


## RESEARCH ARTICLE

# Neutrophil to lymphocyte ratio predicts early growth of traumatic intracerebral haemorrhage

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## Abstract

**Objective:** The neutrophil to lymphocyte ratio (NLR) has been proposed to capture the inflammatory status of patients with various conditions involving the brain. This retrospective study aimed to explore the association between the NLR and the early growth of traumatic intracerebral haemorrhage (tICH) in patients with traumatic brain injury (TBI). **Methods:** A multicentre, observational cohort study was conducted. Patients with cerebral contusion undergoing baseline computed tomography for haematoma volume analysis within 6 h after primary injury and follow-up visits within 48 h were included. Routine blood tests were performed upon admission, and early growth of tICH was assessed. Prediction accuracies of the NLR for the early growth of tICH and subsequent surgical intervention in patients were analysed. **Results:** There were a total of 1077 patients who met the criteria included in the study cohort. Univariate analysis results showed that multiple risk factors were associated with the early growth of tICH and included in the following multivariate analysis models. The multivariate logistic regression analysis results revealed that the NLR was highly associated with the early growth of tICH ( $p < 0.001$ ) while considering other risk factors in the same model. The prediction accuracy of the NLR for the early growth of tICH in patients is 82%. **Interpretation:** The NLR is easily calculated and might predict the early growth of tICH for patients suffering from TBI.

## Introduction

Intracerebral haemorrhage (ICH) is a type of cerebral bleeding within the brain tissue or ventricles.<sup>1</sup> The main causes of ICH include brain tumours, brain trauma, aneurysms and arteriovenous malformations. Among various types of ICH, traumatic intracerebral haemorrhage (tICH) is a common complication after traumatic brain injury (TBI) and a leading cause of long-term disability and mortality worldwide.<sup>2,3</sup>

tICH is associated with a high risk of coagulopathy and leads to an increased risk of haemorrhage growth.<sup>4</sup> This secondary damage of tICH resulted from progressive intraparenchymal haemorrhage, which is defined as a haematoma growth >33% or 5 cm<sup>3</sup> on subsequent computed tomographic (CT) scanning,<sup>5,6</sup> has been reported to occur in 25–50% of all patients with head injury.<sup>7</sup> The growth of tICH is also associated with increased morbidity, and 13–19% of patients with growing tICH will require delayed surgery.<sup>6</sup>

A large amount of evidence has suggested that neuroinflammation is an important injury mechanism that contributes to ongoing neurodegeneration and neurological impairments associated with tICH. Meanwhile, neuroinflammation may also contribute to haematoma growth. Following TBI, patients who survive the initial injury are susceptible to secondary cerebral insults which are initiated by the release of neurotoxic and inflammatory endogenous mediators by resident cells of the central nervous system (CNS).<sup>8</sup> This post traumatic neuroinflammation activates leucocytes and induces the release of inflammatory factors.<sup>9</sup>

Neutrophils are among the first leucocytes that can enter the CNS through blood vessels of meninges and the damaged blood–brain barrier. Evidence showed that neutrophils increase dramatically in the peripheral blood during the early 48 h after TBI.<sup>10</sup> On the other hand, T-lymphocytes play an important role in the damaged brain tissues by releasing growth factors and regulating functions.<sup>11</sup> A decrease in the number of lymphocytes after TBI is considered as a marker of brain injury with poor clinical results.<sup>12</sup>

The neutrophil to lymphocyte ratio (NLR) has been proposed to capture the inflammatory status of patients with various conditions involving the brain, including glial tumours, ischaemic stroke, haemorrhagic stroke and convulsive status epilepticus.<sup>13–17</sup> These studies have indicated that higher NLR levels are linked to poorer functional outcomes and higher mortality rates in severe TBI cases. Our previous study also showed that NLR is associated with long-term outcomes for patients with severe tICH.<sup>18</sup>

Despite the continuous advance in critical care, it is still difficult to predict the early growth of tICH. Moreover,

there is still a lack of research on the association between NLR and the early growth of tICH. Our study aimed to assess the potential of NLR for predicting early growth of tICH in patients with TBI, and the results showed an association between high NLR and early growth of tICH. It suggests that NLR is an objective indicator that helps physicians to judge the early growth of tICH.

