

Original Article

Red blood cell distribution width as a prognostic biomarker for mortality in traumatic brain injury

Biao Zhang, Jin Zhao

Department of Critical Care Medicine, Suzhou Integrated Chinese and Western Medicine Hospital, Suzhou, Jiangsu, China

Received June 22, 2015; Accepted September 18, 2015; Epub October 15, 2015; Published October 30, 2015

Abstract: *Objective:* Traumatic brain injury (TBI) often cause morbidity and mortality, but it is hard to obtain predictive biomarkers. Red blood cell distribution width (RDW) has been reported as a biomarker in cardiovascular disease. But it is unknown whether RDW is associated with the mortality of TBI patients. The aim of this study is to identify whether RDW is a prognostic biomarker for TBI mortality. *Methods:* A total of 122 patients with TBI were included retrospectively. Patients were divided into Survival Group and Non-survival Group, RDW was compared between 2 groups. Receiver Operating Curve (ROC) was used to evaluate the mortality predictive performances. *Results:* 122 patients were included, the male-female ratio was 2.59 (88/34) with their median age of 49.5 (17-89) years. 13 (11.93%) of them were divided into Non-survival Group. We observed significant difference in RDW between two groups ($P < 0.05$). The cut-off level for RDW in TBI was ≥ 12.85 , with the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were 65.4%, 95.7%, 69.7%, 82.6%, respectively; and area under the curve was 0.805 (95% confidence interval [CI]: 0.703-0.906). *Conclusions:* Red cell distribution width is a predictor of mortality in patients with TBI.

Keywords: Traumatic brain injury, red blood cell distribution width, prognostic biomarker, mortality, glasgow coma scale scores

Introduction

Traumatic brain injury (TBI) causes worldwide concern, as one of the leading causes of mortality and morbidity, continued. In case of an urgent concern or emergency, especially in young and older adults [1]. However, few biomarkers were reported in clinical practice when evaluating the brain damage. Recent researchers found that protein S-100 beta (β), neuron-specific enolase (NSE), glial fibrillary acidic protein (GFAP) and myelin basic protein (MBP) etc. could be used as promising markers of TBI [2-6]. However, considering the convenience and operability of clinical practice, none of these could be easy and widely used prognostic biomarkers for TBI mortality evaluating.

Complete blood count is a laboratory test widely used in clinical practice and comprises. As a part of the complete blood count, red cell distribution width (RDW) is often used to differentiate the etiology of anemia [7]. Previous studies

have indicated that the RDW was associated with mortality and other severe adverse outcomes of cardiovascular disease [8], severe acute pancreatitis (SAP) [9] and many other diseases [10, 11]. Recent study exhibits that RDW may be a prognostic biomarker for mortality even for the general population [12]. These researches inspired us to explore whether RDW could be used as a prognostic biomarker for mortality in traumatic brain injury. In this study, we retrospectively analyzed the RDW in traumatic brain injury patients.

Methods

Collected data

The primary endpoint of this retrospective study was 28-day mortality. According to survival or death results, patients were divided into two groups: Survival Group and Non-survival Group. RDW was compared between two groups. The values of RDW in predicting mortality was eval-

Red blood cell distribution width prognostic traumatic brain injury

Table 1. Demographic and clinical characteristics between two groups

	Survival Group (n = 113)	Non-survival Group (n = 13)	P value
Age	49 (36-63)	63 (34-83)	0.054
Hematocrit	38.9 (36.1-41.3)	35.4 (31.6-41.3)	0.120
Hemoglobin (g/L)	135 (125-148)	138 (129-147)	0.718
RDW (%)	12.1 (11.8-12.7)	12.9 (12.45-13.45)	0.00
GCS scores	14 (14-15)	4 (3.5-12)	0.00

Data are presented as median value (interquartile range).

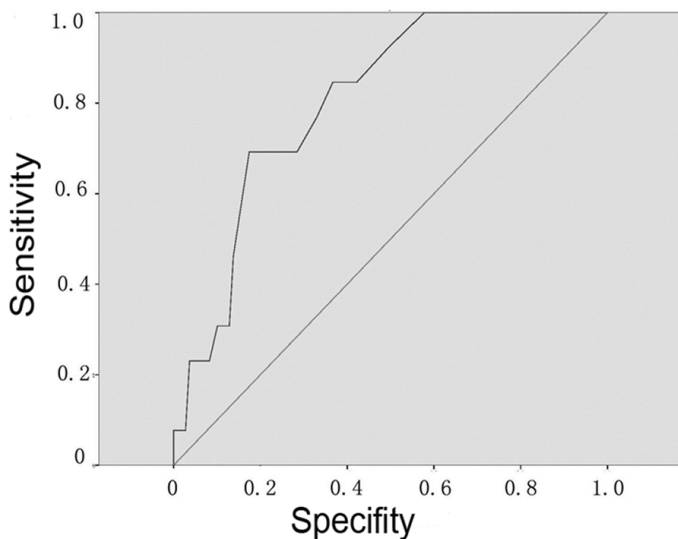


Figure 1. Receiver operating characteristics curve of the RDW.

