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Systematic Inflammation Index as Predictors of CT Findings in Pediatric Traumatic Brain Injury: A Retrospective Study

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Background: Pediatric traumatic brain injury (TBI) is a common cause of emergency department (ED) visits. Although head computed tomography (CT) remains the gold standard for the acute evaluation of TBI, it is associated with ionizing radiation exposure. The aim of this study was to evaluate the association between SII and head CT positivity in pediatric patients with TBI.

Methods: This retrospective study included children aged ≤18 years presenting to the emergency department with TBI who underwent head CT. Demographic, clinical, and laboratory data were collected, and SII was calculated from complete blood count parameters. The primary outcome was CT positivity. ROC curve analysis was performed to assess diagnostic performance.

Results: A total of 52 pediatric patients (mean age 13.1 ± 3.4 years) were included, of whom 33 (63.5%) had a positive head CT scan. Median SII was significantly higher in CT-positive patients compared with CT-negative patients [1891 (646–2892) vs 1128 (428–1712); p = 0.025]. ROC analysis demonstrated moderate discriminative ability of SII for predicting CT positivity (AUC 0.687, 95% CI 0.543–0.832). Using the Youden index, the optimal SII cut-off value was 1837.7, yielding a sensitivity of 51.5% and specificity of 89.5%. In multivariable analysis adjusted for age and GCS, SII was not independently associated with CT positivity (p = 0.118).

Conclusions: SII was associated with CT positivity in univariable analysis but not after adjustment, suggesting a potential role as an exploratory adjunctive biomarker. Larger prospective multicenter studies are warranted to clarify the potential role of SII as an adjunct to clinical decision rules in pediatric TBI.

Keywords: pediatric head trauma, traumatic brain injury, biomarkers, systemic immune-inflammation index, neuro-inflammation.

INTRODUCTION

Traumatic brain injury (TBI) remains one of the leading causes of emergency department (ED) visits in the pediatric population [1]. TBI is defined as a disruption of normal brain function resulting from a direct or indirect external force to the head and represents a significant cause of morbidity, mortality, and long-term disability in children aged 1–18 years [2]. Nevertheless, the majority of pediatric TBIs are classified as mild injuries.

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In the ED, computed tomography (CT) remains the fastest and most accurate diagnostic tool for the acute evaluation of TBI [2]. However, CT imaging exposes patients to ionizing radiation, which has been associated with an increased lifetime risk of malignancy, including brain tumors such as gliomas [3,4]. Importantly, the risk of radiation-induced malignancy is inversely related to age, with infants and young children representing the most vulnerable population [4]. It has been estimated that the risk of developing cancer following a head CT scan may be up to ten times higher in children compared with adults undergoing the same examination [5].

Currently, the Pediatric Emergency Care Applied Research Network (PECARN) clinical decision rule is the primary tool used to guide CT utilization in children with mild TBI [6,7]. While PECARN has high sensitivity for identifying clinically significant brain injury, its positive predictive value remains low (approximately 5%), potentially leading to a substantial number of unnecessary CT scans in this population [8].

TBI triggers a complex neuroinflammatory cascade, the prolonged or excessive activation of which may lead to secondary brain injury [9]. In pediatric patients, whose brains are in a critical phase of development, such inflammatory processes may have long-term consequences on neurodevelopmental trajectories and overall functional outcomes [10]. For this reason, early identification of clinically significant brain injury, as well as reliable prediction of its presence without unnecessary exposure to ionizing radiation is of paramount importance.

Over recent years, a wide range of biomarkers related to TBI-associated neuronal damage and outcome prediction have been investigated, including S100B, tau protein, neurofilament light chain, ubiquitin C-terminal hydrolase L1 (UCH-L1), neuron-specific enolase (NSE), and glial fibrillary acidic protein (GFAP) [11]. However, most of these biomarkers are not widely available in routine clinical practice, require specialized assays, or are associated with increased cost and delayed turnaround times.

