

Research Article

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You-Fan Peng[#], Zhao-Xia Zhang, Wei Cao, Cun-Ren Meng, Shen-Sheng Xu, Qiong Zhang^{*,#}

The association between red blood cell distribution width and acute pancreatitis associated lung injury in patients with acute pancreatitis

Abstract: Background: Red blood cell distribution width (RDW) that describes red blood cell volume heterogeneity is a common laboratory test. Our aim was to focus on the association between RDW and acute pancreatitis associated lung injury (APALI). Methodology: A total of 152 acute pancreatitis (AP) patients who conformed to the criteria were included in this study. The demographic data, medical histories and laboratory measures was obtained from each patient on admission, further, the medical histories and biological data were analyzed, retrospectively. Results: Increased RDW at admission was observed in patients with APALI compared with the non-APALI groups. Our results exhibited that RDW was an independent risk factor for APALI after adjusting leukocyte, neutrophil percentage, random blood glucose (RBG), total bilirubin (TB) and total bile acid (TBA) (Crude model) (OR=2.671; CI 95% 1.145-6.230; P=0.023), further adjustment based on Crude model for sex and age did not attenuate the significantly high risk of APALI in patients with AP, RDW still remained a roles as an independent risk factor for APALI (OR=2.653; CI95 % 1.123-6.138; P=0.026). Conclusions: Our

study demonstrate that RDW at admission is associated with APALI and should be considered as an underlying risk factor of APALI.

Keywords: Red blood cell distribution width, Acute pancreatitis, Acute pancreatitis associated lung injury

DOI 10.1515/med-2015-0028

Received: October 30, 2014; accepted: January 15, 2015

Acute pancreatitis (AP) presents with acute abdominal pain with high morbidity and mortality seen in all age groups [1]. Its main complications include lung damage, heart damage, kidney damage and pancreatic encephalopathy, acute pancreatitis associated with lung injury (APALI) is the most common complication. At present, the laboratory medicine plays an important role for diagnosis of APALI. It is known that RDW is supposed to be a common laboratory test that describes red blood cell volume heterogeneity, increased RDW implies discretizations degree of red blood cell volume [2]. Several studies [3-9] have shown that RDW was significantly correlated with alzheimer's disease, heart failure, coronary artery disease, hypertension, diabetes, rheumatoid arthritis, intestinal inflammation and abdominal diseases. Recently, Şenol K, et al [10] indicated that RDW was a predictor of mortality for patients with AP. Kolber, et al [11] further confirmed that RDW was higher in AP patients who died compared with survivors and had correlation with course of AP in early phase. However, there was no study that the relation between RDW and APALI. Then, our aim in this study was to examine the association between RDW and APALI.

***Corresponding author: Qiong Zhang**, Laboratory Medicine Diagnostic Centre, The First Affiliated Hospital, Xin Jiang Medical University, No.1-137, Liyushan Road, Xin'shi Region, Urumqi, Xinjiang, China, 830011, Phone:15022960879, Telephone:0991-4361446, Fax: 0991-4361445, E-mail:3115224002@qq.com
You-Fan Peng, Zhao-Xia Zhang, Cun-Ren Meng, Laboratory Medicine Diagnostic Centre, The First Affiliated Hospital, Xin Jiang Medical University, Xinjiang Urumqi, China
Wei Cao, Hemopathy Research Center, The First Affiliated Hospital, Xin Jiang Medical University, Xinjiang Urumqi, China
Shen-Sheng Xu, Department of Gastroenterology, The First Affiliated Hospital of Xinjiang Medical University, Xinjiang Urumqi, China

[#] These Authors equally contributed to the work.

1 Patients and Methods

AP patients who were admitted to First Affiliated Hospital of Xinjiang Medical University from 2012 to 2014 were followed during hospitalization. The treatment for patients with AP was made on the basis of the treatment guidelines [12]. The study was approved by the ethics committee, and a consent form was obtained from each participant. The primary end point is onset of APALI during follow-up, further, the medical histories and biological data on admission was analyzed, retrospectively.

