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CORRELATION BETWEEN SYSTEMIC IMMUNE INFLAMMATION INDEX AND SEVERITY OF ACUTE ISCHEMIC STROKE

Neurology

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ABSTRACT

Background: Systemic immune inflammation index is a novel marker of peripheral inflammation used to assess multiple diseases. Accumulating evidence demonstrates that inflammation plays a key role in the pathogenesis of stroke. **Aim:** This study aims to assess its usefulness in validating the severity of stroke at the onset and its usefulness in prognosticating the patient on day 1. **Discussion:** From our study, we were able to identify that the mean SII increased with the increasing severity of stroke.All patients were assessed at 2 weeks post stroke, graded with MRS and classified into those with favourable and unfavourable outcome.According to the SII formula. the more the neutrophils the higher is SII value which equates to higher neutrophil count predicting increased stroke severity and poor functional outcome. Increase in platelets contribute to the increase in SII value which converts to a predictor of increased stroke severity or poorer outcome & increase in lymphocyte count is a sign of less severe stroke and good functional outcome. Through an analysis of peripheral blood counts, including neutrophils, lymphocytes, and platelets, SII provides a quantitative measure of the systemic inflammatory response, which is a key determinant of stroke outcomes. **Conclusion:** In the present study, we evaluated the relation between SII and stroke severity and prognosis. We found that statistically significant differences in SII among subgroups as defined by NIHSS scores. Also, SII was the significant predictor of early functional outcomes at discharge in patients with AIS.

KEYWORDS

AIS - Acute ischemic stroke, NIHSS- National institute of health stroke scale , SII Systemic inflammatory index ,MRS- Modified Rankin scale.

Introduction:
Stroke is one of the leading cause of death and disability. According to the most recent Global Burden of Disease (GBD) estimates, there were around 12.2 million incident cases of stroke, 143 million disabilityadjusted life-years (DALYs) lost, and 6.6 million deaths globally in 2019, making stroke the second leading cause of death and third leading cause of disability worldwide(1). The cumulative incidence of stroke in India ranges from 105 to 152/100,000 persons per year, and the crude prevalence of stroke ranges from 44.29 to 559/100,000 persons in different parts of the country during the past decade.(2). About 87% of all stroke are ischemic (3).

Accumulating evidence demonstrates that inflammation plays a key role in the pathogenesis of stroke (4). Peripheral markers of inflammation in stroke has been analysed in various studies to assess the severity and prognostication of stroke. Systemic immune inflammation index is a novel marker of peripheral inflammation used to assess multiple diseases. It's use in Acute ischemic stroke has been relatively recent.

Aim :
This study aims to assess its usefulness in validating the severity of stroke at the onset and its usefulness in prognosticating the patient on day 1.

Methodology :
Study setting:
The study was done in Madras Institute of Neurology, Rajiv Gandhi Government General Hospital. It was a retrospective and prospective study enrolling patients with acute ischemic stroke for the first time

Study population:
Inclusion criteria:
Age more than 18 years, Patients admitted with arterial ischemic stroke, as proven by neuroimaging within 24 hours of onset of illness.

Exclusion criteria: Patients with history of fever in the past 2 weeks, patients with previous history of stroke.

A total of data from 227 patients were collected.

Data collection:
The data collected were obtained from medical records both retrospectively and prospectively . At baseline, demographic data (age and sex), history of vascular risk factors (including hypertension, diabetes mellitus, atrial fibrillation, smoking, and drinking), systolic blood pressure (SBP), diastolic blood pressure (DBP), treatment after admission (antiplatelet, anticoagulation, thrombolysis therapy) were obtained. Hematological markers, including white blood count (W), neutrophil count (N), lymphocyte count (L), platelet (P), and monocyte count (M), were assessed. These counts were used to calculate systemic immune-inflammation index (SII =P×[N/L]).

The National Institutes of Health Stroke Scale (NIHSS) was used to evaluate the stroke severity within 24 hours after admission, which ranged from 0 to 42 and the higher the score, the more severe the disease was. Mild stroke was defined as NIHSS scores<5, moderate stroke as 5 to 15, moderate to severe as 16 to 20 and severe stroke as 21 to 42. The functional outcome were assessed by the modified Rankin scale (mRS) at 2 weeks (favorable outcome, mRS score ≤2; poor outcomes, scores >2).

