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Prognostic value of neutrophil-lymphocyte ratio (NLR) in trauma patients

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Background: Trauma mortality exhibits three peaks: immediate, early, and late post-traumatic. Early deaths are often due to haemorrhage and central nervous system injury, whereas late deaths are associated with sepsis and multi-organ failure. The neutrophil-lymphocyte ratio (NLR) is a readily available and inexpensive marker of inflammation, and its prognostic value under various conditions has been established. However, the predictive ability of the NLR in trauma mortality remains unclear, with conflicting results from previous studies. This study aimed to investigate the correlation between NLR (on admission and at 48-hour post-admission) and trauma outcomes.
Methods: This retrospective study analysed data of trauma patients (≥ 18 years old) of which 372 were admitted to a level one trauma unit between January and June 2017. The data collected included demographics, mechanism of injury, injury severity score (ISS), new injury severity score (NISS), abbreviated injury scale (AIS), hospital length of stay (LOS), hospital disposition, and NLR values on admission and at 48 hours. Logistic regression models were used to analyse the association between the NLR and mortality, controlling for age, sex, ISS, and AIS. The sample size was calculated based on the anticipated mortality rate and desired power.
Results: The study included 288 patients for admission NLR analysis and 165 patients for the 48-hour NLR analysis. While factors such as ISS, NISS, emergency department (ED) probability of survival, NISS EU probability, and hospital disposition significantly predicted mortality, NLR at both 24 and 48 hours was not significantly associated with mortality. Although NLR showed good diagnostic accuracy, it did not improve the predictive power of the models, including established prognostic factors. The small sample size for 48-hour NLR analysis is a limitation.
Conclusion: Although the NLR is a simple indicator of systemic inflammation, this study found that it does not independently predict mortality in trauma patients when other established prognostic markers are included. These findings suggest that NLR has limited additional prognostic value in this context, highlighting the importance of incorporating established injury severity scores and other clinical factors for accurate mortality risk assessment. Further research with larger sample sizes is needed to confirm these findings and explore the potential role of the NLR in predicting other trauma outcomes.
Keywords: trauma, surgery, resuscitation, injury, neutrophil, lymphocyte

Introduction

The traditional distribution of trauma deaths is described as having three peaks: immediate, early, and late post-traumatic deaths.[1] As expected, the early causes of post-trauma death include haemorrhage and the central nervous system, while sepsis and multi-organ failure are the main contributors to late causes of death.[2] The pathological sequelae of pro- and anti-inflammatory responses that occur early in trauma along with the physiological trauma response may be difficult to distinguish.[3] The neutrophil-to-lymphocyte ratio (NLR) is a basic tool used to assess the inflammatory status of a patient.[4] It has been shown to be valuable in demonstrating mortality in cardiovascular events, malignancies, infectious diseases, and postoperative complications.[5] The normal range of the NLR (0.78–3.53) was demonstrated in the study by Forget et al.[6] in a non-geriatric adult population (aged between 21 and 66 years) without acute or chronic illnesses.However, the use of illicit substances, tobacco, and oral contraceptives in each patient is unknown, which may have influenced this ratio.[7] An elevated NLR (> 4.00) on day one was shown to be a strong predictor of survival during the first 30 days after trauma.[8] However, it is not independent of other factors.[9]

NLR is a simple, sensitive marker of the clinical severity of tissue injury and a low-cost marker of the inflammatory response.[10] Some studies have shown that NLR is a valuable predictor of outcomes in patients with traumatic brain injury (TBI).[11] In particular, an increased NLR at admission is associated with poor outcomes in such patients.[12,13] A meta-analysis by Liu et al.[14] commented that NLR is not necessarily a predictor of in-hospital mortality, even though it is a major predictor of disability and mortality in patients with intracerebral haemorrhage. On the converse of this, there are studies that have shown patients with poor clinical outcomes elicit a more severe and sustained inflammatory response than those with better outcomes.[15-17]

A study showed that an NLR > 5.27 on admission was associated with a two-fold higher risk of hospital mortality, particularly in patients who were older than 65 years and had

systolic blood pressures lower than 90 mmHg.[18] However, an NLR > 5.27 on admission was linked to poorer outcomes and was considered an independent prognostic indicator of hospital mortality in trauma patients.[19-21] Considering that immediate and early deaths after trauma are associated with the pro-inflammatory immune response, while late trauma-related deaths are associated with the anti-inflammatory response, measuring the NLR may be important in predicting such deaths.[22-24]

Trauma is an important health problem worldwide, with especially high incidence rates in low- to middle-income countries. The ability to predict the trauma risk of mortality is helpful for subsequent interventions, resource allocation, and quality assessment.[25]

Aim

This study aimed to evaluate the correlation of the NLR with the outcome in trauma subjects at a level one trauma unit in Johannesburg, and to compare NLR on admission and at 48 hours post-admission to outcomes in trauma.

