

Research Article

The Combination of Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio on Admission was an Independent Predictor for Post-traumatic SIRS

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Abstract

Background: Posttraumatic Systemic Inflammatory Response Syndrome (SIRS) was a common trauma-related complication with increased mortality. Numbers of studies has been conducted to discover alarming factors for posttraumatic SIRS. In this study, we evaluate the predictive value of Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR) and combination of NLR and PLR(CNP) for posttraumatic SIRS.

Methods: A total of 285 traumatic patients were involved. The NLR and PLR on admission were separately calculated by dividing absolute neutrophil count or platelet count by the lymphocyte count. Receiver Operating Characteristic (ROC) curves and the optimum cut-off point for NLR and PLR were got. The CNP was calculated and a CNP value of 2 denoted that both NLR and PLR were beyond the optimum cut-off point. All statistical analyses were performed by using PASW Statistics 18.0.

Results: 102 of the 285 traumatic patients (35.79%) were diagnosed with post-traumatic SIRS. The NLR and PLR were significantly higher in patients with post-traumatic SIRS than in traumatic patients without SIRS (NLR: 23.07 ± 12.30 VS. 12.15 ± 9.05 ; PLR: 271.62 ± 135.64 vs. 180.08 ± 113.76). CNP value of 2, WBC, neutrophil count, NLR and the interval between injury and blood analysis were independently predictive of the risk of posttraumatic SIRS. CNP was a much better predictive parameter than WBC, neutrophil count and NLR (OR=3.268 vs. 1.101 or 1.090 or 1.059).

Conclusion: Compared with WBC count and NLR, CNP on admission was a better predictor for posttraumatic SIRS.

Keywords: Combination of NLR and PLR; NLR; PLR; SIRS; Trauma

MODS : Multiple organ dysfunction syndrome

OR : Odds ratio

CI : Confidence interval

ROC : Receiver operating characteristic curves

AUC : Area under curve

Abbreviations

NLR : Neutrophil lymphocyte ratio

PLR : Platelet lymphocyte ratio

CNP : Combination of NLR and PLR

WBC : White blood cell count

SIRS : Systemic inflammatory response syndrome

Introduction

Traumatic injuries are becoming an increasingly prevalent cause of death especially in less developed countries [1].

Systemic inflammatory response syndrome (SIRS), a potentially life-threatening trauma-related complication characterized by tremendous inflammatory response, is found in about 30% of trauma patients [2,3]. It was demonstrated that post-traumatic SIRS was significantly associated with increased infection and Multiple Organ Dysfunction Syndrome (MODS) and increased mortality [2,4]. In the past decades, a variety of biomarkers and scoring system have been explored in the prediction for SIRS and other complications, such as IL-6, the mitochondrial DNA (mt DNA) and the Boehme's score system [5,6]. But few of them have been routinely used in practice partially because of relatively poor clinical practicality. Thus, it is worthy of making full use of existed clinical tests to obtain a simple and useful predictor for SIRS.

Routine whole blood assay is one of the most common examinations in clinic and White Blood Cell Count (WBC) has long been used for the assessment of SIRS [7]. Some investigators also conducted trials to evaluate the predictive value of subtypes of leukocyte to improve the predictive ability [8,9]. Recently, there are increasing interests in evaluating the prediction ability of the Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) in systemic inflammatory response in chronic diseases [10,11]. Some other studies showed that the combination of NLR and PLR (CNP) might be a better predictor [12]. Nonetheless, the prediction value of CNP for SIRS in trauma patients was not well understood and we conducted this study to evaluate the potent capacity of CNP for predicting SIRS in traumatic patients.

Patients and Methods

Patients

This present study was approved by Jingling Hospital's Institutional Review Committee on Human Research. A total of 285 eligible patients that were admitted for hospitalization at the Department of Emergency, Jinling Hospital in Nanjing China because of acute trauma from December 2016 to April 2018 were recruited for this study. The exclusion criteria were as follows: 1) younger than 18 years or older than 80 years old; 2) the first recorded routine blood assay after hospital admission was taken beyond 24 hours since the occurrence of trauma; 3) essential data could not be obtained; 4) any of the following concomitant situation: pregnancy, uncured malignant disease, acute ischemic stroke, immunomodulation drug using, chronic renal failure, liver cirrhosis, diagnosis of SIRS or infection at admission.

