mean $\pm$ SD)

Analyte	COPD group	Aged group	Control group	F	P
WBC	10.03 $\pm$ 4.76	7.42 $\pm$ 2.05	7.28 $\pm$ 1.71	69.84	<.0001
Neut	7.51 $\pm$ 4.24	3.90 $\pm$ 1.31	3.67 $\pm$ 1.22	75.80	<.0001
Lym	1.17 $\pm$ 0.63	2.16 $\pm$ 1.07	2.28 $\pm$ 0.51	18.23	<.0001
RBC	4.27 $\pm$ 0.86	4.25 $\pm$ 0.45	4.52 $\pm$ 0.46	49.24	<.0001
Hb	124.60 $\pm$ 19.32	135.14 $\pm$ 15.01	141.48 $\pm$ 13.94	53.88	<.0001
Plt	167.61 $\pm$ 59.04	199.20 $\pm$ 57.19	215.98 $\pm$ 40.45	17.00	<.0001
RCI	4.90 $\pm$ 5.66	1.81 $\pm$ 1.28	1.42 $\pm$ 0.49	20.72	<.0001

RCI: the red cell index $[(RBC \times Hb)/(Lym \times Plt)]$. **FIGURE 1** ROC curve for various cutoff levels of the RCI between COPD and control group. AUC: area under the curve; RCI: the red cell index**TABLE 3** Positive rates of the RCI in the different groups

Groups	N	Positive number	Positive rate (%)	P	
				A vs B	B vs C
COPD (A)	45	29	64.4		
Aged (B)	85	18	21.2	<.001	<.001
Control (C)	239	13	5.4		

RCI: the red cell index $[(RBC \times Hb)/(Lym \times Plt)]$, that RCI > 2.3 is considered as an abnormal increase.

4 | DISCUSSION

An increase in the RBC count and the Hb level is known to reflect susceptibility to the hypoxia response.^{11,12} Impairment of respiratory function (mainly chronic respiratory function impairment) indicates the presence of chronic hypoxic conditions, which in turn lead to a compensatory increase in the RBC count and Hb level. When patients develop respiratory failure, the body is often in a

poor condition, and the general level of blood cell proliferation may be abnormal. Hence, it is necessary to identify a variable that accurately reflects the changes in the level of blood cell proliferation. A decrease in such a variable would serve as a suitable context based on which changes in the RBC count and Hb level can be interpreted; a reduction in the RBC count and Hb level is caused by the poor general condition of the body, whereas a compensatory increase in the RBC count and Hb level is caused by hypoxia resulting from poor respiratory function. Lym and Plt counts are rarely affected by other factors, and a significant relationship between $RBC \times Hb$ and $Lym \times Plt$ was observed in the present study, thus indicating that Lym and Plt counts could serve as a better indicator of general proliferation in the blood cell count. Hence, we selected Lym and Plt as reference cells to indicate the proliferative activities of blood cells. Our results show that the Lym and Plt counts in the elderly and COPD groups were lower than those in the control group, thus suggesting that Lym and Plt can accurately reflect general proliferation in the blood cell levels. Therefore, the RCI $[(RBC \times Hb)/(Lym \times Plt)]$ ratio) was considered as an index that reflects the compensatory increase in the RBC count and Hb level secondary to poor lung function.

Our results proved that there was a significant relationship between the RCI and PCO_2 values, and also showed that there was a significant relationship between RCI and FEV1/FVC. However, no significant difference in PO_2 was observed among the 3 groups divided based on the RCI values, which may be due to oxygen therapy received prior to examination. When the influence of environmental factors was excluded (such as the oxygen content in the air), the RCI appeared to serve as a simple and effective tool for evaluating respiratory function. As mentioned earlier, the RCI was inversely proportional to respiratory function.

The respiratory function gradually deteriorates in elderly subjects. Similarly, patients with COPD exhibit respiratory function impairment. Our results showed that the RCI in the COPD and elderly groups was all significantly higher than that in the control group ($P < .05$). Consequently, our results showed that the RCI could reflect the actual respiratory function status.

The increase in RCI can serve as an objective quantitative index of poor respiratory function. We performed an ROC analysis and estimated that <2.3 was the normal range for the RCI. Accordingly, the abnormal rate (based on a cutoff value of 2.3) in each observation

group was higher than that in the control group, further confirming that the RCI was an effective and reliable index for evaluating chronic pulmonary dysfunction.

We do not believe that arterial blood gas analysis is an ideal method for evaluating pulmonary dysfunction, as the procedure itself can be technically difficult and may require several attempts.¹³⁻¹⁵ It is also painful when performed via the radial artery at the wrist. Moreover, arterial puncture is associated with the risk of complications, such as local hematoma, arterial thrombosis, or embolization, with consequent ischemic injury to the digits. The use of RCI, based on complete blood count parameters, to evaluate pulmonary function appears to be technically easier and may be applicable to a majority of patients suffering from respiratory disease. The sensitivity will increase with the regulation of the cutoff value based on the need for a clinical diagnosis or screening for occupational diseases. Thus, the RCI may be a useful alternative method to evaluate pulmonary dysfunction.

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ORCID

Liu Hui <http://orcid.org/0000-0002-1262-1168>

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