Table 2. Sensitivity, specificity, +LR, -LR, PPV and NPV of RDW

RDW	Sensitivity	Specificity	+LR	-LR	PPV	NPV
> 12.85%	65.4	95.7	8.13	0.76	69.2%	82.6%

uated by Receiver Operating Curve. Patients with traumatic brain injury were included from the Suzhou Integrated Chinese and Western Medicine Hospital between January 2013 and June 2013. Traumatic brain injury diagnosis was based on the American Congress of Rehabilitation Medicine TBI criteria [13]; patients with age of over 16 years were included. Patients with severe multiple injury, visceral hemorrhage, anemia, cardiovascular disease or with incomplete medical record were excluded. The information recorded includes demographics, etiology, Glasgow Coma Scale (GCS) scores and the 28-day mortality. The following laboratory measurements were obtained from each patient record on admission: RDW, Hemoglobin (Hb), and Hematocrit (Hct).

Statistical analysis

The collected data were found to be non-normally distributed. Accordingly, all data are presented as median value (interquartile range), with non-parametric analyses being used to assess groups' differences. Univariate analysis was performed using the Mann-Whitney U test and χ^2 test when appropriate. We measured the prognostic performance of the variables, receiver operating characteristic curves was used to calculate sensitivity and specificity; cutoff values were used for positive predictive value (PPV) and negative predictive value. Statistical analyses were performed with SPSS 19.0 software for Windows (SPSS, Chicago, IL, USA). *p* value < 0.05 is considered to indicate statistical significance.

Results

A total of 122 patients with TBI were included. There were 34 male and 88 female, with a median age of 49.5 (17-89) years old. 13 (11.93%) patients were divided into Non-survival Group and the others were included in survival group. The baseline characteristics of Hb and Hct have no significant difference between two groups ($P > 0.05$). While their RDW and GCS scores have statistical difference ($P < 0.05$, **Table 1**). ROC curves of RDW levels were used to identify non-survivors on a statistically significant level (area under the curve of 0.805; 95% confidence interval [CI], 0.703-0.906). As shown in **Figure 1** the best cut-off level for RDW in TBI was 12.58%, (**Figure 1**). RDW in the diagnosis of TBI mortality had a sensitivity of 65.4% and a specificity of 95.7%. Their +LR, -LR, PPV and NPV of RDW for mortality in TBI could be seen **Table 2**.

Discussion

In this study, we observed a significant increase of RDW in the non-survival group compared with survival group for TBI patients. The cutoff of 12.85% in ROC curve showed that RDW is a specific but not a sensitive biomarker for diagnosis of TBI mortality (sensitivity 65.4%, speci-

ficity 95.7%). The NPV in RDW was as high as 82.6%. However, there were many inconsistent with other reports. Kazim Şenol et al. [9] reported that with a cutoff value of 14.8 for RDW, mortality could be correctly predicted, RDW in non-survivors with median value of 15.6 and interquartile range of 14 to 21, but we found the median value in non-survivors was 12.9 and interquartile range were 12.45 to 13.45 for RDW, the largest RDW value of non-survival group was 15.6 (The expected RDW values in our laboratory ranged between 11.4% and 14.3%). In contrast, Chizobam et al. demonstrated that mean RDW was significantly higher among persons with stroke compared to individuals without a stroke (13.7% (12.75-13.9), 13.2%, $P < 0.001$) [11]. To our knowledge, there was few studies investigated the value of RDW in patients with TBI. Most studies investigated the value of RDW in anemia [7], cardiovascular disease [8], SAP [9], acute appendicitis [14] and other disease [10, 11], none of these study involved in patients with TBI, it is hard to obtain valid reference values from these studies.

Considering the small sample size of the non-survival group, and no similar research data could be referred, there were several limitations in present study: as a single-center study, only 13 patients were enrolled in the non-survival group; there was no comparison with other assessment indicators for survival analysis, this also makes credibility of our study Limited. In the further study, we hope more large multi-center studies could be performed to resolve these limitations. In conclusion, RDW might be a strong specificity prognostic biomarker for TBI mortality. Clinicians should pay more attention to the RDW level during their assessments of patients with TBI.