Methodology

Retrospective data were collected from all adult patients (18 years and older) requiring resuscitation and admission at a level one trauma unit between January and June 2017. The following data were collected – age, sex, mechanism of injury (MOI), injury severity score (ISS), new injury severity score (NISS), NISS probability of survival, abbreviated injury scale (AIS) score, emergency department (ED) disposition, hospital length of stay (LOS), hospital disposition, admission neutrophil count, lymphocyte count, and NLR, and 48-hour neutrophil count, lymphocyte count, and NLR; descriptive analysis of study data for admission and 48-hour cohorts and determination of the prognostic value of each NLR metric for death, controlling for age, sex, ISS, and AIS.

Sample size estimation was based on the key research question, in this case, the estimation of the predictive ability of NLR for death. Based on an anticipated mortality rate of 7% and 80% power, a 5% significance level, and an expected area under the curve (AUC) of 0.70, a sample size of 240 was required. The median LOS was estimated using the Kaplan-Meier method, censoring for death. The predictive ability of NLR for death was assessed using receiver operating characteristic (ROC) curve analysis. The natural logarithm of each of the continuous variables included in the models was used to transform the data into (approximate) normal distributions, thereby meeting the assumptions of the technique. Cut points were chosen to maximise the sensitivity and specificity. Data analysis was performed using the SAS v9.4 Windows. A significance level of 5% was used.

This study was approved by the Human Research and Ethics Committee (M180435). Patient data and records were anonymised and informed consent for the use of data was obtained.

Results

Descriptive analysis of the overall group (n = 372), the group used for the admission NLR analyses (n = 288), and the group used for the 48h NLR analyses (n = 165). The data provide information on the correlation of the NLR with various characteristics, including age, sex, MOI, ISS, NISS probability of survival, AIS score, ED disposition,

Table I: Overall variables of patients

Variable	(n = 218)
Patient age	n (%)
Median (Q1, Q3)	39.0 (30.0, 54.0)
Gender	
Female	48 (22.0%)
Male	170 (78.0%)
EDRTS score	
Median (Q1, Q3)	4.1 (4.1, 7.8)
ISS Score	
Median (Q1, Q3)	16.0 (9.0, 25.0)
ISS score category	
< 15	105 (48.2%)
> = 15	113 (51.8%)
NISS score	
Median (Q1, Q3)	22.0 (12.0, 33.0)
ED probability of survival	
Median (Q1, Q3)	98.0 (82.0, 99.0)
NISS EU probability	
Median (Q1, Q3)	97.0 (70.0, 99.0)
ED Disposition	
High care	97 (44.5%)
High care via radiology	14 (6.4%)
High care via theatre	2 (0.9%)
ICU	83 (38.1%)
ICU via radiology	12 (5.5%)
ICU via theatre	9 (4.1%)
Ward	1 (0.5%)
Days in hospital	
Median (Q1, Q3)	19.0 (11.0, 36.0)
Hospital disposition	
Died	13 (6.0%)
Discharged home	170 (78.0%)
Transferred	35 (16.1%)
N count	
Median (Q1, Q3)	78.0 (70.0, 82.5)
L count	
Median (Q1, Q3)	13.1 (9.7, 19.1)
24-hour N/L ratio	
Median (Q1, Q3)	5.9 (3.6, 8.4)
24-hour NL ratio: categorical	
< 4	63 (28.9%)
> = 4	155 (71.1%)
48-hour N count	
Median (Q1, Q3)	73.0 (66.7, 79.0)
48-hour L count	
Median (Q1, Q3)	14.8 (10.1, 19.5)
48-hour N/L ratio	
Median (Q1, Q3)	5.0 (3.3, 7.7)
48-hour NL ratio: categorical	
< 4	75 (34.4%)
> = 4	143 (65.6%)
Abbreviated injury scale	
Median (Q1, Q3)	9.0 (5.0, 18.0)