1.1 Definitions

The diagnosis for AP was based on typical clinical presentation, plasma amylase level exceeding 3 times the upper normal level and/or confirmed pancreatitis by abdominal computed tomographic scanning or ultrasonography. APALI was defined according to following criteria that bases on the onset of clinical signs with acute hypoxemic: (1) progressive dyspnea or embarrassed, arterial blood oxygen partial pressure (PaO_2) < 60 mm/Hg, oxidative index ($\text{PaO}_2/\text{FiO}_2$) < 200 mm/Hg, (2) respiratory failure is only corrected by breathing machine, and patchy shadows change on the lung computed tomographic scanning and X-ray, (3) $\text{PaO}_2/\text{FiO}_2$ < 300 mm/Hg with the exception of chronic lung diseases and left heart function failure [13].

1.2 Exclusion criteria on admission were

(1) presence of hematologic disease, hypertension, and diabetes (2) presence of malignant tumor, active infections, respiratory diseases and serious cardiovascular disease, (3) presence of known chronic liver and/or kidney diseases, immune system disease (4) patients with recent transfusion history, recurrent AP, chronic pancreatitis and pregnancy.

On admission, the past medical history and imaging findings was obtained from each patient with AP, serum amylase (AMY), serum calcium (Ca), serum urea nitrogen (UREA), random blood glucose (RBG), total protein (TP), total bilirubin (TB), total bile acid (TBA), creatine kinase (CK), creatinine (Cr) and blood routine examination including RDW were measured in this research, the data was recorded on the study forms.

1.3 Statistical analysis

The data used SPSS16.0 (SPSS Inc, Chicago, IL, USA) statistical software for statistical analysis, normal distribution was tested with the Kolmogorov-Smirnov test. Two independent sample t-test, Mann-Whitney U test and χ^2 test were used for the comparison in between the groups. Multivariate logistic regression analysis also was used to analysis risk factors associated with APALI. The P value of < 0.05 was considered as significant.

2 Results

According to the criteria, a total of 152 eligible patients with AP were enrolled in our study in which there were 32 (21.1%, 32/152) patients in APALI groups and 120 (78.9%, 120/152) patients in non-APALI groups. The demographic features and experimental indicators at admission were presented in Table 1. APALI patients with high RDW remained significant difference compared with non-APALI patients (14.0 ± 1.2 vs. 12.7 ± 1.8 , $P = 0.003$), the statistically difference for other variables was found in service patients as well ($P < 0.05$), including leukocyte, neutrophil percent, RBG, TB and TBA.

Stepwise multiple logistic regression analysis was used to analysis the risk factors related with APALI possibly. Only RDW at admission was exhibited a significant difference when the different factors were incorporated into Multivariate logistic regression analysis (Table 2). After adjusting leukocyte, neutrophil percentage, RBG, TB and TBA (Crude model), our results exhibited RDW was an independent risk factor for APALI (OR = 2.671; CI 95% 1.145-6.230; $P = 0.023$), further adjustment based on Crude model for sex and age (Adjusting model) did not attenuate the significantly high risk of APALI in patients with AP, RDW still plays a role as an independent risk factor for APALI (OR = 2.653; CI 95% 1.123-6.138; $P = 0.026$).

3 Discussion

In the present study, high RDW was associated with APALI in patients with AP. More important, we demonstrated that elevated RDW at admission was an independently risk factor of APALI in AP patients.