## Materials and Methods

### Patient population

Consecutive patients with a primary traumatic cerebral contusion, who were admitted to one of four hospitals (First and Second Affiliated Hospitals of Shantou University Medical College, Jieyang People's Hospital and Fuzhou General Hospital of Xiamen University) between 1 January 2012, and 30 April 2019, were enrolled in this cohort study. The inclusion criteria were as follows: (1) at least 18 years old; (2) documentation of a baseline CT scan within 6 h after brain injury and a follow-up CT within 48 h after the initial CT; (3) documentation of an initial blood test within 24 h of the occurrence of the injury; and (4) haematoma volume of at least 2 cm<sup>3</sup> at baseline CT scan. The exclusion criteria were as follows: (1) surgery performed before the follow-up CT scan, (2) previous head trauma, (3) previous coagulopathy or (4) use of antiplatelet or anticoagulant medication.

### Data collection

All patients underwent a brain CT scan immediately after admission. The follow-up CT scan was routinely performed within 48 h of the initial CT or when the patient's condition deteriorated. The haematoma volume was calculated based on CT scan results using the volumetric computer on Advantage Windows 3D Workstation 4.1 (Shantou, China). Inter-reader variability was determined by having the CT image analysed by two independent neuroradiologists who were blinded to the details of the study (the number of 5-mm slices containing haemorrhage was multiplied by 0.5).<sup>19</sup> Briefly, the area of interest was manually selected and automatically separated from the environment according to the software's fixed threshold in Hounsfield units (HU). The separated areas were visually inspected and manually adjusted to ensure that bleeding was visible in all three projections. The surrounding haematomas were distinguished using thresholds (fixed windows of 110 and 50 HU), and the adjacent voxels that provide the haematoma volume were automatically summarized. When there were multiple intraparenchymal haematomas in the contusion area, the total volume was calculated. Haematoma expansion was

defined as a 33% or more than 5 mL increase in volume on the follow-up CT scan compared with that on the baseline CT.

Venous blood samples were drawn on admission and stored in tubes containing various anticoagulants for routine blood tests. Routine blood examinations, including examinations of the leucocyte count (reference range, 3.5–9.5  $10^9/L$ ), neutrophil count (reference range, 1.8–6.4  $10^9/L$ ), lymphocyte count (reference range, 1.1–3.2  $10^9/L$ ) and mononuclear cell count (reference range, 0.1–0.6  $10^9/L$ ), were performed for all patients by the routine laboratory assays. The NLR is defined as the number of neutrophils divided by the number of lymphocytes.

The following factors were also included for statistical analysis to expand the spectrum of the information gathered: (1) the potential risk factors related to the growth of tICH, such as primary haematoma volume, time to early CT scan and Glasgow Coma Scale (GCS)<sup>20–23</sup>; (2) the novel predictors for early haematoma growth in patients with TBI, including leucocyte counts,<sup>24</sup> coagulopathy<sup>25,26</sup> and the haematoma shape as visualized by head CT<sup>27</sup>; (3) the presence of intraventricular haemorrhage, subarachnoid haemorrhage (SAH), subdural haemorrhage (SDH), epidural haematoma (EDH), contrecoup injury and intracranial surgery during the initial 24 h; (4) comorbidities.

## Statistical analysis

Data were analysed using SPSS 22 (SPSS Inc., Chicago, IL). Continuous variables are expressed as the means  $\pm$  standard deviations, and categorical variables are expressed as counts (percentages). Continuous variables were compared using a two-sample *t*-test, whereas categorical data were analysed using the Pearson  $\chi^2$  test or Fisher's exact test.

Three statistical models (univariate analysis [NLR model], reduced multivariate model without NLR, and full model with NLR) were used to evaluate the relationship between NLR and tICH by considering their corresponding risk factors. The results are presented as odds ratios (ORs) and 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive performance for haematoma expansion by the NLR values obtained at admission. The cut-off values were estimated using the ROC curve, and the corresponding sensitivities and specificities were calculated based on the area under the curve (AUC). Statistical significance was set at  $p < 0.05$ . Finally, prediction accuracies of the early growth of tICH and receiving subsequent surgical intervention in patients by NLR model and full model were calculated respectively.