Clinical Assessment and Data Collection

Patients' demographic data were recorded at admission. Medical records including the Injury Severity Score (ISS), the length of ICU stay and the length of hospital stay were recorded at the discharge. Data on blood cell counts were extracted in a retrospective fashion from the electronic medical records database. All patients received daily examination of body temperature, heart rate and respiratory rate. Patients were diagnosed with SIRS if they meet at least two of the following concurrent conditions: 1) a body temperature $<36^{\circ}\text{C}$ or $>38^{\circ}\text{C}$; 2) a heart rate $> 90/\text{min}$, 3) a

respiratory rate $> 20/\text{min}$ or $\text{aPaCO}_2 < 32 \text{ mmHg}$; 4) a white blood cell count (WBC) $< 4000/\text{mm}^3$ or $> 12000/\text{mm}^3$. No standardized treatment protocol was routinely requested in the present study because of its nature as observational research.

NLR, PLR and CNP evaluation

The NLR was defined as the ratio of absolute neutrophil count divided to the absolute lymphocyte count and PLR was defined as the ratio of absolute platelet count to the absolute lymphocyte count. The data of the absolute neutrophil count and the absolute lymphocyte count were obtained from the first routine blood assay on the day of admission. Receiver operating characteristic (ROC) curves for the prediction of SIRS were separately plotted to verify the optimum cut-off point for NLR and PLR. As shown in Figure 1, the optimum cut-off values for NLR and PLR were 16.5617 and 238.9394, respectively. The CNP was calculated as follows: CNP=2: both an elevated NLR (over 16.5617) and an elevated PLR (over 238.9394); CNP=1: either an elevated NLR or an elevated PLR; CNP=0: neither an elevated NLR nor an elevated PLR = 0.

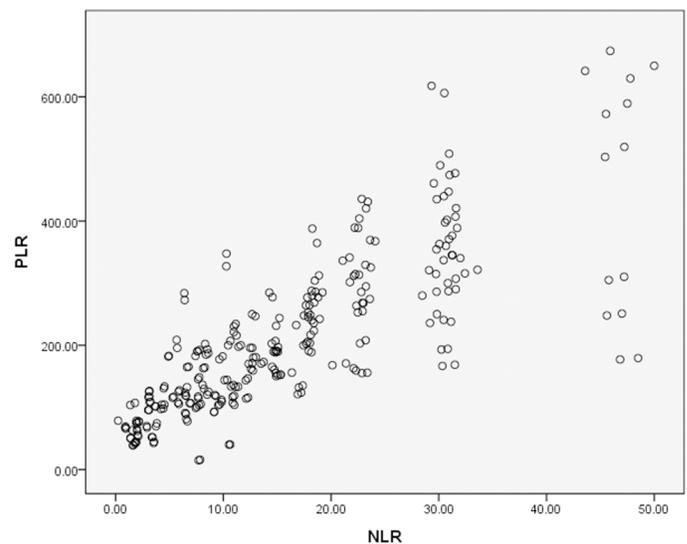


Figure 1: Correlation between NLR and PLR. The NLR and PLR were positively related and the Pearson Correlation was 0.802.

Statistical Analysis

All statistical analyses were performed by using PASW Statistics 18.0 (IBM Corporation, Armonk, NY, USA). Data were presented as the mean \pm SD and absolute numbers (percentages). The test of normality was performed in age, ISS score, hospital stay duration, ICU stay duration, interval between injury and blood analysis, platelet count, white blood cell count, lymphocyte count, neutrophil count, PLR, NLR and CRP. Receiver operating characteristics curves (ROC) and associated areas under the curve (AUCs) with 95% CIs were constructed for potential predictors and the optimum cut-off point for NLR and PLR were obtained. After the calculation of CNP, a stepwise logistic regression analysis was

performed to identify factors with potential independent predictive value for the risk of post-traumatic SIRS.