In contrast, inflammatory indices derived from routine complete blood count testing, such as the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), are immediately available, inexpensive, and easily reproducible [12]. Previous research has demonstrated that neutrophils are among the first immune cells activated following TBI and can be detected in brain tissue within as little as two hours after injury, supporting the biological plausibility of inflammation-based biomarkers in acute brain injury assessment [13].

The systemic immune-inflammation index (SII), which integrates neutrophil, lymphocyte, and platelet counts, represents a composite marker of both immune activation and inflammatory burden [14]. In adult populations, elevated SII values have been associated with worse clinical outcomes in TBI [15]. However, data regarding its role in pediatric populations remain limited [14,16].

The present study aimed to explore the association between SII and head CT positivity in pediatric patients with TBI and to assess its potential role as an adjunctive biomarker for CT findings.

MATERIALS AND METHODS

Study design

We conducted a retrospective, single-center observational study using the medical records of pediatric patients with TBI who presented to the ED between January 1st , 2022, and December 31st, 2025. Fifteen patients (28.8%) from the present cohort were also included in a previous study from our institution [12]

All patients aged ≤18 years who presented to the ED with TBI and had available blood examination results were identified through the hospital electronic database and reviewed. The study was approved by the local institutional review board. Due to the retrospective nature of the study, the requirement for informed consent was waived.

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Inclusion and exclusion criteria

Patients were eligible for inclusion if they had a diagnosis of TBI, were ≤18 years old, underwent a head CT scan, and had complete blood count laboratory results available at the time of ED presentation.

Patients were excluded if they had missed complete blood count data, did not undergo a head CT scan, or if complete medical records could not be retrieved.

Data collection

Medical records of pediatric patients presenting to the ED with TBI were reviewed, and relevant variables were extracted. Collected data included demographic characteristics (age and sex), Glasgow Coma Scale (GCS) score, laboratory parameters (neutrophil count, lymphocyte count, platelet count, and serum glucose), and radiological findings.

The systemic immune-inflammation index (SII) was calculated by multiplying the absolute platelet count by the absolute neutrophil count and dividing by the absolute lymphocyte count.

The primary objective of the present study was to evaluate the association between SII and CT positivity. NLR and PLR were analyzed as supportive inflammatory indices (Supplementary material).

Head CT scan evaluation

Head CT scans were classified as positive when at least one acute traumatic finding, including skull fracture or intracranial traumatic abnormality, was identified. CT positivity was considered a radiological outcome and was not intended to represent PECARN-defined clinically important traumatic brain injury (ciTBI) [2].

Statistical analysis

Continuous variables were summarized as median and interquartile range (Q1, Q3), while categorical variables were presented as counts (n) and percentages. Data normality was assessed using the Shapiro–Wilk test, which demonstrated non-normal distributions (all $p < 0.01$); therefore, non-parametric statistical methods were applied.

Continuous variables were compared using the Mann–Whitney U test, whereas categorical variables were compared using Fisher's exact test. Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the diagnostic performance of SII for CT positivity. The area under the curve (AUC) with 95% confidence intervals (CI) was calculated using the DeLong method. Optimal cut-off values were determined using the Youden index, and corresponding sensitivity and specificity values were reported.

Age, GCS score, and SII were included in the exploratory multivariable logistic regression model. SII was included as the primary biomarker of interest, whereas age and GCS score were included as clinically relevant covariates reflecting patient age and injury severity.

An exploratory subgroup analysis was performed in patients presenting with a GCS score of 15. SII values were compared between CT-positive and CT-negative patients using the Mann–Whitney U test, and ROC analysis was performed to assess discrimination for CT positivity. Given the limited subgroup sample size, no multivariable analysis was performed.

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All statistical analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria) through RStudio (RStudio, PBC). A p-value < 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 52 pediatric patients (13.1 ± 3.4 years) with TBI were included in the analysis. Of these, 33 patients were CT-positive, and 19 patients were CT-negative. The median age was 12 years (11.0–15.0) in the CT-negative group and 13 years (11.0–16.0) in the CT-positive group. The median time from injury to blood sampling was 120 minutes (IQR, 60–120), and 85.1% of patients with available injury-pattern data had isolated trauma.