Table II: Factors related to mortality

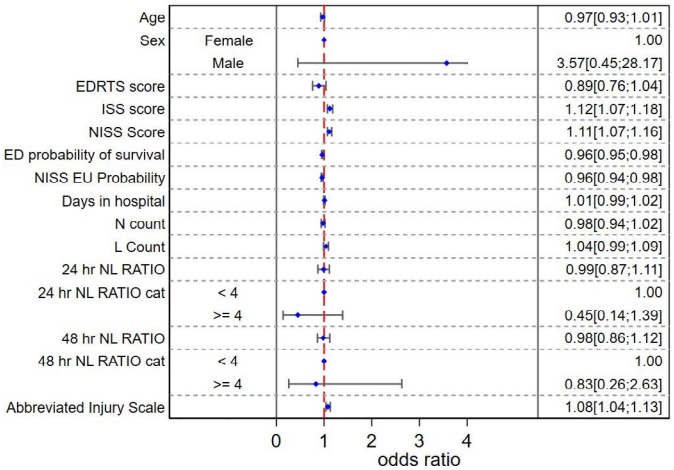
Variable		OR [95% CI]	*p*-value
Patient Age		0.97 [0.93, 1.01]	0.095
Sex	Female	1.00 (Ref)	
	Male	3.57 [0.45, 28.17]	0.227
EDRTS score		0.89 [0.76, 1.04]	0.152
ISS score		1.12 [1.07, 1.18]	< 0.001
NISS score		1.11 [1.07, 1.16]	< 0.001
ED probability of survival		0.96 [0.95, 0.98]	< 0.001
NISS EU probability		0.96 [0.94, 0.98]	< 0.001
Days in hospital		1.01 [0.99, 1.02]	0.336
N count		0.98 [0.94, 1.02]	0.298
L count		1.04 [0.99, 1.09]	0.086
NL ratio 24-hour		0.99 [0.87, 1.11]	0.807
24-hour NL ratio: categorical	< 4	1.00 (Ref)	
	> = 4	0.45 [0.14, 1.39]	0.166
48-hour NL ratio		0.98 [0.86, 1.12]	0.806
NL ratio 48-hour: categorical	< 4	1.00 (Ref)	
	> = 4	0.83 [0.26, 2.63]	0.751
Abbreviated injury scale		1.08 [1.04, 1.13]	< 0.001

hospital disposition, and outcome. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. It is a simple and inexpensive marker of systemic inflammation and the immune response. ISS and AIS were highly correlated (rho = 0.84); therefore, they could not be used together in one model. Table I presents the results of the logistic regression model. All models without NLR had good diagnostic accuracy as measured by AUC, sensitivity, and specificity.

The addition of NLR to these models was non-significant, and consequently did not improve diagnostic accuracy.

Discussion

While several factors such as EDRTS, ISS, NISS, ED probability of survival, NISS EU probability, ED and hospital disposition, and the AIS were significantly associated with mortality (Table II), the NLR at 24-hours and 48-hours did not appear to have a statistically significant association with mortality in this analysis. This result is consistent with the outcomes shown by some studies that the initial NLR was not predictive of trauma outcomes,



