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Systemic inflammation response index as a clinical outcome evaluating tool and prognostic indicator for hospitalized stroke patients: a systematic review and meta-analysis

Yong-Wei Huang^{1†}, Ye Zhang^{1†}, Cui Feng^{2†}, Yin-Hua An^{3†}, Zong-Ping Li^{1*} and Xiao-Shuang Yin^{4*}

Abstract

Background Stroke, which is the main element of cerebrovascular disease (CVD), has become the foremost reason for death and disability on a global scale. The systemic inflammation response index (SIRI), a newly developed and comprehensive indicator, has demonstrated promise in forecasting clinical results for diverse ailments. Nevertheless, the uncertainty surrounding the assessment and prediction of clinical outcomes for stroke patients by SIRI persists, and the conflicting findings from the limited studies conducted on this matter further complicate the situation. Consequently, we performed a thorough systematic review and meta-analysis to explore the correlation between SIRI and the clinical results in individuals suffering from stroke.

Methods This research was registered in PROSPERO and carried out following the PRISMA guidelines. A thorough investigation was carried out on PubMed, Embase, the Cochrane Library, Web of Science, and Scopus databases. Furthermore, we conducted a manual search in Chinese databases, such as China national Knowledge Infrastructure (CNKI), WanFang, VIP, and China Biology Medicine (CBM). We assessed the potential for bias in the studies included by utilizing the Newcastle–Ottawa Scale (NOS) tool. Adverse clinical outcomes were the main focus of the study, with secondary endpoints including mortality, the predictive value of SIRI, SIRI values across various endpoints, and clinical parameters associated with subarachnoid hemorrhage (SAH) in relation to low and high SIRI group.

Results Following rigorous evaluation, a grand total of 22 investigations, encompassing a populace of 12,737 individuals, were considered suitable for incorporation in the final analysis. The findings from our meta-analysis indicate a strong and consistent correlation between elevated SIRI levels and adverse functional outcomes, irrespective of the method used to evaluate unfavorable outcomes. Furthermore, increased SIRI values have a strong correlation with mortality rates in both the short and long term. Besides, SIRI is a useful indicator of the severity of SAH. SIRI demonstrates strong predictive ability in identifying unfavorable outcomes and stroke-related pneumonia (SAP), as higher SIRI values are typically linked to negative endpoints. Nevertheless, the meta-analysis indicated that there

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was no significant increase in the risk of early neurological deterioration (END) and acute hydrocephalus (AHC) in high SIRI group when comparing to low SIRI.

Conclusion This study could potentially pave the way for groundbreaking insights into the relationship between SIRI and stroke patient outcomes, as it appears to be the first meta-analysis to explore this association. Given the critical role of the inflammatory response in stroke recovery, closely monitoring patients with high SIRI levels could represent a promising strategy for mitigating brain damage post-stroke. Thus, further investigation into SIRI and its impact on clinical outcomes is essential. While our initial findings offer valuable insights into this area, continued research is necessary to fully elucidate the potential of SIRI, ideally through dynamic monitoring and large-scale, multi-center studies. Ultimately, this research has the potential to inform clinical decision-making and improve patient outcomes following stroke.

Systematic review registration: <https://www.crd.york.ac.uk/prospero/>; Identifier CRD42023405221.

Keywords Systemic inflammation response index, Stroke, Intracerebral hemorrhage, Subarachnoid hemorrhage, Clinical outcome

Introduction

Studies in epidemiology have shown that the prevalence of cerebrovascular disease (CVD) has exceeded that of heart disease, emerging as the primary factor for death and impairment in the adult population [1, 2]. The occurrence of stroke is increasing as it is the main element of CVD. Accounting for 84.4% of all strokes, ischemic stroke (IS) is a prevalent sub-type [3]. Hemorrhagic stroke (HS), a more severe sub-type, consists of intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). ICH experiences an annual increase of 3.41 million cases [4], while SAH contributes to 5% of total stroke cases [5]. Both IS and HS result in elevated mortality rates and prolonged disability [6–8]. With the population getting older, there will be a substantial rise in the burden of stroke in the coming years. Hence, it is imperative to create a straightforward, user-friendly, economical indicator that can anticipate the likelihood of unfavorable results and offer supplementary details grounded in clear pathophysiological principles for subsequent treatment. Since blood routine tests are essential for every admitted patient, a new indicator that relies on the absolute values of blood cell counts demonstrates potential.

The SIRI, an innovative and comprehensive indicator, relies on the absolute counts of neutrophils, monocytes, and lymphocytes ($N \times M/L$) in the peripheral blood as a measure. The body's inflammatory status can be more comprehensively reflected by these three blood cells, which represent distinct pathways of inflammation and immunity, as compared to peripheral blood cell ratios like neutrophil/lymphocyte ratio (NLR), lymphocyte/monocyte ratio (LMR), and platelet/lymphocyte ratio (PLR) [9–12]. Previous studies have extensively utilized SIRI to evaluate the regression of tumor patients and forecast unfavorable clinical treatment regression in pancreatic, gastric, and hepatocellular cancers [13]. Moreover, research has indicated that SIRI additionally mirrors

the extent of atherosclerosis and forecasts the medical results in individuals with ICH, SAH, and those receiving intravascular mechanical thrombectomy for large artery occlusive stroke [14–16]. In patients with rheumatoid arthritis, there has been a connection between SIRI and the potential for developing acute ischemic stroke (AIS) [17]. Nevertheless, despite certain research indicating that SIRI holds promise as a valuable instrument for diagnosing and forecasting results in individuals with stroke, its ability to anticipate functional outcomes in stroke patients is restricted, and the results are contradictory, leaving the connection between SIRI and clinical outcomes uncertain. Hence, we conducted a comprehensive review and meta-analysis to investigate the correlation between SIRI and the clinical results in individuals affected by stroke.