In the CT-negative group, 21% of patients were female and 79% were male, while in the CT-positive group, 33% were female and 67% were male. Among the 51 patients with available GCS data, 49 had mild TBI and only two patients had severe TBI (GCS scores of 5 and 7), and both were in the CT-positive group (Table 1).

Table 1: Characteristics of the patients and p-values from univariable analyses.

Characteristic	CT negative (N = 19)	CT positive (N = 33*)	p-value
Age, years	12.0 (11.0, 15.0)	13.0 (11.0, 16.0)	0.70
Gender, n (%)			0.50
Female	4 (21%)	11 (33%)	
Male	15 (79%)	22 (67%)	
Neutrophils, $\times 10^9$/L	8.1 (5.1, 10.4)	11.4 (6.7, 13.6)	**0.020**
Lymphocytes, $\times 10^9$/L	2.55 (1.63, 2.98)	1.81 (1.16, 3.20)	0.20
Platelets, $\times 10^9$/L	275 (249, 333)	280 (236, 324)	0.80
SII	1128 (428, 1712)	1891 (646, 2892)	**0.025**
Glucose, mg/dL	101 (91, 111)	107 (93, 117)	0.50
GCS score			**0.028**
5	0	1	
7	0	1	
14	1	11	
15	18	19	

[1]Median (Q1, Q3), n (%)

*GCS data were available for 51 of 52 patients; one patient in the CT-positive group had missing GCS data.

Continuous variables are presented as median (interquartile range) and compared using the Mann–Whitney U test. Categorical variables are presented as number (percentage) and compared using Fisher's exact test. CT: computed tomography; GCS: Glasgow Coma Scale; SII: systemic immune-inflammation index.

Among CT-positive patients, skull fractures were the most common abnormality (n = 26, 78.8%), followed by acute subdural hematoma (n = 4, 12.1%), cerebral contusion (n = 3, 9.1%), epidural hematoma (n = 2, 6.1%), subarachnoid hemorrhage (n = 2, 6.1%), pneumocephalus (n = 2, 6.1%), and diffuse axonal injury (n = 1, 3.0%) (Table 2). Multiple CT abnormalities coexisted in 7 patients.

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Table 2: Computed Tomography (CT) findings in the CT-positive group

CT findings among CT-positive patients (n=33)	
Skull fracture	26 (78.8%)
Acute subdural hematoma	4 (12.1%)
Cerebral contusion	3 (9.1%)
Epidural hematoma	2 (6.1%)
Subarachnoid hemorrhage	2 (6.1%)
Pneumocephalus	2 (6.1%)
Diffuse axonal injury	1 (3.0%)
Not available	1 (3.0%)

CT findings were recorded separately and were not mutually exclusive. Patients with multiple CT abnormalities were included in each applicable category, and percentages do not sum to 100%. Percentages were calculated using all CT-positive patients (n=33) as the denominator.

Univariable and Multivariable Comparisons Between CT-Negative and CT-Positive Groups

Univariable Analysis – Association of SII and CT result

Univariable analysis demonstrated that SII was significantly higher in CT-positive patients than in CT-negative patients. Median SII was 1891 (646–2892) in CT-positive patients compared with 1128 (428–1712) in CT-negative patients (p = 0.025) (Table 1).

GCS scores were slightly lower in the CT-positive group and showed a statistically significant difference between groups (p = 0.028), although median values were similar, reflecting the narrow distribution of GCS in this predominantly mild TBI cohort (Table 1).

Multivariable Analysis

In the exploratory multivariable logistic regression analysis including age, GCS score, and SII. One patient was excluded because of missing GCS data. GCS score was associated with CT positivity (OR 0.11, 95% CI 0.005–0.69, p = 0.049). Age was not independently associated with CT positivity (OR 0.90, 95% CI 0.72–1.09, p = 0.30). SII was also not an independent predictor after adjustment (OR 1.0005, 95% CI 0.9999–1.0013, p = 0.12) (Table 3 and Figure 1).