In order to avoid the selection bias, the missing data of the variables included in the full model are not excluded.

## RESULTS

### General information

The initial screening identified 3101 subjects who had been admitted to the hospital due to TBI. Based on the predetermined criteria, 2024 patients were excluded. A total of 1077 patients (815 men and 262 women) were included in the final analysis cohort (Fig. S1). The results of univariate analysis for all study variables to growth and no growth of tICH are listed in Table 1. The mean GCS score upon admission is  $11.54 \pm 3.39$  overall included patients, the mean time from injury to the first CT scan is  $2.92 \pm 2.13$  h and the mean initial tICH volume was  $4.72 \pm 9.73$  mL. GCS score, time to baseline CT, contrecoup injury, SAH, SDH, baseline CT haematoma volume, inflammatory index parameters (leucocyte, neutrophil, lymphocyte and mononuclear cell counts) and NLR were found to be statistically discriminative between groups with and without growth of tICH ( $p < 0.001$ ). These parameters were all included in the following multivariate statistical models.

### Surgical intervention group versus non-intervention group

In Table 1, receiving surgery at baseline for cleaning intracranial haematoma also exhibited a statistically significant difference ( $p < 0.001$ ) between patients with and without growth of tICH (34.0% vs. 13.5%). This fact raised our interest and intention for further exploring the association among surgery, NLR and tICH. We conducted another analysis for the 544 patients with haematoma expansion measured at the follow-up CT scan. Among them, 185 patients have received surgery at baseline. As shown in Table 2, a univariate analysis was performed to identify risk factors for surgical intervention among patients with the growth of tICH. GCS scores, mean arterial pressure, the occurrence of contrecoup injury and encephalatrophy, SAH, SDH, EDH, initial haematoma volume and NLR were significantly different ( $p < 0.05$ ) between those patients.

### NLR as a predictor for haematoma expansion and surgical intervention

Multivariate analysis results are summarized in Table 3 to demonstrate the associations between NLR and the outcome variables, including the growth of tICH and baseline surgery. To further evaluate the predictive

**Table 1.** Differences between with growth of tICH and without growth of tICH (univariate analysis).

Term	Total (N = 1077)	Population (N = 1077)		p value
		With growth of tICH (n = 544)	Without growth of tICH (n = 533)	
Age	48.63 ± 17.92	49.68 ± 18.28	47.56 ± 17.49	0.053
Gender				0.508
Male	815 (75.7%)	407 (74.8%)	408 (76.5%)	
Female	262 (24.3%)	137 (25.2%)	125 (23.5%)	
GCS score	11.54 ± 3.39	11.03 ± 3.41	12.06 ± 3.30	<b>&lt;0.001</b>
Baseline CT time, h	2.92 ± 2.13	2.67 ± 1.92	3.17 ± 2.30	<b>&lt;0.001</b>
Hypertension	114 (10.6%)	67 (12.3%)	47 (8.8%)	0.112
MAP, mmHg	99.82 ± 16.66	100.78 ± 18.54	98.85 ± 14.48	0.094
Diabetes	51 (4.7%)	28 (5.2%)	23 (4.4%)	0.502
Smoking	170 (15.8%)	90 (16.9%)	80 (15.5%)	0.544
Alcohol abuse	104 (9.7%)	50 (9.4%)	54 (10.5%)	0.550
Combine injury	430 (39.9%)	227 (41.7%)	203 (38.2%)	0.232
Contercoup injury	255 (23.7%)	225 (41.4%)	30 (5.6%)	<b>&lt;0.001</b>
Lobe of contusion				0.056
Frontal	472 (43.8%)	247 (45.4%)	225 (42.2%)	
Temporal	473 (43.9%)	245 (45.0%)	228 (42.8%)	
Parietal	56 (5.2%)	19 (3.5%)	37 (6.9%)	
Occipital	24 (2.2%)	12 (2.2%)	12 (2.3%)	
Others	52 (4.8%)	21 (3.9%)	31 (5.8%)	
IVH	68 (6.3%)	37 (6.9%)	31 (5.8%)	0.491
SAH	802 (74.5%)	445 (82.1%)	357 (67.1%)	<b>&lt;0.001</b>
SDH	672 (62.4%)	413 (75.9%)	259 (48.7%)	<b>&lt;0.001</b>
EDH	226 (21.0%)	122 (22.5%)	105 (19.5%)	0.234
Encephalatrophy	53 (4.9%)	28 (5.2%)	25 (4.7%)	0.740
Initial haematoma volume, mL	4.72 ± 9.73	5.99 ± 9.26	3.43 ± 10.03	<b>&lt;0.001</b>
Inflammatory index parameters				
Leucocyte count	15.33 ± 5.56	16.40 ± 5.41	14.24 ± 5.50	<b>&lt;0.001</b>
Neutrophil count	13.02 ± 5.16	14.40 ± 4.93	11.61 ± 5.02	<b>&lt;0.001</b>
Lymphocyte count	1.35 ± 0.93	1.00 ± 0.60	1.71 ± 1.06	<b>&lt;0.001</b>
Mononuclear cell count	0.85 ± 0.50	0.88 ± 0.48	0.82 ± 0.48	<b>0.047</b>
NLR	13.11 ± 10.49	17.84 ± 12.31	8.28 ± 4.63	<b>&lt;0.001</b>
Surgery for cleaning intracranial haematoma	257 (23.9%)	185 (34.0%)	72 (13.5%)	<b>&lt;0.001</b>