Results

Patient Characteristics

A total of 285 traumatic patients (213 males; age 45.95±14.58 years) were recruited in this study. 102 of the 285 patients (35.79%) were diagnosed with post-traumatic SIRS during hospital stay. The baseline characteristics of the included patients are presented in Table 1. Traffic accident counted for over 67% of all the causes of injury. Only two patients who were diagnosed with post-traumatic SIRS died during the hospital. The overall mean length of stay in hospital and ICU was respectively 14.04 and 6.26 days. The overall mean interval between the occurrence of injury and the first routine blood analysis was 6.62 hours and no statistically significant difference was found between these two groups. The percentage of male patients, the ISS score, the duration of ICU stay, WBC, NLR and PLR were significantly higher in patients with post-traumatic SIRS than those without post-traumatic SIRS. As there was no significant difference in the interval between the injury and the first routine blood analysis between these two groups, it did not cause bias in this issue.

	None-SIRS (183)	SIRS (102)	Total (285)	p-value
Age, year	45.34±15.50	47.04±14.01	45.95±14.58	0.361*
Male/Female	129 /54	84 /18	213/72	0.034 [§]
Mechanism of injury				
Traffic accident	116 (63.39%)	75 (73.53%)	191 (67.02%)	0.176 [§]
Falling accident	31 (16.94%)	14 (13.73%)	45 (15.79%)	0.666 [§]
Fighting	25 (13.67%)	9 (8.82%)	34 (11.93%)	0.460 [§]
Other	11 (6.01%)	4 (3.92%)	15 (5.26%)	0.720 [§]
ISS score	17.8±10.9	23.6±12.5	19.8±11.8	0.017*
Length of hospital stay, days	13.24±8.03	15.47±11.39	14.04±9.42	0.087 [#]
Length of ICU stay, days	5.08±6.60	8.35±7.97	6.26±7.28	<0.001 [#]
Interval between injury and blood analysis, hours	6.13±6.09	7.51±6.74	6.62±6.36	0.079*
WBC, × 10 ⁹ /L	13.17±5.12	16.36±4.67	14.32±5.19	<0.001*
CRP, mg/L	12.37±22.18	14.15±21.54	13.01±20.51	0.590*
NLR	12.15±9.05	23.07±12.30	16.06±11.57	<0.001 [#]
PLR	180.08±113.76	271.62±135.64	212.84±129.50	<0.001 [#]
CNP score				
0	129 (70.5%)	26 (25.5%)	155 (54.4%)	<0.001 [§]
1	24 (13.1%)	15 (14.7%)	39 (13.7%)	0.835 [§]
2	30 (16.4%)	61 (50.8%)	91 (31.9%)	<0.001 [§]

NOTE: Data are presented by mean±SD or n (percentage).

*One-way analysis of variance (ANOVA)

[§]Chi-square test

[#]Kolmogorov-Smirnov test

Table 1: Baseline characteristics of study groups.

NLR, PLR and CNP in Patients

The NLR and PLR were significantly higher in post-traumatic SIRS patients than in patients without SIRS (NLR: 23.07±12.30 vs. 12.15±9.05; PLR: 271.62±135.64 vs. 180.08±113.76). As shown in (Figure 1), the NLR and PLR were positively related. As shown in ROC curve (Figure 2), the Area Under Curve (AUC) was separately 0.762 for NLR and 0.722 for PLR. The optimal cutoff

point for NLR was 16.5617 with a sensitivity of 0.725 and a specificity of 0.743. The optimal cutoff point for PLR was 238.9394 with a sensitivity of 0.618 and a specificity of 0.798. Based on this, the NLR of 121 patients and the PLR of 100 patients was separately beyond their cutoff value. The CNP was calculated and the percentage of patients with a score of 2 was significantly higher in patients with posttraumatic SIRS than those without SIRS (50.8% vs. 16.4%, $p < 0.001$). There was no significant difference in a CNP score of 1 between posttraumatic SIRS patients and none-SIRS patients.