Very recently, the association between RDW and adverse events was examined in previous studies [3-11]. And it was implied marks for severity and mortality of

Table 1: Demographical and Laboratory Data for Participants

	APALI groups	non-APALI groups	p-value
Male, n (%)	22(68.8%)	100(83.3%)	0.066
Age(y)	43.3±14.9	46.2±13.8	0.465
Biliary calculi, n (%)	16(50%)	40(33.3%)	0.082
Overeating history, n (%)	10(31.3%)	38(31.6%)	0.964
Smoking history, n (%)	6(18.8%)	16(13.3%)	0.623
Leukocyte (×10 ⁹ /L)	14.8±5.8	10.9±5.2	0.004
Neutrophil percent (%)	85.3±7.7	77.4±11.3	0.010
Red blood cell (×10 ¹² /L)	5.0±0.7	4.7±0.6	0.135
Hemoglobin (g/L)	157.3±19.2	149.3±19.3	0.159
Red blood cell distribution width (%)	14.0±1.2	12.7±1.8	0.003
Random blood glucose (mmol/L)	7.9±3.2	8.8±1.6	0.009
Total bile acid (μmol/L)	24.6±28.12	15.3±28.1	0.030
Total bilirubin (μmol/L)	57.3±46.9	35.9±39.6	0.013
Total protein	66.0±12.9	70.0±8.6	0.163
Creatine kinase (IU/L)	109.8±140.7	77.0±44.4	0.404
Serum calcium (mmol/L)	2.2±0.3	2.3±0.2	0.084
Serum urea nitrogen (mmol/L)	5.5±2.9	4.3±1.3	0.156
Creatinine (μmol/L)	99.0±75.1	64.8±20.9	0.101
Serum amylase (IU/L)	688.0±511.0	571.7±828.8	0.065

Table 2: Results of Stepwise multiple logistic regression analysis of red blood cell distribution width

	B	SE	Wald	p-value	OR	95% Confidence interval
Crude model	0.982	0.432	5.168	0.023	2.671	1.145-6.230
Adjusting model	0.965	0.433	4.962	0.026	2.653	1.123- 6.138

Crude model: adjusting leukocyte, neutrophil percent, random blood glucose, total bilirubin and total bile acid.

Adjusting model: adjustment for sex, age, leukocyte, neutrophil percent, random blood glucose, total bilirubin and total bile acid.

disease [14]. In addition, a large of laboratory tests associated with APALI were found in laboratory such as heme oxygenase start factor and lipid oxygen element A4 [15,16]. Nonetheless, those laboratory tests are rarely used in our clinical practice. In this study, our research showed that RDW, as easily available and affordable laboratory tests, was associate with outcomes of APALI in patients with AP.

Clinically the AP ranges from a mild form, edema and necrosis of the parenchyma, to severe AP involving a systemic inflammatory response syndrome, multi-organ failure including APALI. Although, the pathophysiologic mechanisms for the relationship between high RDW and APALI still remains unknown, the systemic inflammatory response probably help to explain the potentially association between RDW and APALI. Several studies [17-22] have shown that vascular endothelial cells, lymphocytes, neutrophils, macrophages were activated when pancreatic

acinar cell was damaged in early phase, releasing a large of inflammatory cytokine such as phospholipase, protease, elastase, tumor necrosis factor, nitric oxide, oxide enzyme, interleukin-6 (IL-6) and interleukin-8 (IL-8) etc. What is important is that oxidative stress and MAP kinase expands inflammatory response induced by inflammation factors, contributing to damage of pulmonary capillaries and alveolar epithelial cell through various channels. As a result, systemic inflammation impacts bone marrow function and iron metabolism, and inflammatory cytokines inhibits erythrocyte maturation, leading to newer, larger reticulocytes into the blood circulation, which is relevant with RDW increase [23], in addition, increased oxidative stress is able to increase RDW by reducing RBC survival and releasing large premature RBC into the circulation. Besides inflammation alters the ion channels and

glycoproteins of RBC membrane, which contributes to the change of RBC morphology and increases RDW [24,25].

Our study has several limitations. Initially, our study was limited by the smaller samples for patients, the large-scale investigations should be further performed in future work, additionally, the samples were collected and measured from a single laboratory, leading to the values of RDW that may have been slightly different in the different races and regions. However, our study demonstrate that RDW at admission is associated with APALI and should be considered as an underlying risk factor of APALI, AP patients with high RDW levels at admission should be additional concerned by clinicians to alert APAIL.

Conflict of interest: The authors state that they have no conflicts of interest.

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