Graph I: Odds ratio

Table III: 24-hour NLR category bivariate

	NLR < 4 (*n* = 63)	NLR > = 4 (*n* = 155)	*p*-value
Patient Age			0.856
Median (Q1, Q3)	39.0 (30.0, 53.0)	40.0 (29.0, 55.0)	
Gender			0.753
Female	13 (20.6%)	35 (22.6%)	
Male	50 (79.4%)	120 (77.4%)	
EDRTS score			0.089
Median (Q1, Q3)	4.1 (4.1, 7.8)	7.3 (4.1, 7.8)	
ISS score			0.445
Median (Q1, Q3)	16.0 (9.0, 24.0)	16.0 (9.0, 25.0)	
ISS score cat			0.844
1	31 (49.2%)	74 (47.7%)	
2	32 (50.8%)	81 (52.3%)	
NISS score			0.956
Median (Q1, Q3)	18.0 (12.0, 34.0)	22.0 (12.0, 29.0)	
ED probability of survival			0.195
Median (Q1, Q3)	97.0 (72.0, 99.0)	98.0 (85.0, 99.0)	
NISS EU probability			0.216
Median (Q1, Q3)	95.0 (55.0, 99.0)	97.0 (81.0, 99.0)	
ED disposition			0.714
High care	24 (38.1%)	73 (47.1%)	
High care via radiology	4 (6.3%)	10 (6.5%)	
High care via theatre	1 (1.6%)	1 (0.6%)	
ICU	25 (39.7%)	58 (37.4%)	
ICU via radiology	5 (7.9%)	7 (4.5%)	
ICU via theatre	4 (6.3%)	5 (3.2%)	
Ward	0 (0.0%)	1 (0.6%)	
Days in hospital			0.065
Median (Q1, Q3)	16.0 (9.0, 30.0)	19.0 (13.0, 37.0)	
Hospital disposition			0.196
Died	6 (9.5%)	7 (4.5%)	
Discharged home	50 (79.4%)	120 (77.4%)	
Transferred	7 (11.1%)	28 (18.1%)	
N count			<0.001
Median (Q1, Q3)	65.9 (55.6, 69.3)	80.5 (77.4, 84.4)	
L count			<0.001
Median (Q1, Q3)	24.4 (20.3, 31.1)	11.1 (8.4, 13.9)	
48-hour N count			0.033
Median (Q1, Q3)	71.4 (61.6, 75.9)	73.7 (67.8, 80.4)	
48-hour L count			0.064
Median (Q1, Q3)	16.0 (12.2, 20.4)	14.4 (9.5, 19.1)	
48-hour N/L ratio			0.054
Median (Q1, Q3)	4.5 (2.8, 6.3)	5.1 (3.4, 8.5)	
Hour NL ratio 48 cat			0.464
1	24 (38.1%)	51 (32.9%)	
2	39 (61.9%)	104 (67.1%)	
Abbreviated injury scale			0.522
Median (Q1, Q3)	8.0 (5.0, 19.0)	10.0 (5.0, 18.0)	

Table IV: 48-hour NLR category bivariate

	NLR < 4	NLR >= 4	
	(*n* = 75)	(*n* = 143)	*p*-value
Patient age			0.595
Median (Q1, Q3)	40.0 (30.0, 48.0)	39.0 (30.0, 56.0)	
Gender			0.387
Female	14 (18.7%)	34 (23.8%)	
Male	61 (81.3%)	109 (76.2%)	
EDRTS score			0.708
Median (Q1, Q3)	4.1 (4.1, 7.8)	4.1 (4.1, 7.8)	
ISS score			0.199
Median (Q1, Q3)	14.0 (9.0, 25.0)	16.0 (9.0, 26.0)	
ISS score_cat			0.269
1	40 (53.3%)	65 (45.5%)	
2	35 (46.7%)	78 (54.5%)	
NISS score			0.257
Median (Q1, Q3)	18.0 (9.0, 27.0)	22.0 (12.0, 34.0)	
ED probability of survival			0.078
Median (Q1, Q3)	98.0 (87.0, 99.0)	97.0 (72.0, 99.0)	
NISS EU probability			0.159
Median (Q1, Q3)	98.0 (79.0, 99.0)	97.0 (64.0, 99.0)	
ED disposition			0.462
High care	40 (53.3%)	57 (39.9%)	
High care via radiology	4 (5.3%)	10 (7.0%)	
High care via theatre	1 (1.3%)	1 (0.7%)	
ICU	22 (29.3%)	61 (42.7%)	
ICU via radiology	4 (5.3%)	8 (5.6%)	
ICU via theatre	4 (5.3%)	5 (3.5%)	
Ward	0 (0.0%)	1 (0.7%)	
Days in hospital			0.385
Median (Q1, Q3)	17.0 (7.0, 39.0)	20.0 (12.0, 35.0)	
Hospital disposition			0.024
Died	5 (6.7%)	8 (5.6%)	
Discharged home	65 (86.7%)	105 (73.4%)	
Transferred	5 (6.7%)	30 (21.0%)	
N count			0.395
Median (Q1, Q3)	77.9 (69.0, 81.0)	78.1 (70.0, 83.3)	
L count			0.130
Median (Q1, Q3)	14.0 (10.0, 20.0)	12.5 (9.1, 18.7)	
24hr N/L ratio			0.174
Median (Q1, Q3)	5.6 (3.6, 7.9)	6.2 (3.6, 9.0)	
Hour NL ratio 24_cat			0.464
1	24 (32.0%)	39 (27.3%)	
2	51 (68.0%)	104 (72.7%)	
48-hour N count			< 0.001
Median (Q1, Q3)	63.8 (56.0, 68.7)	76.2 (73.0, 82.5)	
48-hour L count			< 0.001
Median (Q1, Q3)	22.0 (19.3, 28.1)	11.9 (8.7, 14.7)	
Abbreviated injury scale			0.074
Median (Q1, Q3)	7.0 (5.0, 16.0)	10.0 (6.0, 19.0)	