Statistical analysis: Statistical analysis was performed using SPSS 22.0 software. Normally distributed data were expressed as mean ± SD. Comparison between groups was performed by MannWhitney U test, chi-square test where appropriate. Receiver operating characteristic (ROC) analysis was performed to identity the optimal cut-off values of SII for discrimination of clinical outcome after stroke. P value <0.05 were considered as statistically significant.

Results and analysis:
The basic demographic data of the study population are tabulated in the tables. Based on figure 1, people with minor stroke were 51% and strokes of more than minor severity were 49%.

Table 1

PARAMETERS	MEAN	SD
AGE	56.60	14.392
WBC	8.641	9.1924
NEUTROPHILS	5.253	1.4672

LYMPHOCYTES	2.177	0.3276
PLATELETS	219.20	63.271
SII	544.69	239.42
NIHSS	6.84	4.780
MRS	3.29	1.189

Table 2

	NUMBER OF PATIENTS	PERCENTAGE
MALE	165	73%
FEMALE	60	27%
SHT	156	69%
DM	81	36%
AF	36	16%
CAD	75	33%
SMOKING	153	68%
ALCOHOLIC	102	45%
ANTIPLATELETS	183	81%
ANTICOAGULANTS	42	19%
THROMBOLYSIS	18	8%

Table 3

NIHSS SEVERITY	NUMBER OF PATIENTS	PERCENTAGE
MINOR STROKE	114	51%
MODERATE STROKE	99	44%
MODERATE TO SEVERE STROKE	9	4%
SEVERE STROKE	3	1%

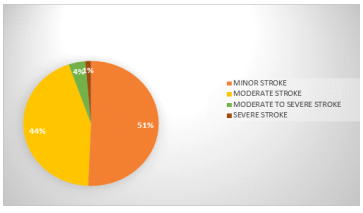

Figure 1

Table 4

MRS AT 2 WEEKS	NUMBER OF PATIENTS	PERCENTAGE
FAVOURABLE	72	32%
UNFAVOURABLE	153	68%

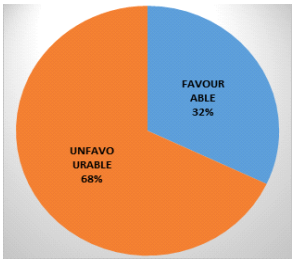

Figure 2

Association between SII and severity of stroke:

From our study, we were able to identify that the mean SII increased with the increasing severity of stroke as we can see in table and figure 3, being 354.97 for minor stroke , 736.21 for moderate stroke, 826.42 for moderate to severe stroke and 589.04 for severe stroke. The difference in mean SII between all 4 grades were statistically significant, tested by anova test(p value- 0.001)(Table 6). The lesser mean SII in severe stroke when compared to moderate and moderate to severe stroke could be probably due to limited data. The mean SII for minor stroke was 354.97, whereas the mean SII for all other stroke grades were 739.54. This difference was also statistically significant tested by unpaired t test (p value- 0.001). We had also found a positive correlation between increasing SII and stroke severity. This was tested by spearman's correlation test and the correlation coefficient was 0.695(Table 8),with positive correlation being greater than 0.5. ROC curve was constructed to determine the value of SII above which the severity of stroke increased and this was found to be 551.79.

Table 5- Mean SII in various stroke severities

NIHSS STROKE SEVERITY	SYSTEMIC IMMUNE INFLAMMATION INDEX	
	MEAN	SD
MINOR STROKE	354.97	75.52
MODERATE STROKE	736.21	193.73
MODERATE TO SEVERE STROKE	826.42	88.57
SEVERE STROKE	589.04	0
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		

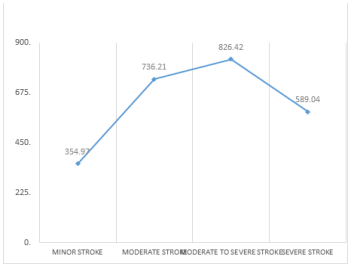

Figure 3

Table 6- Difference in Mean SII in minor versus other strokes

	SYSTEMIC IMMUNE INFLAMMATION INDEX	
	MEAN	SD
MINOR (<5)	354.97	75.52
OTHERS (>5)	739.54	187.75
UNPAIRED T TEST		
P VALUE - 0.001		
SIGNIFICANT		

Association between SII and functional outcome at 2 weeks:

All patients were assessed at 2 weeks post stroke, graded with MRS and classified into those with favourable and unfavourable outcome. Mean MRS of patients with favourable outcome was 364.79 and for those with unfavourable MRS or poor functional outcome was 629.35. This difference was analysed by unpaired t test and was found to be statistically significant(p value 0.001)(Table 7). There was also a significant positive correlation between higher SII and poor functional outcome at 2 weeks as analysed by spearman correlation with a correlation coefficient of 0.752, (Table 8). An ROC curve was also constructed to find the cutoff value of SII above which patients had a poor outcome and this was at 385.4. This cutoff value was considerably lesser than the cutoff value of SII above which patients had a severe stroke.