tICH, traumatic intracerebral haemorrhage; CT, computed tomographic; GCS score, Glasgow Coma Scale; MAP, mean arterial pressure; IVH, Intra-ventricular haemorrhage; SAH, subarachnoid haemorrhage; SDH, subdural haematoma; EDH, epidural haematoma; NLR, neutrophil/lymphocyte ratio.

The bold values are the parameters with statistically significant difference in the included patients with and without tICH. Those may underlying the growth of tICH therefore deserve further analysis.

performance of NLR, two multivariate logistic regression models (a reduced model without NLR and a full model with NLR) were introduced. Statistically, significant variables identified in the previous univariate analysis were all included in the multivariate analysis. In the full multivariate model, after adjusting for confounders such as age and gender, NLR has exhibited an OR of 1.309 (95% CI = 1.254–1.367) for predicting the growth of tICH at a statistically significant level ( $p < 0.001$ ). A deviance test was also conducted for the same multivariate model. The result (goodness-of-fit statistics = 264.7) indicated that a full multivariate model including NLR has better

predictability than a reduced model without NLR for growth of tICH, at a statistically significant level.

A ROC curve analysis was performed to obtain the optimal NLR cut-off value for predicting the growth of tICH, and the results are listed in Table 3. Results showed that the AUC of the NLR-only model is 0.864 (95% CI = 0.842–0.885) (Fig. 1). Even though the ROC analysis suggested that the predictive performance of the full model (AUC = 0.908 with NLR) was better than the reduced model (AUC = 0.805 without NLR), NLR itself still exhibited predictive potential for growth of tICH in the reduced model at a cut-off point of 10.94 ( $p < 0.001$ ).