even if it may provide predictive outcomes at various time points.[26] The particular outcome shown in this study may have been influenced by different inclusion criteria (head injury patients, early mortality within first 24 hours), the varying time from injury to arrival, and the severity of the trauma itself.[27] This analysis (Tables III and IV) suggests that injury severity scores (ISS and NISS), ED probability of survival, NISS EU probability, and AIS are significantly associated with mortality. However, factors such as patient age, sex, EDRTS score, days in the hospital, N count, L count, and N/L ratios at 24 and 48 hours did not show statistically significant associations with mortality in this study. The N/L ratio categories at 24 and 48 hours may be associated with some aspects of hospital stay and outcome. However, the relationship between injury severity scores and probability of survival was not consistently observed across these time points. These findings suggest that the N/L ratio may be relevant to early clinical course and outcomes in this population.

Therefore, NLR remains a good indicator of the severity of trauma injury that may have less favourable outcomes, but it does not add to the prediction of mortality already shown by the ISS and AIS. Studies have shown that an elevated NLR is associated with worse outcomes in trauma patients, including higher mortality rates and increased risk of complications, such as sepsis and organ failure.[8,10-12,14] The mechanism underlying this correlation is thought to be related to the inflammatory response to injury.[7] Several studies have investigated the correlation between NLR and prognosis in trauma patients, and the results have been mixed.[18-20] Some studies have shown that a high NLR is associated with worse outcomes, such as longer hospital stay, increased morbidity and mortality, and higher rates of complications. Other studies have not found a significant association between NLR and outcomes in patients with trauma. One possible explanation for these mixed results is that the relationship between NLR and prognosis may depend on the severity and type of trauma.[21-23] For example, some studies found that NLR was only associated with worse outcomes in patients with severe TBI, but not in those with other types of injuries.[10-14]

Several studies have investigated the association between NLR and outcomes in trauma patients and found that an NLR value of ≥ 12 was associated with a significantly increased risk of mortality, while others concluded that higher NLR values were associated with an increased risk of mortality and longer hospital stays, and found that higher NLR values were consistently associated with increased mortality, longer hospital stays, and worse outcomes in trauma patients.[10-12]

Overall, the available evidence suggests that NLR may be a useful marker for predicting prognosis and outcomes in trauma patients. However, further research is needed to fully understand the relationship between NLR and trauma outcomes and to determine the optimal NLR cutoff values for predicting poor outcomes in this patient population.[25-27]

Limitations

The actual sample size of 288 for admission NLR was adequate, but the sample size of 165 for 48-hour NLR was low; this means that only a more discriminating variable, corresponding to an AUC of 0.74 or more, was found to be statistically significant. Increasing the length of the study could have yielded greater numbers to allow results to be

statistically significant. A recommendation from this study would be to increase the research time frame, and thus allow for larger inclusion numbers to produce statistically significant results.

Conclusion

Overall, the data provide a comprehensive view of the NLR distribution across different categories and metrics. While some trends can be observed, the differences in NLR values are generally not substantial, indicating that NLR might have limited utility as a standalone prognostic marker in patients with trauma. Other factors and markers should be considered in conjunction with the NLR to accurately assess the severity of injury and patient outcomes. It is essential to remember that this analysis was based on the data provided, and further studies are needed to draw more definitive conclusions about the correlation of NLR in trauma patients. It is a simple and inexpensive marker of systemic inflammation and immune response. The addition of NLR to the current measurement scales of ISS and AIS does not improve the mortality rate prognostic value, even though the NLR did show good diagnostic accuracy in keeping with that of the ISS and AIS. Therefore, the association between NLR and in-hospital mortality in trauma patients may be nonlinear. While NLR may be a useful marker of inflammation and prognosis in some trauma patients, its clinical utility may be limited by the heterogeneity of trauma patients and the need for further research to determine its specific role in predicting outcomes. Therefore, while further research is needed to fully understand the relationship between NLR and prognosis in trauma patients, current evidence suggests that elevated NLR may be a useful prognostic marker in this population.

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

This study was approved by the University of the Witwatersrand Human Research and Ethics Committee (M180435). Patient data and records were anonymised and informed consent for the use of data was obtained.

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