Table 7- Mean SII in favourable and unfavourable outcome.

MRS AT 2 WEEKS	SYSTEMIC IMMUNE INFLAMMATION INDEX	
	MEAN	SD
FAVOURABLE	364.79	71.92
UNFAVOURABLE	629.35	243.95
UNPAIRED T TEST		
P VALUE - 0.001		
SIGNIFICANT		

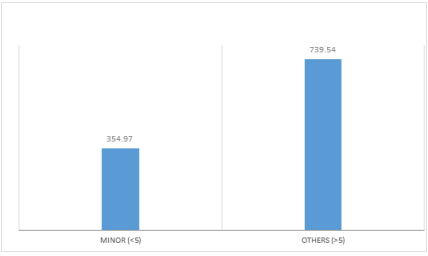

Figure 4- Mean SII in minor stroke versus others

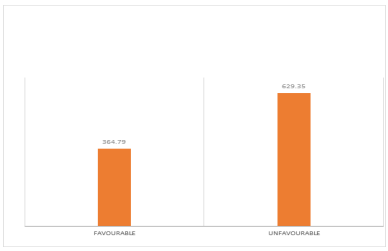

Figure 5 - Mean SII in patients with favourable MRS versus unfavorable MRS

Table 8

SPEARMAN CORRELATION		NIHSS	MRS
SII	Correlation Coefficient	.695**	.752**
	Sig. (2-tailed)	0.000	0.000
	N	225	225

Discussion:

In the present study, we evaluated the relation between SII and stroke severity and prognosis. We found that statistically significant differences in SII among subgroups as defined by NIHSS scores. Also, SII was the significant predictor of early functional outcomes at discharge in patients with AIS.

Firstly we would like to analyse the role of neutrophils, platelets and lymphocytes in acute stroke pathophysiology and why do they correspondingly increase or decrease contributing to a increased SII.

Role of neutrophils in acute ischemic stroke:

Neutrophils play a significant role in the pathophysiology of acute ischemic stroke. Their involvement includes both beneficial and detrimental aspects, and their count typically increases in response to the stroke event. They are the first responders to tissue injury, including ischemic stroke. They migrate to the site of damage and release pro-inflammatory mediators, contributing to the initial inflammatory cascade(5) In acute ischemic stroke, there is a notable increase in circulating neutrophil counts. This elevation is part of the immune response aimed at clearing debris, combating pathogens, and initiating tissue repair processes (6).They can release neutrophil extracellular traps, which are web-like structures composed of DNA, histones, and antimicrobial proteins. While NETs can trap pathogens, they can also contribute to tissue damage and exacerbate inflammation in stroke (7). Upon recruitment to the ischemic brain tissue, neutrophils become activated and release a variety of inflammatory mediators, including cytokines, chemokines, and reactive oxygen species (ROS). These molecules contribute to the inflammatory cascade and tissue damage(7). They can also interact with endothelial cells and contribute to blood-brain barrier disruption, allowing immune cells and molecules to enter the brain parenchyma and exacerbate neuronal injury (8). While neutrophils contribute to tissue damage through their inflammatory actions, they also play a role in tissue repair and remodeling by clearing cellular debris and modulating immune responses(9). According to the SII formula. the more the neutrophils the higher is SII value which equates to higher neutrophil count predicting increased stroke severity and poor functional outcome.