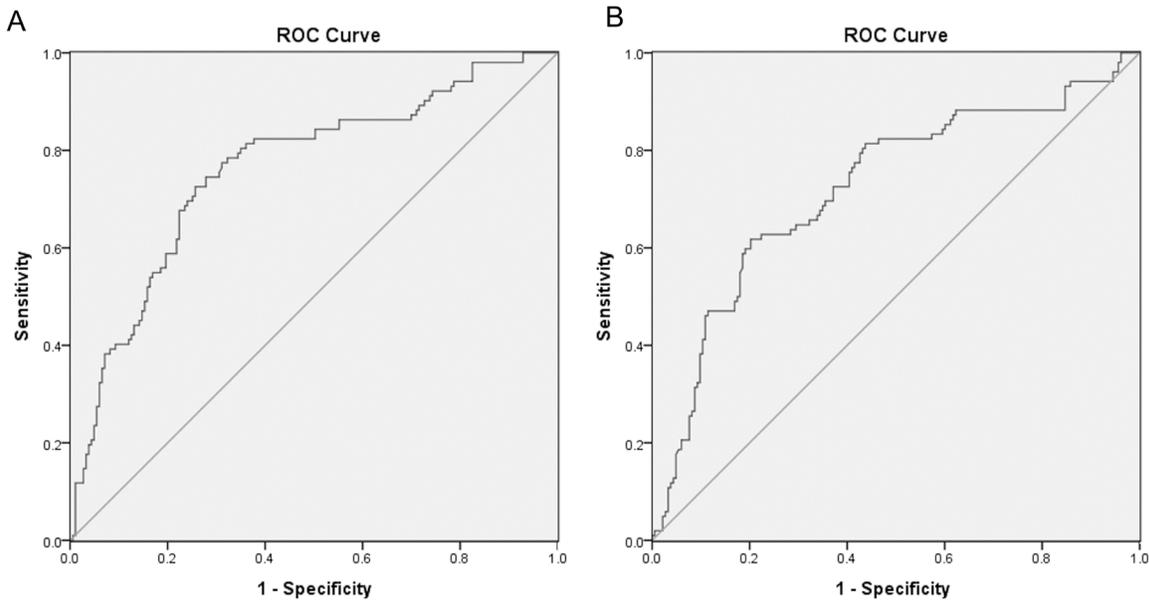


Figure 2: ROCs for NLR (A) and PLR (B).

CNP and Posttraumatic SIRS

As WBC, CRP, count of neutrophil, platelet and lymphocyte, PLR and NLR might be associated with posttraumatic SIRS, we further performed logistic regression analysis to compare those various factors. Among the factors used in the logistic regression (i.e., age, sex, ISS, interval between injury and blood analysis, WBC, CRP, neutrophil count, platelet count, lymphocyte count PLR and NLR), only CNP value of 2, WBC, neutrophil count, lymphocyte count, NLR and the interval between injury and blood analysis were independently predictive of the risk of posttraumatic SIRS. The OR of CNP value of 2 was much bigger than any other three parameters (3.268 vs. 1.101, 1.090, 1.498, 1.059 or 1.060). Other parameters including age, sex, ISS, CRP, platelet count and PLR on admission were not statistically associated with posttraumatic SIRS, Table 2.

Variables	OR	95% C.I.		p-value
		Lower	Upper	
Male	1.823	0.885	3.757	0.103
Age	1.013	0.992	1.035	0.219
ISS	1.877	0.869	4.368	0.087
Interval time	1.060	1.011	1.112	0.016*
WBC	1.101	1.036	1.149	0.002*
CRP	0.989	0.974	1.005	0.177
PLT	0.999	0.988	1.010	0.803
Neutrophil	1.090	1.015	1.170	0.017*
Lymphocyte	1.498	1.036	2.166	0.032*

PLR	0.998	0.993	1.003	0.395
NLR	1.059	1.005	1.116	0.033*
CNP				
CNP=1	1.066	0.514	4.410	0.455
CNP=2	3.268	1.447	8.499	0.004*
NOTE: *p<0.05 was considered as significant. OR: Odds ratio; CI: Confidence interval				

Table 2: Results of logistic regression analysis.

Discussion

This present study demonstrated that WBC, NLR, PLR and CNP were significantly higher in post-traumatic SIRS patients than in traumatic patients without SIRS and CNP was a much better independent predictor of posttraumatic SIRS. To the best of our knowledge, this is the first study investigating the potential predictive value of CNP on admission for posttraumatic SIRS.