Table 3: Multivariable logistic regression analysis for CT positivity

OR: odds ratio; CI: confidence interval; GCS: Glasgow Coma Scale; SII: systemic immune-inflammation index

Variable	**OR**	**95% CI**	**p-value**
GCS score	0.11	0.005–0.69	**0.049**
Age, years	0.90	0.72–1.09	0.30
SII	1.0005	0.9999–1.0013	0.12

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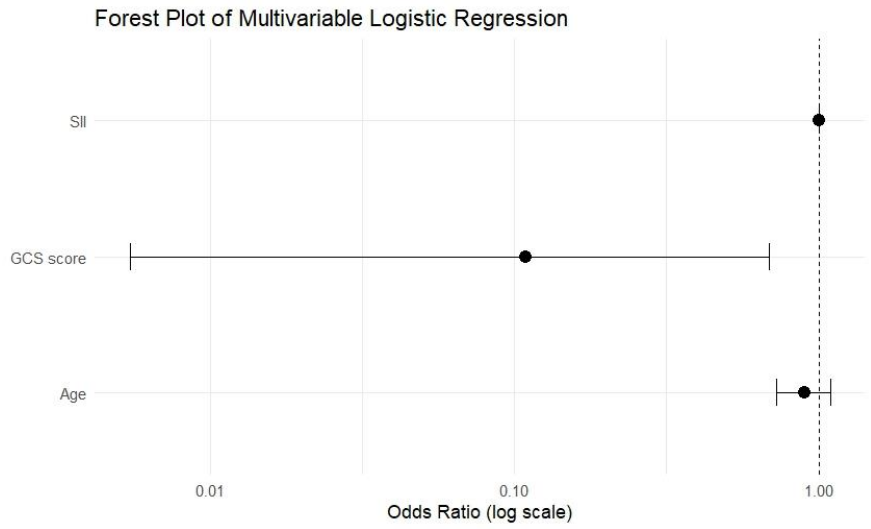

Figure 1: Forest plot of multivariable logistic regression analysis for predictors of CT positivity. The model included age, GCS score, and SII. Odds ratios (ORs) with 95% confidence intervals are shown on a logarithmic scale. The dashed vertical line indicates OR =1

ROC analysis and cut-off value for SII

ROC analysis demonstrated moderate discriminative ability for SII predicting CT positivity with an AUC of 0.687 (95% CI 0.543–0.832).

Using the Youden index, the optimal cut-off value for SII was 1837.7, yielding a sensitivity of 51.5%, a specificity of 89.5% , positive predictive value of 89.5%, and negative predictive value of 51.5% for predicting CT positivity (Figure 2).

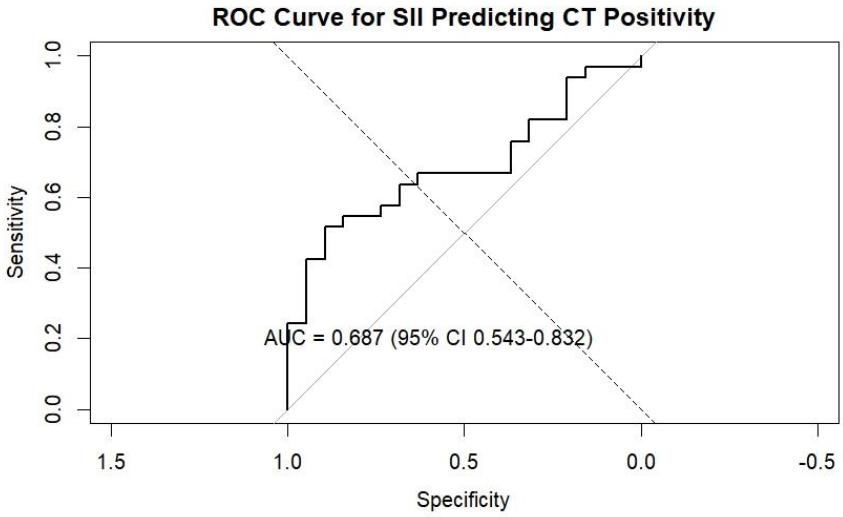

Figure 2: Receiver operating characteristic (ROC) curve for the SII in predicting head CT positivity in pediatric traumatic brain injury. The AUC was 0.687 (95% CI 0.543–0.832), indicating moderate discriminative ability. The optimal cut-off value determined by the Youden index was 1837.7, yielding a sensitivity of 51.5% and specificity of 89.5%

