A STUDY ON THE MORTALITY PROGNOSTIC VALUE OF NEUTROPHIL TO LYMPHOCYTE RATIO AT ADMISSION IN POLYTRAUMA PATIENTS

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Abstract

Objectives: To evaluate the mortality prognostic value of neutrophil/lymphocyte ratio (NLR) at admission in patients with polytrauma. ***Methods:*** A retrospective, descriptive study on 196 polytrauma patients diagnosed using the criterion of the Berlin Consensus 2014, treated at Military Hospital 103 from June 2020 to June 2023. Severity was assessed based on ISS scales, and NLR was calculated at admission prior to any treatment intervention. ***Results:*** Polytrauma predominantly affected males (80.1%) aged between 20 and 59, polytrauma cases were primarily attributed to traffic accidents (66.8%). The group experiencing mortality exhibited lower Glasgow scores, Revised Trauma Score (RTS) at admission, and length of hospital stay compared to the survival group. Additionally, the mortality group demonstrated a higher Injury Severity Score (ISS), lactate level, INR, and aPTT scores, all statistically significant. The NLR value at admission demonstrated predictive value for mortality in polytrauma patients, with an AUC of 0.724, a cut-off of 10.8, sensitivity of 80%, and specificity of 67.2%. ***Conclusion:*** Polytrauma predominantly affected working-age males, with traffic accidents being the primary cause. The NLR value at admission emerges as a meaningful predictor of mortality in polytrauma patients.

Keywords: Polytrauma; Mortality prognosis; Neutrophil to lymphocyte ratio.

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INTRODUCTION

Polytrauma stands as the primary cause of severe complications and fatalities among trauma patients. It is defined as a condition wherein a patient sustains two or more severe injuries in distinct body regions or organ systems, with at least one injury, or a combination thereof, posing a life-threatening risk.

The pathophysiological cascade following polytrauma, traumatic shock, and severe trauma typically involves the activation of immune function cells. This process triggers the release of pro-inflammatory and anti-inflammatory chemical mediators at both local and systemic levels, culminating in a systemic inflammatory response syndrome (SIRS), where leukocytes play a pivotal role. Notably, neutrophils, the primary contributors to this mechanism, undergo an increase in both quantity and functional differentiation in response to the severity of the injury. This robust immune cell response occurs promptly post-injury. Conversely, lymphocytes, adaptive immune cells, require time to differentiate and proliferate after receiving activation signals and antigen presentation. In the initial stages following severe injury, the number of lymphocytes may even decrease, disrupting the adaptive immune response. Consequently, during the early days of polytrauma, NLR tends to rise, indicating a higher response in more severe injuries. NLR serves as an objective index that is rapid, cost-effective, repeatable, and covered by health insurance [1]. Therefore, NLR emerges as a simple yet effective predictor of outcomes in polytrauma patients. Despite the scarcity of specific studies on NLR in patients with multiple injuries in Vietnam, it remains an unexplored area. This study aims: *To examine the mortality prognostic value of NLR in polytrauma patients*.

MATERIALS AND METHODS

1. Subjects

196 polytrauma patients who were admitted to the Surgical Intensive Care Unit, Military Hospital 103, from June 2020 to June 2023.

** Inclusion criteria:*

- Patients aged ≥ 18 years;

- Patients diagnosed with polytrauma according to the Berlin Consensus criteria in 2014 [2]: Patients have > 2 lesions with an AIS ≥ 3 and at least one of the following additional conditions:

+ Hypotension (systolic blood pressure ≤ 90 mm Hg);

+ Coma (Glasgow Coma Scale [GCS] ≤ 8);

+ Acidosis (Base Excess [BE] ≤ - 6.0);

+ Coagulation disorders (activated partial thromboplastin time [aPTT] ≥ 50 seconds or international normalized ratio [INR] ≥ 1.4);

+ Age ≥ 70;

- Patients' relatives provided consent to participate in the study.

Table 1. Abbreviated injury scale AIS - 2005.

Point	Injuries
1	Minor injury
2	Average injury
3	Severe injury, not life-threatening
4	Severe injury, life-threatening, still capable of living
5	Severe injury, life-threatening, unlikely to live
6	Injury cannot be survived

* *Exclusion criteria:* Hospitalized > 12 hours after the accident; patients who have had surgery or treatment at previous level hospitals; pregnant woman; have chronic diseases such as cirrhosis, end-stage chronic kidney failure, congestive heart failure, and malignancy; patients who had cardiac arrest before entering the hospital and were successfully resuscitated.

* *Criteria for removal from the study:* Transfer to another hospital before discharge after 30 days; insufficient collection of research data.

2. Methods

* *Research design:* A retrospective, descriptive study.