**Table 2.** Characteristic of growth of tICH stratified by surgical intervention.

Variables	Surgical intervention		p value
	Yes (n = 185)	No (n = 359)	
Age, years	49.82 ± 18.12	49.61 ± 18.38	0.900
Gender			0.589
Male	141 (76.2%)	266 (74.1%)	
Female	44 (23.8%)	93 (25.9%)	
GCS score	10.36 ± 3.39	11.38 ± 3.37	<b>0.001</b>
Baseline CT time, h	2.86 ± 2.38	2.58 ± 1.63	0.148
Hypertension (%)	25 (14.2%)	42 (12.0%)	0.482
MAP, mmHg	103.58 ± 20.64	99.44 ± 17.32	<b>0.032</b>
Diabetes (%)	13 (7.2%)	15 (4.2%)	0.266
Smoking (%)	31 (17.2%)	59 (16.7%)	0.882
Drink abuse (%)	18 (10.0%)	32 (9.0%)	0.719
Combined injury (%)	80 (43.2%)	147 (40.9%)	0.607
Contrecoup injury (%)	99 (53.8%)	126 (35.1%)	<b>&lt;0.001</b>
Lobe of contusion			0.819
Frontal (%)	79 (42.7%)	168 (46.8%)	
Temporal (%)	89 (48.1%)	156 (43.5%)	
Parietal (%)	7 (3.8%)	12 (3.3%)	
Occipital (%)	3 (1.6%)	9 (2.5%)	
Other (%)	7 (3.8%)	14 (3.9%)	
IVH (%)	17 (9.3%)	20 (5.6%)	0.108
SAH (%)	169 (91.8%)	276 (77.1%)	<b>&lt;0.001</b>
SDH (%)	152 (82.2%)	261 (72.7%)	<b>0.014</b>
EDH (%)	57 (31.0%)	65 (18.2%)	<b>0.001</b>
Encephalatrophy (%)	4 (2.2%)	24 (6.7%)	<b>0.024</b>
Initial haematoma volume, mL	8.97 ± 10.68	4.36 ± 7.95	<b>&lt;0.001</b>
NLR	19.79 ± 17.52	16.84 ± 8.32	<b>0.031</b>

tICH, traumatic intracerebral haemorrhage; CT, computed tomographic; EDH, extradural haemorrhage; GCS, Glasgow Coma Scale; IVH, intraventricular haemorrhage; MAP, mean arterial pressure; NLR, neutrophil to lymphocyte ratio; SAH, subarachnoid haemorrhage; SDH, subdural haemorrhage.

The bold values are the parameters with statistically significant difference in the included patients required surgical intervention or not in the group of growth of tICH. Those may underlying the risk factors for surgical intervention among patients with growth of tICH therefore deserve further analysis.

The same multivariate analysis models were also performed for associating NLR and baseline surgery, and the results were presented in Table 3. NLR has exhibited an OR of 1.027 (95% CI = 1.003–1.053) in predicting baseline surgery at a significant level ( $p = 0.029$ ). The results of the deviance test (goodness-of-fit statistics = **1.017**) were not statistically significant. Results of the ROC curve analysis showed that the full model with NLR could demonstrate a good predictive value (**AUC = 0.744, 95% CI = 0.698–0.790**) comparing to the NLR-only model (AUC = 0.538) (Fig. 1).

The positive prediction accuracy of the early growth of tICH in patients by NLR model was 82%, which is

higher than the full model of **80%** (Table 4). The positive prediction accuracy of patients with tICH receiving subsequent surgical intervention by NLR model was 37.6%, lower than the full model of **55.6%** (Table 4). The positive prediction accuracy of **82%** by the NLR model for predicting the early growth of tICH in patients demonstrated that the NLR model might properly predict the early growth of tICH for patients suffering from TBI.

We further explored the association between NLR level and the 6-month outcome of patients with TBI (Fig. 2). A total of 409 patients (38.73%) with available 6-month GOS were included in the analysis dataset. The NLR was significantly higher in the unfavourable 6-month outcome (GOS  $\leq 3$ ) group than in the favourable 6-month outcome (GOS  $> 3$ ) group ( $14.50 \pm 8.62$  vs.  $12.17 \pm 7.68$ ,  $p = 0.014$ ) (Fig. 2A). The result of the univariable logistic regression indicated that NLR level was significantly associated with an unfavourable outcome (crude OR, 1.04; 95% CI, 1.01–1.06;  $p = 0.016$ ). Figure 2B shows that NLR level was positively associated with the probability of an unfavourable outcome.

## DISCUSSION

For patients suffering from TBI, the growth of tICH induces subsequent biochemical and metabolic changes leading to progressive tissue damage and associated cell death that contribute to poor outcomes. In this study, we explored the possibility of using routine laboratory tests to run a new indicator for easily predicting patient's outcome in terms of the growth of tICH. NLR, an indicator of neuroinflammation, has demonstrated predictive potential for the growth of tICH on TBI patients. Results of various univariate and multivariate models showed that NLR was significantly associated with the growth of tICH.