Subgrouping analysis

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In an exploratory subgroup analysis restricted to patients with a GCS score of 15 (n = 37), median SII was higher in CT-positive compared with CT-negative patients [1445 (408–2411) vs 1117 (434–1677), respectively], although the difference was not statistically significant (p = 0.438). ROC analysis demonstrated limited discriminative ability (AUC 0.576, 95% CI 0.385–0.768). The optimal Youden-derived SII threshold was 1837.7, yielding a sensitivity of 36.8%, specificity of 88.9%, positive predictive value of 77.8%, and negative predictive value of 57.1% (Figure 3).

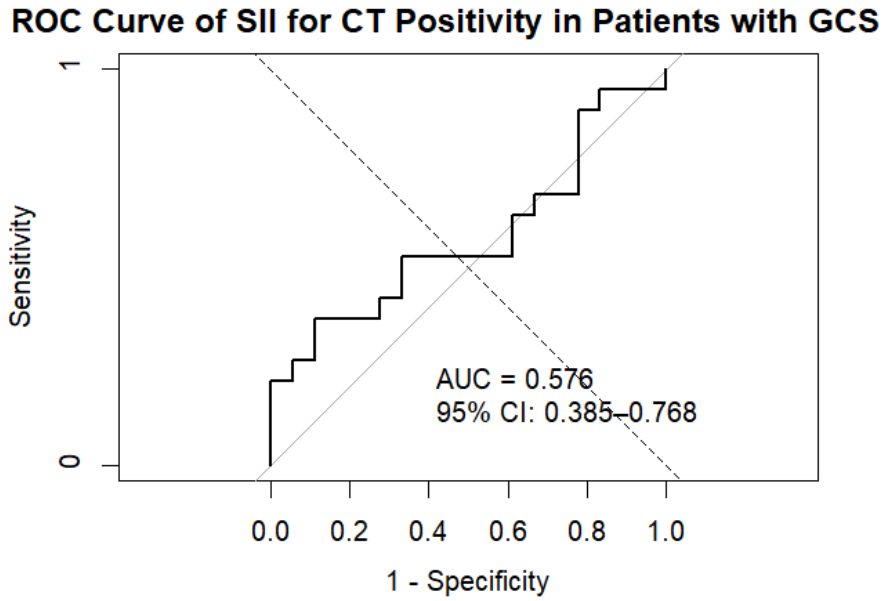

Figure 3: Receiver operating characteristic (ROC) curve for the SII in predicting head CT positivity in patients with GCS 15/15. The AUC was 0.576 (95% CI 0.385-0.768), indicating moderate discriminative ability. The optimal cut-off value determined by the Youden index was 1837.7, yielding a sensitivity of 36.8% and specificity of 88.9%

DISCUSSION

In this retrospective cohort, we evaluated the potential role of the SII as a biomarker for predicting head CT positivity in pediatric patients with TBI. While the PECARN clinical decision rule remains the cornerstone of clinical triage in pediatric mild TBI, it primarily provides guidance on whether CT imaging is indicated and does not incorporate biological markers of injury or inflammation [6-8]. As a result, reliance on clinical criteria alone may contribute to a substantial number of unnecessary CT scans, exposing children to radiation without clear clinical benefit [17]. Therefore, there is a growing need to identify novel, readily available biomarkers that could be integrated into clinical decision tools to improve risk stratification and potentially reduce unnecessary imaging.