* *Data collection:* Vital signs, Glasgow score, RTS, Trauma score (TS), and ISS were documented upon admission. Blood samples, including biochemical, complete blood count, and blood gas tests, were obtained within 30 minutes of admission. Patient outcomes were assessed 30 days after admission, considering patients dead if they expired in the hospital or were in serious condition

with a family request for discharge. Compiled information is recorded in the research medical record.

* *Treatment protocols:*

Coma patients (GCS ≤ 8 points) received volume-controlled ventilation (Tidal volume = 8 mL/kg, respiratory rate 16 - 20 breaths/minute, PEEP 5 - 10 cmH_2O, I:E ratio of 1:2, FiO_2 40%), adjusted parameters to keep end-tidal CO_2 pressure ($EtCO_2$) within the range of 35 - 45 mmHg, arterial blood gas PaO_2 80 - 100 mmHg.

Treatment followed the 2014 Berlin Consensus guidelines for polytrauma patients, involving vasopressors (Noradrenalin, Adrenalin, etc.), fluid infusion to maintain mean blood pressure ≥ 65 mmHg, aggressive management of visceral bleeding and cerebral edema (in traumatic brain injury) with 3% hypertonic saline and tranexamic acid, use of antibiotics, analgesics, and sedatives as needed.

Nutritional support targeted 25 - 35 kcal/kg/day, initiated promptly post-injury unless contraindicated.

* *Statistical analysis:* Qualitative variables are presented as percentages. The Kolmogorov-Smirnov test was performed to check the normal distribution of the variables. Quantitative variables that are not normally distributed are presented as medians (interquartile range: Q1 - Q3). Test the difference between two quantitative variables that do not have a normal distribution using the Mann - Whitney test. Kaplan-Meier failure curve and log-rank test were fitted to explore the survival difference among groups. After the bivariable and multivariable Cox regression analysis, an Adjusted Hazard Ratio with 95% Confidence Intervals (CI) was reported to declare the strength of association and statistical significance, respectively.

* *Data processing:* Using the SPSS 26.0 software.

3. Ethics

All patients (without consciousness disorders) in the study were informed and consented by their relatives. Patients' names are kept anonymous. The main variable of the article is NLR, which is an objective paraclinical parameter in complete blood count. This parameter and other clinical characteristics are collected and recorded in the medical record on a regular basis. Obtaining research data does not affect diagnosis, treatment, patient costs, or health insurance. The research has no conflicts of interest among any individual or organization.

RESULTS

Table 2. General characteristics of research subjects.

Characteristics		Quantity (n)	Proportion (%)
Age	< 20	24	12.2
	20 - 40	76	38.8
	41 - 59	64	32.7
	≥ 60	32	16.3
	Mean age	41.75 ± 18.2	
Gender	Male	157	80.1
	Female	39	19.9
Causes	Traffic accidents	131	66.8
	Occupational accidents	32	16.3
	High fall	23	11.7
	Others	10	5.1
ISS	18 - 25	38	19.4
	26 - 40	98	50.0
	41 - 75	60	30.6
Outcome	Survival	116	59.2
	Death	80	40.8
Total		196	100

The patients with multiple injuries in the study were mainly working age, with an average age of 41.75 ± 18.2 years old. The lowest age was 18, and the highest was 82. The majority were men (80.1%).

The main cause of multiple injuries was traffic accidents (66.8%). The mortality rate due to multiple injuries in hospitalized patients was 40.8%.

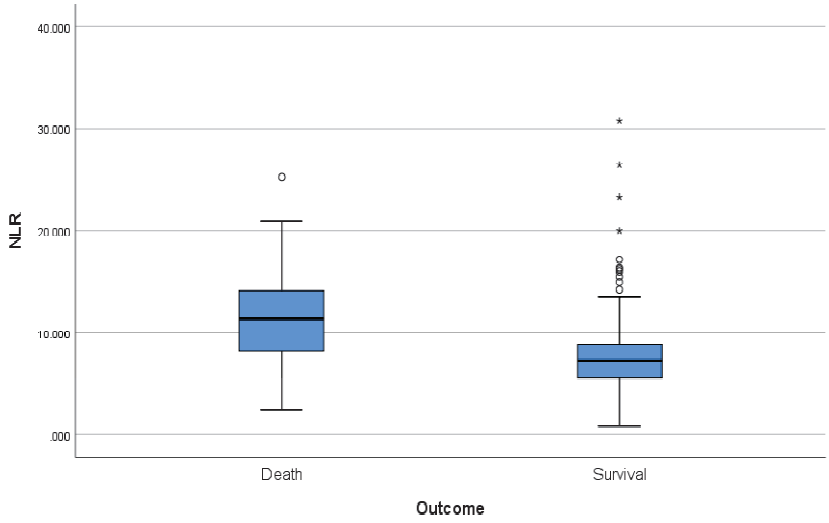
Most patients with multiple injuries had ISS scores ranging from 26 to 40 (50%). The lowest ISS score was 18 (4 patients accounting for 2%), and the highest ISS score was 75 (1 patient).