Role of platelets in acute ischemic stroke:

Platelets play a critical role in the pathophysiology of acute ischemic stroke, particularly in the formation of thrombi that can occlude cerebral arteries and lead to ischemic injury(10). It is clear that platelets are increased in ischemic stroke due to their pivotal role in thrombus formation and vascular occlusion. The activation and aggregation of platelets contribute significantly to the pathophysiology of ischemic stroke, leading to increased platelet counts in response to the vascular insult. Understanding platelet biology and their involvement in vascular diseases like ischemic stroke is essential for developing targeted interventions and improving patient outcomes(11). Thrombo-inflammation refers to the interplay between thrombotic processes and inflammatory responses in stroke, where platelets, leukocytes, and endothelial cells contribute to both clot formation and inflammatory cascades(12).Following vascular injury or endothelial dysfunction in ischemic stroke, platelets become activated and aggregate at the site of injury, forming a primary hemostatic plug that can evolve into a thrombus(13). Activated platelets release pro-inflammatory mediators such as thromboxane A2, P-selectin, and cytokines, contributing to the recruitment and activation of immune cells and amplifying the inflammatory response(14).While platelets are essential for initial clot formation, their persistence in the thrombus can impede thrombus resolution and contribute to reperfusion injury during thrombolytic or endovascular treatments(15). Increase in platelets contribute to the increase in SII value which converts to a predictor of increased stroke severity or poorer outcome.

Role of lymphocytes in acute ischemic stroke:

Lymphocytes, including T cells and B cells, play a crucial role in the adaptive immune response. They contribute to the resolution of inflammation, tissue repair, and modulation of the immune system post-stroke(16). During the acute phase of ischemic stroke, there is often a decrease in peripheral blood lymphocyte counts. This decrease is attributed to lymphocyte redistribution, apoptosis, and stress-related immunosuppression following the stroke event(17). They also exert immunomodulatory effects post-stroke by regulating the balance between pro-inflammatory and anti-inflammatory processes, which can influence the extent of tissue damage and functional recovery(18). Specific subsets of lymphocytes, such as regulatory T cells (Tregs), have been associated with better stroke outcomes by dampening excessive inflammation and promoting tissue repair mechanisms(19). Thereby increase in lymphocyte count is a sign of less severe stroke and good functional outcome.

Review of literature:

Association between SII and stroke severity:

SII was significantly higher in moderate-to-severe group than in the mild stroke group [932.73 vs. 581.21 P <0.001 in a study by Huang et al (20). Wei at al and Weng et all also in their studies found a positive association between SII and NIHSS (21,22). These are concordance with our study. Acar et al in his study had researched on the usefulness of SII as not only a predictor of severity but also a predictor of successful and unsuccessful reperfusion after thrombectomy (23).

A case control analysis done in Turkey revealed a higher SII in acute ischemic stroke patients vs normal population and also high SII was associated with a high risk of mortality (24). We did not have a control arm in our study and analysed only the differences in mean SII of various grades of stroke patients. A control arm could have analysed if there is any significant difference in mean SII between minor stroke patients and normal population. A study by Fei et al corroborate that higher SIRI, SII, and Inflammatory prognosis index values indicate greater disease severity at admission and an increased incidence of poor outcomes at 90-day prognosis. They however found that SII was less accurate than the other two parameters in predicting stroke severity and outcome(25). In our study our main goal was to analyse SII and did not analyse other indices. Wu et al in their study concluded that Elevated SII of patients with acute ischemic stroke increased the risk of 30-day all-cause mortality (26).

Association between SII and functional outcome:

Comparative analyses have demonstrated that SII may outperform traditional prognostic factors in predicting stroke severity, including age, comorbidities, and initial neurological status(27). In a study by Zhou et al, SII was an independent risk factor for 90-day adverse outcomes in stroke patients (28).

Similar results of higher SII predicting unfavourable outcome at 3 months was also identified by weng et al (22). This was a limitation in our study as we had only assessed functional outcome at 2 weeks and did not have a long term follow up. According to a Taiwanese study Common significant predictors of in-hospital complications and unfavorable outcomes were age > 72 years, female sex, NIHSS > 4, diabetes mellitus, and three immune-inflammatory markers, namely SII > 651, NLR > 2.9, and NC > 7.2 × 103/mL. (29). Cut off for unfavourable outcome at 3 months had been 504.99 in a study by Wei et al (21).Research done by Wang et al had revealed that patients with higher SIIs after an acute ischemic stroke were more likely to have poor functional outcomes at the 90-day and 1-year follow-ups. Furthermore, patients with higher SIIs were more likely to experience all-cause death and recurrent stroke (30). A meta analysis by Han et al had also established the predictive capacity of higher SII with poorer outcome (31).

In summary, the Systemic Immune Inflammation Index (SII) has

demonstrated consistent associations with stroke severity in multiple studies, highlighting its potential as a valuable prognostic tool for risk assessment and treatment planning in acute ischemic stroke patients.