Over the past several years, multiple biomarkers and inflammatory indices have been proposed for this purpose. Among the most widely studied are the NLR and serum glucose, largely due to their immediacy, low cost, rapid availability, and widespread use in routine clinical practice [18]. In addition, several brain-specific biomarkers been investigated and of these, S100B and GFAP have shown particular promise and have been used in selected settings to help identify low-risk patients who may safely avoid CT imaging [4,19].

SII has been only sparsely investigated in pediatric populations, and data on its role in pediatric TBI is limited [14,16]. Prior studies have primarily focused on adult cohorts or on clinical outcomes rather than CT findings. In one pediatric study including 206 patients, inflammatory indices, including SII, differed significantly across injury severity categories (mild, moderate, and severe TBI). However, SII was not significantly associated with clinical outcomes [14]. These findings suggest that SII may reflect injury

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burden and systemic inflammatory activation, but its diagnostic and prognostic utility in children remains incompletely defined.

In the present study, SII was significantly higher in CT-positive patients in univariable analysis and demonstrated moderate discriminative ability in ROC analysis (AUC 0.687, 95% CI 0.543–0.832). Using the Youden index, we identified an optimal SII cut-off value of 1837.7, which yielded a sensitivity of 51.5% and a specificity of 89.5% for predicting CT positivity. However, the relatively low sensitivity (51.5%) and negative predictive value (51.5%) indicate that SII cannot be used as a stand-alone rule-out marker to safely withhold CT imaging. These findings suggest a potential association between SII and traumatic CT abnormalities. However, in multivariable logistic regression adjusting for GCS score and age, SII did not remain independently associated with CT positivity. This suggests that SII may primarily reflect injury severity and systemic inflammatory response rather than provide substantial incremental diagnostic value beyond established clinical predictors such as GCS.

Nevertheless, the potential clinical value of SII may lie in identifying patients with a higher probability of radiologically detectable traumatic abnormalities. This may be particularly relevant in patients with a normal GCS (15/15) and clinical uncertainty regarding the need for CT imaging. In this context, elevated SII could potentially serve as an adjunctive marker of underlying traumatic pathology, even in the absence of reduction in GCS. To explore this hypothesis, we performed an exploratory analysis restricted to patients with GCS 15. In this subgroup, SII did not significantly differ between CT-positive and CT-negative patients and showed limited overall discriminative performance. However, high SII values retained relatively high specificity for CT positivity. Given the small sample size and low sensitivity, this finding should be considered hypothesis-generating and requires validation in larger prospective cohorts.

Importantly, 15 patients (28.8%) from the present cohort were also included in a previously published retrospective study from our institution that focused on other inflammatory indices, including NLR, PLR, and serum glucose [12]. In that prior analysis, children with positive CT demonstrated higher NLR values while PLR and glucose showed no significant associations [12]. In the present study, we aimed to extend these prior findings by evaluating SII as the primary inflammatory biomarker of interest. Accordingly, other indices were not emphasized in the current results in order to minimize overlap with prior publications derived from a similar institutional cohort and highlights the unique contribution of the present analysis.

Age-related physiological differences in leukocyte differentials should also be considered when interpreting inflammatory indices in pediatric populations. Younger children may exhibit relative lymphocyte predominance compared with older children and adults, a phenomenon known as leukocyte differential reversal [20]. Although only a small proportion of patients in the present cohort were younger than 10 years of age, this physiological variation may influence SII values and could contribute to inter-individual variability. This underscores the importance of age-specific interpretation of inflammatory biomarkers in pediatric TBI [14]. A recent study revealed significant age-related variation in inflammatory biomarkers, emphasizing the necessity for age-specific reference values in children and supporting cautious interpretation of indices such as SII in pediatric TBI [16].