Systemic Inflammatory Response Syndrome (SIRS) was one of the common complications of trauma and has been considered as a remarkable predictor of outcomes in trauma [13]. Traumatic patients might develop SIRS even 3 weeks or later after the initial of injury. It was indicated that posttraumatic SIRS was associated with higher mortality, higher rate of nosocomial infection and longer hospital stay [13,14]. In this sense, it is quite meaningful and helpful to recognize high risk patients for posttraumatic SIRS by exploring certain parameters or biomarkers. In this study, it was shown that the WBC, neutrophil count, lymphocyte count, NLR and PLR on admission were remarkably elevated. Receiver operating characteristic curves (ROC) for NLR showed that the Area Under Curve (AUC) was 0.762 and the optimal cutoff point was 16.5617 with a sensitivity of 0.725 and a specificity of 0.743. And the AUC for PLR was 0.722 and the optimal cutoff point for PLR was 238.9394 with a sensitivity of 0.618 and a specificity of 0.798. Logistic analysis showed that NLR was independently associated with increased risk of post-traumatic SIRS (OR= 1.059, 95% CI= 1.005 - 1.116). Neutrophils were activated following trauma and contributed to succeeding inflammation and organ dysfunction like lung injury and gut injury [15]. Platelet, an effector of both thrombosis and inflammation was also activated following trauma [16]. Previous studies indicated that platelet might interact with neutrophil and contribute to increased neutrophil activity [17]. A fall in total lymphocyte and change of CD4+/CD8+ T cell subset were also found to be associated with organ dysfunction in trauma patients [16,18]. Thus, NLR and PLR might be a reliable index for both inflammation and immunosuppression.

CNP was a new index for systemic inflammation and it has been proved to be associated with outcomes in diverse diseases like lung cancer [12], esophageal squamous cell carcinoma and myocardial infarction. It seems that CNP was an index for both chronic and acute inflammation. In our study, it was shown that

the AUCs for NLR and PLR were quite closed but the NLR got a better sensitivity while the PLR got a better specificity. In this sense, the combination of NLR and PLR (CNP) should be much better than a separated one. It was shown that patients with a CNP score of 2 was much easier to develop posttraumatic SIRS. Further logistic analysis also indicated that CNP was an independent risk factor for posttraumatic SIRS. A CNP value of 2 was an extremely high-risky maker of posttraumatic SIRS with an OR of 3.268.

Except for posttraumatic SIRS, some other studies also indicated that lymphocytosis and increased WBC in trauma patients was associated with significantly higher death rate and ISS [19]. NLR is also associated with mortality in patients with critically ill trauma [20] and severe traumatic brain injury [21]. Since the mortality in this study is relatively low and is not applicable for further analysis, we failed to investigate the prognostic role of CNP in trauma patients. And the number of involved patients was relatively small, and we did not evaluate the early dynamic change of CNP in the prediction of posttraumatic SIRS. Further prospective study in this field is needed.

Conclusion

In conclusion, it was indicated that NLR and CNP on admission were positively related and WBC, neutrophil count and lymphocyte count NLR and CNP on admission were independently associated with posttraumatic SIRS. CNP was a predictor for posttraumatic SIRS with an OR of 3.268 which was bigger than other index.

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Conflict of Interest

We declare that no economic interest or any conflict of interest exists.

References

1. Vecino-Ortiz AI, Jafri A, Hyder AA (2018) Effective interventions for unintentional injuries: a systematic review and mortality impact assessment among the poorest billion. *The Lancet. Global health* 6: e523-e534.