Conclusion:

The Systemic Immune-Inflammation Index (SII) has emerged as a valuable biomarker in the context of acute ischemic stroke, offering insights into the complex interplay between systemic inflammation and stroke pathophysiology. Through an analysis of peripheral blood counts, including neutrophils, lymphocytes, and platelets, SII provides a quantitative measure of the systemic inflammatory response, which is a key determinant of stroke outcomes. The prognostic utility of SII extends beyond traditional risk factors, highlighting its potential as a simple yet effective tool for risk stratification, treatment decision-making, and post-stroke management. Incorporating SII into clinical practice may enhance the ability to identify high-risk patients early, allowing for timely interventions and optimized care pathways. Further research is warranted to validate the clinical utility of SII across diverse patient populations, explore its role in guiding therapeutic strategies, and elucidate the underlying mechanisms linking systemic inflammation to stroke outcomes. By leveraging the insights provided by SII, clinicians can improve risk assessment, prognostication, and ultimately, the overall care and outcomes of patients with acute ischemic stroke.

REFERENCES:

1. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2021 Oct;20(10):795-820. doi: 10.1016/S1474-4422(21)00252-0. Epub 2021 Sep 3. PMID: 34487721; PMCID: PMC8443449.
2. Kamalakannan S, Gudlavalleti ASV, Gudlavalleti VSM, Goenka S, Kuper H. Incidence & prevalence of stroke in India: A systematic review. Indian J Med Res. 2017 Aug;146(2):175-185. doi: 10.4103/ijmr.IJMR_516_15. PMID: 29265018; PMCID: PMC5761027.
3. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, Baker-Smith CM, Beaton AZ, Boehme AK, Buxton AE, Commodore-Mensah Y, Elkind MSV, Evenson KR, Eze-Nliam C, Fugar S, Generoso G, Heard DG, Hiremath S, Ho JE, Kalani R, Kazi DS, Ko D, Levine DA, Liu J, Ma J, Magnani JW, Michos ED, Mussolino ME, Navaneethan SD, Parikh NI, Poudel R, Rezk-Hanna M, Roth GA, Shah NS, St-Onge MP, Thacker EL, Virani SS, Voeks JH, Wang NY, Wong ND, Wong SS, Yaffe K, Martin SS; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. Circulation. 2023 Feb 21;147(8):e93-e621. doi: 10.1161/CIR.0000000000001123. Epub 2023 Jan 25. Erratum in: Circulation. 2023 Feb 21;147(8):e622. Erratum in: Circulation. 2023 Jul 25;148(4):e4. PMID: 36695182.
4. Jayaraj, R.L., Azimullah, S., Beiram, R. et al. Neuroinflammation: friend and foe for ischemic stroke. J Neuroinflammation 16, 142 (2019). https://doi.org/10.1186/s12974-019-1516-2.
5. Gelderblom M, Weymar A, Bernreuther C, Velden J, Arunachalam P, Steinbach K, Orthey E, Arumugam TV, Leypoldt F, Simova O, Thom V, Friese MA, Prinz I, Hölscher C, Glatzel M, Korn T, Gerloff C, Tolosa E, Magnus T. Neutralization of the IL-17 axis diminishes neutrophil invasion and protects from ischemic stroke. Blood. 2012 Nov 1;120(18):3793-802. doi: 10.1182/blood-2012-02-412726. Epub 2012 Sep 13. PMID: 22976954.
6. Wang L, Song Q, Wang C, Wu S, Deng L, Li Y, Zheng L, Liu M. Neutrophil to lymphocyte ratio predicts poor outcomes after acute ischemic stroke: A cohort study and systematic review. J Neurol Sci. 2019 Nov 15;406:116445. doi: 10.1016/j.jns.2019.116445. Epub 2019 Aug 31. PMID: 31521961.