Our findings echo the increasing shreds of evidence that systemic immune response is an important mechanism contributing to ongoing neurological impairments. The inflammatory response after acquiring TBI is characterized by the infiltration of circulating inflammatory cells, including neutrophils and macrophages.<sup>28</sup> Following brain damage, T cells are recruited to the lesion site. The process is shown to be aggravated by reactive oxygen species released from neutrophils.<sup>29</sup> These inflammatory cells release cytokines that can cause secondary injury around the tICH, thereby leading to the growth of tICH. In a previous study, Zhou et al described the role of inflammation in tICH, including its underlying mechanism and clinical translation.<sup>30</sup> Secondary damage of TBI is triggered by the presence of intraparenchymal blood, which subsequently activates cytotoxic, excitotoxic, oxidative and inflammatory pathways.<sup>31,32</sup> Similarly, during the

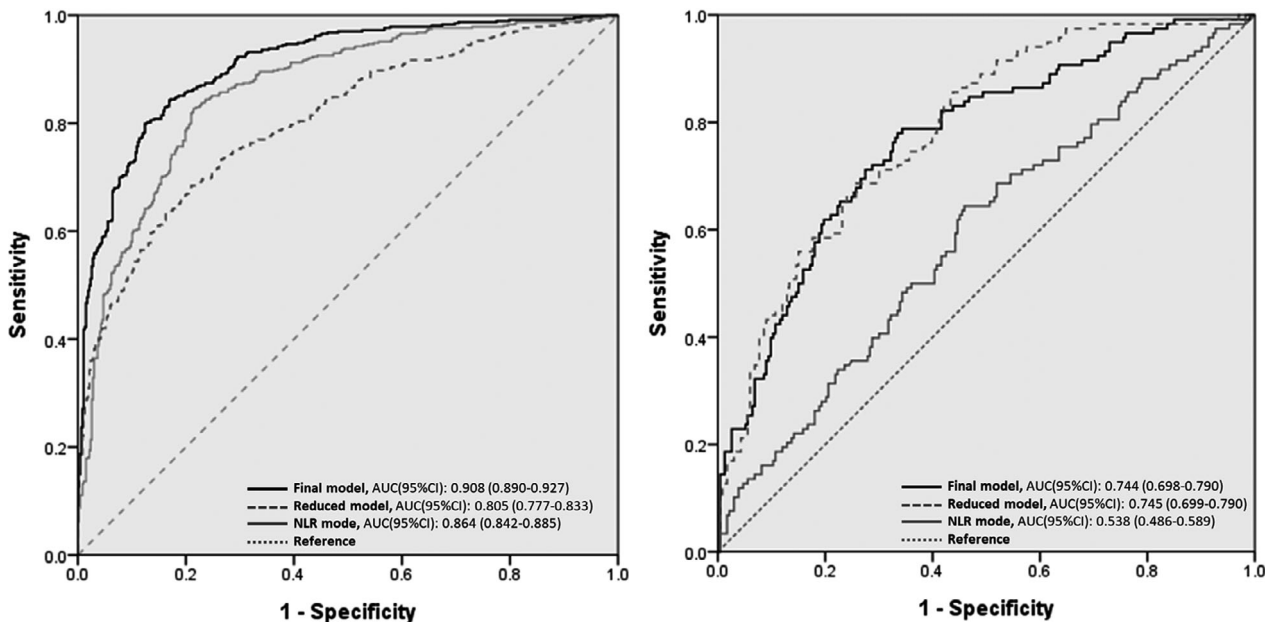
**Table 3.** Statistical analysis for tICH and surgical intervention with different models.