2. Bochicchio GV, Napolitano LM, Joshi M, Knorr K, Tracy JK, et al. (2002) Persistent systemic inflammatory response syndrome is predictive of nosocomial infection in trauma. *The Journal of trauma* 53: 245-250.
3. Malone DL, Kuhls D, Napolitano LM, McCarter R, Scalea T (2001) Back to basics: validation of the admission systemic inflammatory response syndrome score in predicting outcome in trauma. *The Journal of trauma* 51: 458-463.
4. Bochicchio GV, Napolitano LM, Joshi M, McCarter RJ Jr, Scalea TM (2001) Systemic inflammatory response syndrome score at admission independently predicts infection in blunt trauma patients. *The Journal of trauma* 50: 817-820.
5. Gu X, Yao Y, Wu G, Lv T, Luo L, et al. (2013) The plasma mitochondrial DNA is an independent predictor for post-traumatic systemic inflammatory response syndrome. *PLoS one* 8: e72834.
6. Sapan HB, Paturusi I, Jusuf I, Patellongi I, Massi MN, et al. (2016) Pattern of cytokine (IL-6 and IL-10) level as inflammation and anti-inflammation mediator of multiple organ dysfunction syndrome (MODS) in polytrauma. *International journal of burns and trauma* 6: 37-43.
7. Chang DC, Cornwell EE, 3rd, Phillips J, Paradise J, Campbell K (2003) Early leukocytosis in trauma patients: what difference does it make? *Current surgery* 60: 632-635.
8. Heffernan DS, Monaghan SF, Thakkar RK, Machan JT, Cioffi WG, et al. (2012) Failure to normalize lymphopenia following trauma is associated with increased mortality, independent of the leukocytosis pattern. *Critical care* 16: R12.
9. Gouel-Cheron A, Venet F, Allaouchiche B, Monneret G (2012) CD4+ T-lymphocyte alterations in trauma patients. *Critical care* 16: 432.
10. Yao Y, Yuan D, Liu H, Gu X, Song Y (2013) Pretreatment neutrophil to lymphocyte ratio is associated with response to therapy and prognosis of advanced non-small cell lung cancer patients treated with first-line platinum-based chemotherapy. *Cancer immunology, immunotherapy: CII* 62: 471-479.
11. Wang SC, Chou JF, Strong VE, Brennan MF, Capanu M, et al. (2016) Pretreatment Neutrophil to Lymphocyte Ratio Independently Predicts Disease-specific Survival in Resectable Gastroesophageal Junction and Gastric Adenocarcinoma. *Annals of surgery* 263: 292-297.
12. Wu G, Yao Y, Bai C, Zeng J, Shi D, et al. (2015) Combination of platelet to lymphocyte ratio and neutrophil to lymphocyte ratio is a useful prognostic factor in advanced non-small cell lung cancer patients. *Thoracic cancer* 6: 275-287.
13. Jacome T, Tatum D (2018) Systemic Inflammatory Response Syndrome (SIRS) Score Independently Predicts Poor Outcome in Isolated Traumatic Brain Injury. *Neurocritical care* 28: 110-116.
14. Easton R, Balogh ZJ (2014) Peri-operative changes in serum immune markers after trauma: a systematic review. *Injury* 45: 934-941.
15. Xu J, Guardado J, Hoffman R, Xu H, Namas R, et al. (2017) IL33-mediated ILC2 activation and neutrophil IL5 production in the lung response after severe trauma: A reverse translation study from a human cohort to a mouse trauma model. *PLoS medicine* 14: e1002365.
16. Morris RS, Schaffer BS, Lundy JB, Pidcoke HF, Chung KK, et al. (2018) Immunopathological response to severe injury: platelet activation and the Th-17 immune response. *Blood coagulation & fibrinolysis: an international journal in haemostasis and thrombosis* 29: 48-54.
17. Soehnlein O (2018) Decision shaping neutrophil-platelet interplay in inflammation: From physiology to intervention. *European journal of clinical investigation* 48.
18. Manson J, Cole E, De'Ath HD, Vulliamy P, Meier U, et al. (2016) Early changes within the lymphocyte population are associated with the development of multiple organ dysfunction syndrome in trauma patients. *Critical care* 20: 176.
19. Pinkerton PH, McLellan BA, Quantz MC, Robinson JB (1989) Acute lymphocytosis after trauma--early recognition of the high-risk patient? *The Journal of trauma* 29: 749-751.
20. Dilektasli E, Inaba K, Haltmeier T, Wong MD, Clark D, et al. (2016) The prognostic value of neutrophil-to-lymphocyte ratio on mortality in critically ill trauma patients. *The journal of trauma and acute care surgery* 81: 882-888.
21. Chen W, Yang J, Li B, Peng G, Li T, et al. (2018) Neutrophil to Lymphocyte Ratio as a Novel Predictor of Outcome in Patients with Severe Traumatic Brain Injury. *The Journal of head trauma rehabilitation* 33: E53-E59.