7. Zhang S, Cao Y, Du J, Liu H, Chen X, Li M, Xiang M, Wang C, Wu X, Liu L, Wang C, Wu Y, Li Z, Fang S, Shi J, Wang L. Neutrophil extracellular traps contribute to tissue plasminogen activator resistance in acute ischemic stroke. FASEB J. 2021 Sep;35(9):e21835. doi: 10.1096/fj.202100471RR. PMID: 34449927.
8. Huang Y, Chen S, Luo Y, Han Z. Crosstalk between Inflammation and the BBB in Stroke. Curr Neuropharmacol. 2020;18(12):1227-1236. doi: 10.2174/1570159X18666200620230321. PMID: 32562523; PMCID: PMC7770647.
9. Iadecola C, Anrather J. The immunology of stroke: from mechanisms to translation. Nat Med. 2011 Jul 7;17(7):796-808. doi: 10.1038/nm.2399. PMID: 21738161; PMCID: PMC3137275.
10. del Zoppo GJ. The role of platelets in ischemic stroke. Neurology. 1998 Sep;51(3 Suppl 3):S9-14. doi: 10.1212/wnl.51.3_suppl_3.s9. PMID: 9744824.
11. Lebas H, Yahiaoui K, Martos R, Boulaftali Y. Platelets Are at the Nexus of Vascular Diseases. Front Cardiovasc Med. 2019 Sep 11;6:132. doi: 10.3389/fcvm.2019.00132. PMID: 31572732; PMCID: PMC6749018.
12. Stoll G, Nieswandt B. Thrombo-inflammation in acute ischaemic stroke - implications for treatment. Nat Rev Neurol. 2019 Aug;15(8):473-481. doi: 10.1038/s41582-019-0221-1. Epub 2019 Jul 1. PMID: 31263257.
13. Nieswandt B, Pleines I, Bender M. Platelet adhesion and activation mechanisms in arterial thrombosis and ischaemic stroke. J Thromb Haemost. 2011 Jul;9 Suppl 1:92-104. doi: 10.1111/j.1538-7836.2011.04361.x. PMID: 21781245.
14. Mereweather LJ, Constantinescu-Bercu A, Crawley JTB, Salles-Crawley II. Platelet-Neutrophil Crosstalk in Thrombosis. Int J Mol Sci. 2023 Jan 9;24(2):1266. doi: 10.3390/ijms24021266. PMID: 36674781; PMCID: PMC9861587.
15. Ho-Tin-Noé B, Desilles JP, Mazighi M. Thrombus composition and thrombolysis resistance in stroke. Res Pract Thromb Haemost. 2023 May 16;7(4):100178. doi: 10.1016/j.rpth.2023.100178. PMID: 37538503; PMCID: PMC10394565.
16. Malone MK, Ujas TA, Britsch DRS, Cotter KM, Poinsatte K, Stowe AM. The immunopathology of B lymphocytes during stroke-induced injury and repair. Semin Immunopathol. 2023 May;45(3):315-327. doi: 10.1007/s00281-022-00971-3. Epub 2022 Nov 29. PMID: 36446955; PMCID: PMC9708141.
17. Juli C, Heryaman H, Nazir A, Ang ET, Defi IR, Gamayani U, Atik N. The Lymphocyte Depletion in Patients with Acute Ischemic Stroke Associated with Poor Neurologic Outcome. Int J Gen Med. 2021 May 14;14:1843-1851. doi: 10.2147/IJGM.S308325. PMID: 34017192; PMCID: PMC8131088.
18. Lei TY, Ye YZ, Zhu XQ, Smerin D, Gu LJ, Xiong XX, Zhang HF, Jian ZH. The immune response of T cells and therapeutic targets related to regulating the levels of T helper cells after ischaemic stroke. J Neuroinflammation. 2021 Jan 18;18(1):25. doi: 10.1186/s12974-020-02057-z. PMID: 33461586; PMCID: PMC7814595.
19. Wang H, Wang Z, Wu Q, Yuan Y, Cao W, Zhang X. Regulatory T cells in ischemic stroke. CNS Neurosci Ther. 2021 Jun;27(6):643-651. doi: 10.1111/cns.13611. Epub 2021 Jan 20. PMID: 33470530; PMCID: PMC8111493.
20. Huang L. Increased Systemic Immune-Inflammation Index Predicts Disease Severity and Functional Outcome in Acute Ischemic Stroke Patients. Neurologist. 2023 Jan 1;28(1):32-38. doi: 10.1097/NRL.0000000000000464. PMID: 36125980; PMCID: PMC9812414.
21. Wei CJ, Xue JJ, Zhou X, Xia XS, Li X. Systemic Immune-Inflammation Index is a Prognostic Predictor for Patients With Acute Ischemic Stroke Treated With Intravenous Thrombolysis. Neurologist. 2024 Jan 1;29(1):22-30. doi: 10.1097/NRL.0000000000000508. PMID: 37582611.