In addition to blood-based biomarkers, artificial intelligence (AI)–based triage models have recently gained increasing attention for the prediction of the need for head CT in pediatric TBI [21]. Recent studies have demonstrated promising results using machine learning algorithms to support clinical decision-making [22,23]. A recently developed AI-based model demonstrated over 90% accuracy in predicting the need for CT scanning among pediatric patients in a cohort exceeding 1,100 children [24]

Despite these encouraging findings, most currently available AI models lack sufficient external validation and are often derived from single-center or limited datasets [21]. Furthermore, their performance may be affected by data quality, missing variables, and heterogeneity in clinical practice across institutions [25]. Therefore, large multicenter studies with standardized data collection are required before such models can be widely implemented in routine clinical care.

Overall, our findings suggest that SII is associated with CT positivity in univariable analysis and demonstrates moderate diagnostic performance, but it does not independently predict CT findings after

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adjustment for key clinical variables. Future larger, multicenter prospective studies are needed to clarify whether SII may provide additive value when combined with clinical decision rules and to determine its potential role in reducing unnecessary CT imaging in pediatric TBI.

Limitations

This study has several important limitations that should be acknowledged. First, it was a retrospective, single-center analysis with a relatively small sample size, including only 52 pediatric patients, of whom 33 had positive CT findings. This limited sample size reduces statistical power and may partially explain why SII did not remain an independent predictor of CT positivity in multivariable analysis. In addition, the small cohort precluded more detailed subgroup analyses based on age, injury mechanism, or traumatic brain injury severity. Furthermore, CT positivity represented a heterogeneous radiological outcome, including both skull fractures and intracranial traumatic abnormalities, and should not be considered equivalent to PECARN-defined ciTBI. The high proportion of CT-positive patients likely reflects, at least in part, retrospective patient selection and potential spectrum bias, limiting the generalizability of our findings.

Second, 28.8% of the study population overlapped with a previously published cohort from our institution, which focused on other inflammatory indices. However, the present study addressed a distinct research question, with SII evaluated as the primary biomarker of interest, thereby minimizing methodological and analytical overlap with earlier investigations. Moreover, the study included only patients who underwent CT, potentially introducing selection bias, as children deemed low risk and not imaged were excluded.

Age-related physiological differences in leukocyte distributions may also influence SII values in pediatric patients. Although most patients in this cohort were older children and adolescents, age-specific reference ranges for SII were not applied, which may contribute to inter-individual variability and limit interpretability.

CONCLUSION

In this single–center cohort we find that the SII was significantly higher in children with positive head CT findings and demonstrated moderate discriminative ability for predicting CT positivity.

However, SII did not remain an independent predictor of CT positivity after adjustment for established clinical variables, particularly Glasgow Coma Scale score, suggesting that its role is more reflective of injury severity and systemic inflammation rather than a standalone diagnostic marker. Accordingly, SII should be viewed as a supportive biomarker rather than a replacement for established clinical decision rules.

Given its wide availability, low cost, and rapid turnaround, SII may have potential value as an adjunct to clinical assessment by identifying patients with a higher probability of traumatic CT findings. This potential role may be particularly relevant among patients presenting with GCS 15, although our exploratory subgroup analysis was underpowered to establish clinical utility. Future large, prospective, multicenter studies are needed to determine whether SII can provide incremental benefit when combined with validated clinical decision tools and to clarify its role in reducing unnecessary CT imaging while maintaining patient safety.

DISCLOSURES

Ethical approval

This study was performed in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board of the University Hospital of Ioannina (protocol code 28/22-11-2023, item 6; approval number 1/22-1-2020, item 24).

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Consent to participate

Due to the retrospective nature of the study and the use of anonymized patient data, the requirement for informed consent was waived by the Institutional Review Board.

Conflict of interest

Not applicable. The manuscript does not contain identifiable personal information or identifiable patient images**.**

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Artificial intelligence

Artificial intelligence tools were used solely to assist with language editing and improvement of clarity and readability.

CONTRIBUTIONS

Eleni Romeo: Conceptualization; Methodology; Data curation; Formal analysis; Investigation; Writing – original draft; Writing – review & editing.

George A. Alexiou: Conceptualization; Methodology; Project administration; Supervision; Validation; Writing – original draft; Writing – review & editing.

Spyridon Voulgaris: Supervision; Validation; Writing – review & editing.

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