Ethics and dissemination

The Ethics Committee of Suzhou Integrated Chinese and Western Medicine Hospital approved the consent and the procedure of this study.

Disclosure of conflict of interest

None.

Abbreviations

TBI, Traumatic brain injury; NSE, Neuron-specific enolase; GFAP, Glial fibrillary acidic protein; MBP, Myelin basic protein; RDW, Red blood cell

distribution width; Hb, Hemoglobin; Hct, Hematocrit; GCS, Glasgow Coma Scale; ROC, Receiver Operating Curve; RBC, Red Blood Cell; PPV, Positive predictive value; NPV, Negative predictive value; +LR, Positive likelihood ratio; -LR, Negative likelihood ratio; SAP, Severe acute pancreatitis.

Address correspondence to: Dr. Jin Zhao, Department of Critical Care Medicine, Suzhou Integrated Chinese and Western Medicine Hospital, No. 39 Xiashatang Road, Mudu, Suzhou, Jiangsu Province, PR China. Tel: +8618962113305; E-mail: zhaojch@163.com

References

- [1] Roozenbeek B, Maas AI and Menon DK. Changing patterns in the epidemiology of traumatic brain injury. *Nat Rev Neurol* 2013; 9: 231-236.
- [2] Kövesdi E, Lückl J, Bukovics P, Farkas O, Pál J, Czeiter E, Szellár D, Dóczy T, Komoly S and Büki A. Update on protein biomarkers in traumatic brain injury with emphasis on clinical use in adults and pediatrics. *Acta Neurochirurgica* 2010; 152: 1-17.
- [3] Ondruschka B, Pohlers D, Sommer G, Schober K, Teupser D, Franke H and Dressler J. S100B and NSE as Useful Postmortem Biochemical Markers of Traumatic Brain Injury in Autopsy Cases. *J Neurotrauma* 2013; 30: 1862-71.
- [4] Böhmer AE, Oses JP, Schmidt AP, Perón CS, Krebs CL, Oppitz PP, D'Avila TT, Souza DO, Portela LV and Stefani MA. Neuron-specific enolase, S100B, and glial fibrillary acidic protein levels as outcome predictors in patients with severe traumatic brain injury. *Neurosurgery* 2011; 68: 1624-1631.
- [5] Berger RP, Adelson PD, Pierce MC, Dulani T, Cassidy LD and Kochanek PM. Serum neuron-specific enolase, S100B, and myelin basic protein concentrations after inflicted and noninflicted traumatic brain injury in children. *J Neurosurg* 2005; 103: 61-68.
- [6] Demir A, Kavalci C, Yilmaz MS, Yilmaz F, Durdu T, Ceyhan MA, Alagoz F and Yel C. The value of Serum BNP for diagnosis of intracranial injury in minor head trauma. *World J Emerg Surg* 2014; 9: 16.
- [7] Aslan D, Gümrük F, Gürgey A and Altay C. Importance of RDW value in differential diagnosis of hypochrome anemias. *Am J Hematol* 2002; 69: 31-33.
- [8] Kimmenade RR, Mohammed AA, Uthamalingam S, Meer P, Felker GM and Januzzi JL. Red blood cell distribution width and 1-year mortality in acute heart failure. *Eur J Heart Fail* 2010; 12: 129-136.

Red blood cell distribution width prognostic traumatic brain injury

- [9] Şenol K, Saylam B, Kocaay F and Tez M. Red cell distribution width as a predictor of mortality in acute pancreatitis. *Am J Emerg Med* 2013; 31: 687-689.
- [10] Bazick HS, Chang D, Mahadevappa K, Gibbons FK and Christopher KB. Red cell distribution width and all-cause mortality in critically ill patients. *Crit Care Med* 2011; 39: 1913-1921.
- [11] Ani C and Ovbiagele B. Elevated red blood cell distribution width predicts mortality in persons with known stroke. *J Neurol Sci* 2009; 277: 103-108.
- [12] Perlstein TS, Weuve J, Pfeffer MA and Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort. *Arch Inter Med* 2009; 169: 588-594.
- [13] Terrio H, Brenner LA, Ivins BJ, Cho JM, Helmick K, Schwab K, Scally K, Bretthauer R and Warden D. Traumatic brain injury screening: preliminary findings in a US Army Brigade Combat Team. *J Head Trauma Rehabil* 2009; 24: 14-23.
- [14] Narci H, Turk E, Karagulle E, Togan T and Karabulut K. The role of red cell distribution width in the diagnosis of acute appendicitis: a retrospective case-controlled study. *World J Emerg Surg* 2013; 8: 46.