Screening model	Logistic regression			ROC curve			
	OR (95% CI)	p-value	-2likelihood	AUC (95% CI)	p-value	Youden's index	Cut-off point
<b>tICH</b>							
Univariate analysis	1.321 (1.275–1.369)	<0.001	–	0.864 (0.842–0.885)	<0.001	0.602	10.94
Reduced model without NLR	NA	NA	991.275 <sup>1</sup>	0.805 (0.777–0.833)	<0.001	–	–
Full model with NLR	1.309 (1.254–1.367)	<0.001	726.577 <sup>1</sup>	0.908 (0.890–0.927)	<0.001	0.675	0.514
<b>Surgery intervention</b>							
Univariate analysis	1.020 (1.004–1.036)	0.016	–	0.538 (0.486–0.589)	0.149	0.088	14.99
Reduced model without NLR	NA	NA	371.553 <sup>2</sup>	0.745 (0.699–0.790)	<0.001	–	–
Full model with NLR	1.027 (1.003–1.053)	0.029	365.514 <sup>2</sup>	0.744 (0.698–0.790)	<0.001	0.436	0.312

tICH, traumatic intracerebral haemorrhage; NLR, neutrophil to lymphocyte ratio; ROC, receiver operating characteristic; AUC, area under the curve; OR, odds ratio; CI, confidence interval.

<sup>1</sup>Deviance test, goodness-of-fit statistic = 264.70 (> $\chi^2_{1,0.05}$ ), it is significant.

<sup>2</sup>Deviance test, goodness-of-fit statistic = 1.017 (> $\chi^2_{1,0.05}$ ), it is non-significant.



**Figure 1.** Receiver operating characteristic (ROC) curve analysis for a univariate analysis (NLR model), reduced model (without NLR) and final model (with NLR) on (A) growth of tICH, (B) surgery intervention. tICH, traumatic intracerebral haemorrhage; NLR, neutrophil to lymphocyte ratio.

early stages of TBI, many inflammatory cells have been observed around the haematoma in animal studies.<sup>33</sup>

The association between NLR and the outcome variables, tICH growth and surgery at baseline, demonstrates the clinical benefits of this study. The results suggest that higher NLR levels are associated with worse functional outcomes and higher mortality, at least in severe TBI cases. Our previous study showed the association between NLR and the long-term prognosis of patients with severe tICH, and this study further explored the relationship between NLR levels and the 6-month

prognosis of TBI patients. High NLR level and poor prognosis were significantly correlated, indicated by the univariate logistic regression results and by Figure 2B. It is consistent with the previous results. In addition to NLR, other indicators relating to neuroimaging were highly associated with the outcome variable. A key factor for detecting tICH may be the timing of the first CT scans post-injury. Both the time to baseline CT and the baseline CT haematoma volume have shown to be associated with the outcome variable during univariate and multivariate analysis.

**Table 4.** Prediction accuracies of patients with the growth of tICH by different models.

Term	Model	Prediction	Patients with the growth of tICH	
			No	Yes
tICH	NLR model	No	417 (81.0%)	98 (19.0%)
		Yes	116 (21.8%)	<b>446 (82.0%)</b>
	Full model	No	409 (81.3%)	94 (18.7%)
		Yes	58 (13.4%)	<b>375 (80.0%)</b>