Table 3. Comparing the survival group with the death group.

Characteristics	Survival group (n = 116)	Death group (n = 80)	p
Age	37.0 (25.0 - 56.0)	45.0 (28.0 - 58.0)	0.16
Glasgow score	8 (7 - 9)	5 (4 - 5)	< 0.001
RTS	11 (10 - 12)	8 (6 - 10)	< 0.001
ISS	32 (25 - 35)	41 (34 - 45)	< 0.001
Lactate	3.7 (2.5 - 5.5)	6.6 (3.7 - 9.3)	< 0.001
INR	1.13 (1.04 - 1.27)	1.34 (1.12 - 1.60)	< 0.001
aPTT	29.6 (27.0 - 36.4)	38.1 (30.3 - 53.0)	< 0.001
Time elapsed until care (hours)	3.0 (2.0 - 4.0)	3.0 (2.0 - 3.0)	0.241
Duration of mechanical ventilation (days)	5.0 (1.0 - 8.0)	2.0 (1.0 - 6.0)	0.37
Length of intensive care (days)	6.5 (3.0 - 13.0)	2.0 (1.0 - 6.8)	< 0.001
Length of hospital stay (days)	21.5 (11.7 - 30.0)	2.0 (1.0 - 6.8)	< 0.001

The Glasgow scores, TS, and RTS at admission and the length of recovery and hospital stay of the death group were smaller than those of the survival group. In addition, the death group's ISS, creatinine at admission, lactate, blood glucose, INR, and aPTT were statistically significantly greater than those of the survival group.

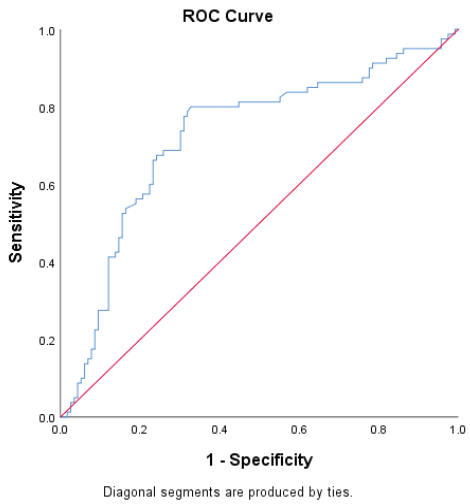
Figure 1. NLR value is in the survival group and death group.



	Survival group (n = 116)	Death group (n = 80)	p
NLR	8.21 (7.36 - 9.05)	11.08 (10.1 - 12.05)	p < 0.05

The mean admission NLR value in the death group was 11.08 ± 0.48 (95%CI: 10.1 - 12.05), in the survival group, it was 8.21 ± 0.42 (95%CI: 7.36 - 9.05); the death group had a higher NLR at the time of admission than the survival group, which was statistically significant with p < 0.05.

Figure 2. ROC curve predicting mortality by NLR at the time of hospitalization in patients with polytrauma.



	AUC	Cut - off	Specificity	Sensitivity
NLR	0.724	10.8	0.672	0.8

The NLR value at the time of admission has a predictive value for mortality in polytrauma patients with $p < 0.01$, area under the curve AUC = 0.724, cut-off point = 10.8 with 80% sensitivity (Se), specificity (Sp) 67.2%.

DISCUSSION

1. General characteristics of the patients

Our study was performed on 196 polytrauma patients with an average age of 41.75 ± 18.2 years. The male patient group accounted for 80.1%, most of whom were of working age. Up to 66.8% of the total patients in the study suffered multiple injuries due to traffic accidents. Research by Farzad Rahmani et al. on 374 multiple trauma patients admitted to the emergency department also found that most multiple trauma patients were men (82.1%), and the average age was 40.42 ± 18.05 years [3], quite similar to our research results. This is because young and middle-aged men are the main group of workers in most occupations, including occupations with heavy, intense labor, with a higher risk of accidents. Moreover, men also account for a high rate of traffic accidents, and is related to alcohol use while driving, etc.

The survival rate at 1 month after hospitalization for treatment in the study patient group was 59.2%, and the death rate was 40.8% (death cases were removed from the study patient population); death before the first 24 hours after admission). The study of Sauaia A et al. on 289 trauma patients showed that the mortality rate was 20%, lower than that of our study [4]. This difference was due to many reasons; it may caused by the larger number of patients studied, and at the same time, the patient population selected for this study was trauma in general; in addition to multiple trauma patients, there were also patients with multiple injuries. The injury was only in one organ, and the level of injury was not severe. In addition, it may also be due to first aid steps at the accident site, patient transportation, the capacity of doctors and hospitals, and good coordination between emergency, resuscitation, and surgical departments than in Western countries.