22. Weng Y, Zeng T, Huang H, Ren J, Wang J, Yang C, Pan W, Hu J, Sun F, Zhou X, Qiu H, Gao Y, Gao B, Chi L, Chen G. Systemic Immune-Inflammation Index Predicts 3-Month Functional Outcome in Acute Ischemic Stroke Patients Treated with Intravenous Thrombolysis. Clin Interv Aging. 2021 May 20;16:877-886. doi: 10.2147/CIA.S311047. PMID: 34040364; PMCID: PMC8143961.
23. Acar BA, Acar T, Vatan MB, Aras YG, Ulaş SB, Eryılmaz HA, Dalkılıç Ş, Zafer AP, Turhan O, Vatan A, Varım P, Kaya T. Predictive value of systemic immune-inflammation index for cerebral reperfusion and clinical outcomes in patients with acute ischemic stroke undergoing endovascular treatment. Eur Rev Med Pharmacol Sci. 2022 Aug;26(16):5718-5728. doi: 10.26355/eurrev_202208_29507. PMID: 36066145.
24. Çakır, Adem & Sener, Kemal & Guven, Ramazan. (2023). Diagnostic Value Of Systemic Immune–Inflammation Index (SIII) in Acute Ischemic Stroke. Journal of Contemporary Medicine. 13. 1-6. 10.16899/jcm.1213716.
25. Ma F, Li L, Xu L, Wu J, Zhang A, Liao J, Chen J, Li Y, Li L, Chen Z, Li W, Zhu Q, Zhu Y, Wu M. The relationship between systemic inflammation index, systemic immune-inflammatory index, and inflammatory prognostic index and 90-day outcomes in acute ischemic stroke patients treated with intravenous thrombolysis. J Neuroinflammation. 2023 Sep 30;20(1):220. doi: 10.1186/s12974-023-02890-y. PMID: 37777768; PMCID: PMC10543872.
26. Wu S, Shi X, Zhou Q, Duan X, Zhang X, Guo H. The Association between Systemic Immune-Inflammation Index and All-Cause Mortality in Acute Ischemic Stroke Patients: Analysis from the MIMIC-IV Database. Emerg Med Int. 2022 Aug 2;2022:4156489. doi: 10.1155/2022/4156489. PMID: 35959219; PMCID: PMC9363175.
27. Chen PY, Chen GC, Hsiao CL, Hsu PJ, Yang FY, Liu CY, Tsou A, Chang WL, Liu HH, Lin SK. Comparison of Clinical Features, Immune-Inflammatory Markers, and Outcomes Between Patients with Acute In-Hospital and Out-of-Hospital Ischemic Stroke. J Inflamm Res. 2022 Feb 9;15:881-895. doi: 10.2147/JIR.S342830. PMID: 35177921; PMCID: PMC8843816.
28. Zhou YX, Li WC, Xia SH, Xiang T, Tang C, Luo JL, Lin MJ, Xia XW, Wang WB. Predictive Value of the Systemic Immune Inflammation Index for Adverse Outcomes in Patients With Acute Ischemic Stroke. Front Neurol. 2022 Mar 18;13:836595. doi: 10.3389/fneur.2022.836595. PMID: 35370926; PMCID: PMC8971364.
29. Chu YW, Chen PY, Lin SK. Correlation between Immune-Inflammatory Markers and Clinical Features in Patients with Acute Ischemic Stroke. Acta Neurol Taiwan. 2020 Dec;29(4):103-113. PMID: 34018169.
30. Wang N, Yang Y, Qiu B, Gao Y, Wang A, Xu Q, Meng X, Xu Y, Song B, Wang Y, Wang Y. Correlation of the systemic immune-inflammation index with short- and long-term prognosis after acute ischemic stroke. Aging (Albany NY). 2022 Aug 19;14(16):6567-6578. doi: 10.18632/aging.204228. Epub 2022 Aug 19. PMID: 35985678; PMCID: PMC9467411.
31. Han J, Yang L, Lou Z, Zhu Y. Association between Systemic Immune-Inflammation Index and Systemic Inflammation Response Index and Outcomes of Acute Ischemic Stroke: A Systematic Review and Meta-Analysis. Ann Indian Acad Neurol. 2023 Sep-Oct;26(5):655-662. doi: 10.4103/aian.aian_85_23. Epub 2023 Jul 20. PMID: 38022472; PMCID: PMC10666886.