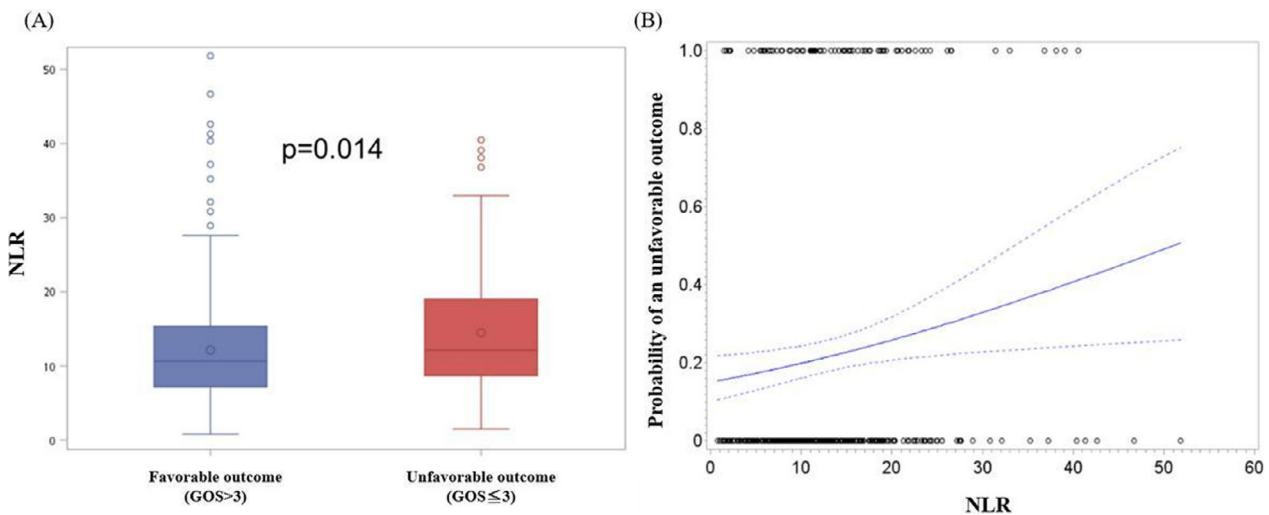
Term	Model	Prediction	Patients with tICH received surgery intervention	
			No	Yes
Surgery intervention	NLR model	No	178 (70.1%)	76 (29.9%)
		Yes	181 (62.4%)	<b>109 (37.6%)</b>
	Full model	No	203 (84.2%)	38 (15.8%)
		Yes	103 (44.4%)	<b>129 (55.6%)</b>

Positive prediction accuracies are in bold. tICH, traumatic intracerebral haemorrhage; NLR, neutrophil to lymphocyte ratio.

In clinical practice, the basis for re-examination of CT is to integrate the patient’s clinical symptoms, GCS score, pupil size, degree of consciousness and other aspects. When a patient’s clinical symptoms aggravate, consciousness changes, the pupil dilates and GCS score declines, re-examination of CT is required. Conventional CT has its limitations. Beam-hardening effects, displacement of the CT signal near metal objects, bone, calcifications and high concentrations of contrast can degrade

the image quality and prevent accurate assessment. CT can miss small amounts of blood that occupy widths less than a slice because of volume averaging. CT findings may lag behind actual intracranial damage, so the examinations performed within 3 h of trauma may underestimate injury. In the absence of changes in neurological status, it is still under debate whether CT scans should be repeated after a normal admission CT. The above concerns about CT scan further raise the value of finding novel indicators for the prognosis of TBI patients. However, we do not suggest replacing CT images with NLR completely. NLR is related to the increase in intracranial haematoma and prognosis to assist clinicians in judging the development of the patient’s condition.

Besides inflammatory factors and CT scans, SDH patients were also associated with a more severe presentation and worse clinical outcomes. A possible underlying mechanism may be the effect of local pressure around the tICH. The growth of tICH frequently occurs during the initial hours after trauma and is attributed to continuous bleeding by microvessels that were ruptured at the early injury.<sup>34</sup> The pressure surrounding the tICH decreases significantly during the early stages, resulting in the rupture of microvessels around the tICH. In this study, the novel data showed that NLR is a highly sensitive indicator while even considering SDH in the same statistical model for predicting the early growth of tICH. Another advantage of NLR is that it is more objective than other predictors such as SAH, SDH and the shape of the tICH on a CT scan.



**Figure 2.** NLR level was positively associated with an unfavourable outcome of the patient with TBI. (A) NLR levels in favourable and unfavourable outcome groups. (B) Relationship between the probability of an unfavourable outcome and NLR level after cerebral contusion. NLR, neutrophil to lymphocyte ratio; TBI, traumatic brain injury.

## Conclusions

In this study, we report that the NLR has predictive potential for the early growth of tICH in patients with TBI. NLR can be easily assessed and calculated using routine laboratory tests. It is precise and sensitive for predicting the growth of tICH, demonstrated by the results of ROC test. These findings suggest that NLR raises the intriguing possibility that neuroinflammation plays a role in the progression of tICH and is a novel and prognostic indicator for the growth of tICH.

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## Conflicts of Interest

The authors declare that they have no conflict of interest.

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## Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Figure S1.** Patient selection flow chart. Inclusion and exclusion criteria for selecting patients with TBI for this study.