RTS in the death group were lower than in the survival group, and ISS in the death group were higher than in the survival group. The difference

between the two groups is statistically significant, with p < 0.001 (*Table 3*). This result is equivalent to the study of Diwakar Verma et al. on 88 multiple trauma patients from June 2016 to November 2016 in New Delhi, India, finding that ISS and RTS had a statistically significant difference between the two groups of living and dead patients, and research also shows that ISS and RTS are highly effective factors in predicting death for patients with multiple injuries [5].

Lactate is a product of anaerobic metabolism, reflecting hypoxia. Research results showed that blood lactate concentration at admission was statistically significantly higher at p < 0.001. This result is equivalent to the study by Divya Jyoti et al. (2022) on 90 patients with polytrauma, showing that lactate concentration at the time of admission is valuable in predicting both severity and the possibility of death in internal hospitals [6]. Normalization of lactate in polytrauma patients within the first 48 hours after injury significantly improves in-hospital mortality.

Coagulation disorder is one of the three deadly triads in polytrauma patients. The parameters assessing basic coagulation status at the time of hospitalization of most patients with multiple injuries are disordered. The study results showed that PT/INR and APTT at the time of admission in the group of patients who died were higher than those who survived; this difference was statistically significant with p < 0.001. This was similar to the results of a study by Gururaj N Puranik, et al. on 142 polytrauma patients in the pathology department of a tertiary care center for 20 months from December 2012 to July 2014, PT/INR, aPTT, and D-Dimer were independent predictors of mortality in polytrauma patients [7].

2. The mortality prognostic value of NLR at the time of hospitalization in polytrauma patients.

NLR at the time of hospitalization in the death group was higher than the survival group, with a statistical significance of p < 0.001. This result was similar to the study by Jinghong Xu et al. on 3865 trauma patients at 335 ICU centers in 208 hospitals, showing that the NLR at many time points between the polytrauma patients who died and survived group had different statistical significance [8].

NLR at the time of hospitalization could predict the outcome of polytrauma patients on a moderate level with p < 0.001 and AUC = 0.724. The cut-off point at NLR value = 10.8 because it has the highest J index with Se = 0.8 and Sp = 0.672.

This result is quite similar to the study by author Soulairman ES et al. on 566 patients with multiple injuries from July 2017 to November 2017: NLR at the time of admission has the ability to predict the outcome of the disease. Multiply the moderate level by AUC = 0.63. The cut-off point of NLR at time T_0 that best predicts the risk of death in this study is at NLR T_0 = 4 with Se = 0.70, Sp = 0.56 [9]. There are differences in the location of the cutting point that can be caused by many reasons. The subjects and design of the two studies are quite different. In Soulairman's study, subjects with ISS $\geq$ 15 were selected, while in our study, patients with ISS $\geq$ 18 were selected. Differences in acute conditions research and treatment in the two centers, study race, and tumor size also make a difference.

Our research results are also quite like the results of Jinghong Xu et al. in 2022: NLR at the time of hospitalization is a factor in predicting outcomes in trauma patients. With the area under the curve AUC = 0.681 and the optimal cut-off point of 9.75, Se = 65.3% and Sp = 65.8%. Meanwhile, in patients with traumatic brain injury, the area under the curve is 65.8%. Under the curve of NLR at the time of hospitalization, predicting outcomes is AUC = 0.725, and the optimal cut-off point is 7.439, Se = 77.7%, and Sp = 60.2%, respectively [8]. This shows that the value of NLR at the time of admission predicts mortality in patients with traumatic brain injury better than in patients with trauma. However, the time of death assessment in the two studies is different. Our study assessed death after 30 days, while the study by Jinghong Xu et al. was 15 days with many patients. In multicenter settings, this resulted in differences in the two study results.

In patients with severe TBI, research by Weiqiang Chen and colleagues on 688 patients from January 2007 to March 2012 found that NLR at the time of admission may be an effective new marker to predict mortality in patients with severe TBI with AUC = 0.704 (95%CI = 0.66 - 0.744), Se = 60.1% and Sp = 72.5%, respectively. The optimal cut-off point of the NLR value at the time of admission is 16.23 [10]. This result was like our study on the group of patients with polytrauma but with a higher NLR cut-off point.

CONCLUSION

Patients with multiple injuries were mainly men in the working age group, with traffic accidents being the main cause of multiple injuries. NLR at the time of admission in the group of patients who died was higher than that

of the group who survived, with $p < 0.001$. NLR at the time of hospital admission is meaningful in predicting mortality in patients with polytrauma. The higher the NLR at the time of admission, the greater the mortality rate of polytrauma patients.

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