Methods

Search strategy

The systematic review and meta-analysis followed the PRISMA guidelines [18] and was registered on PROSPERO with the identifier CRD42023405221 (<https://www.crd.york.ac.uk/PROSPERO/>) [19]. Additional file 1: Table S1 contains the PRISMA checklist. PubMed was searched using the keywords (“Systemic inflammation response index” OR “System inflammation response index” OR “Systemic inflammatory response index” OR “SIRI”) AND (“Patients”). We used the identical search approach for Embase, Cochrane Library, Web of Science, and Scopus. Furthermore, we conducted a manual search in Chinese databases, such as China National Knowledge Infrastructure (CNKI), WanFang, VIP, and China Biology Medicine (CBM). To minimize selection bias, articles in both English and Chinese were taken into account during the search, which spanned from the beginning to February 12, 2023. Additional file 1: Table S2 presents the detailed search strategy.

Study selection

We included studies that satisfied the following PICO criteria: (1) Population: individuals who have experienced a stroke, including IS and HS (ICH and SAH); (2) Intervention: mechanical thrombectomy, intravenous thrombolysis, surgical procedures (coiling or clipping), conservative treatment, or no treatment; (3) Comparisons: low SIRS vs. high SIRS; evaluating different SIRS values at different endpoints; (4) Outcomes: functional outcomes (measured by modified Rankin Scale [mRS] or Glasgow Outcome Score [GOS] at follow-up), mortality, predictive value of SIRS, SIRS values between poor and good outcomes, stroke-associated pneumonia (SAP) and non-SAP, early neurological deterioration (END) and non-END; SAH-associated clinical parameters between high SIRS and low SIRS, including Hunt-Hess Scale (HHS), modified Fisher Scale (mFS), delayed cerebral ischemia (DCI), vasospasm, and acute hydrocephalus (AHC). We did not include reviews, editorials, commentaries, case reports, letters to the editor, systematic reviews and meta-analyses, notes, replies, and conference abstracts because these types of records are insufficient for data.

Both reviewers (H Y-W and Z Y) individually examined the titles and abstracts of all the records that were obtained. Two reviewers independently assessed the relevant studies in their entirety and made decisions on article inclusion or exclusion according to the eligibility criteria. In case of discordance, the corresponding authors (L Z-P and Y X-S) would adjudicate.

Data extraction

Data were independently extracted into separate Excel spreadsheets by two reviewers, namely F C and A Y-H. To ensure accuracy, the source material and the spreadsheets were cross-checked with each other. Data collection included the first author's name, year of publication, country, study design, sample size, age, range, gender, stroke type, intervention type, SIRS cutoff ($\times 10^9/L$), primary and secondary endpoints, as well as the duration of follow-up. If any discrepancies were found, they were resolved by the corresponding author (L Z-P and Y X-S).

Study outcomes

The primary outcome of this study was the assessment of functional outcomes, as measured by the mRS or GOS at follow-up. The definition of mRS and GOS is presented in Additional file 1: Table S3. The secondary outcomes included mortality, the predictive value of SIRS, SIRS values between poor/good outcomes, the SAP/non-SAP, and END/non-END. Additionally, the study analyzed

the differences in HHS, mFS, DCI, vasospasm, and AHC between patients with low SIRS and high SIRS.

Bias assessment

Two independent reviewers (H Y-W and F C) assessed the risk of bias of the included studies using the Newcastle–Ottawa Scale (NOS) tool [20] in a blind manner. The risk of bias summaries was then cross-checked, and any unresolved discrepancies were resolved by the corresponding author (LZ-P and YX-S).

Statistical analysis

We computed odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) for binary variables. Continuous variables were used to calculate the mean difference (MD) along with their corresponding 95% CIs. If there is a substantial difference in the values of continuous variables, we employed the standard mean difference (SMD) for conducting meta-analysis. We extracted ORs and their corresponding 95% CIs from studies that had adjusted for confounding factors. The mean and standard deviation (SD) were estimated by utilizing the sample size, median, and interquartile range. These estimates were obtained using the optional estimation techniques described in McGrath et al.'s publication [21], which can be accessed at <https://smcgrath.shinyapps.io/estmeansd/>. To consider the variation in clinical characteristics, we performed meta-analyses and subgroup analyses utilizing the random-effects approach if the heterogeneity exceeds 50%, or the fixed-effects approach if the heterogeneity is less than 50% [22]. When there were more than five studies included, subgroup analyses were conducted based on the sub-type stroke. Significant heterogeneity was assessed by conducting the Cochrane Q test ($P < 0.1$ or $I^2 > 50\%$) [23]. Statistical significance was determined using a significance level of $P < 0.05$. Funnel plots were utilized to evaluate publication bias. The statistical analyses were conducted using Review Manager software (version 5.3.3), which can be found at <https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman>.

Results

Study selection

We acquired a total of 2435 publications using the search method on June 30, 2023. After eliminating 796 duplicates, we evaluated the remaining 1644 publications by their article type, title, and abstracts and we excluded 1620 publications that were not relevant. We thoroughly reviewed the remaining 24 publications for potential eligibility [9, 10, 14–16, 24–42]. Two studies [15, 40] shared almost the same data and were from the same author; thus, we combined the data and treated them as a single

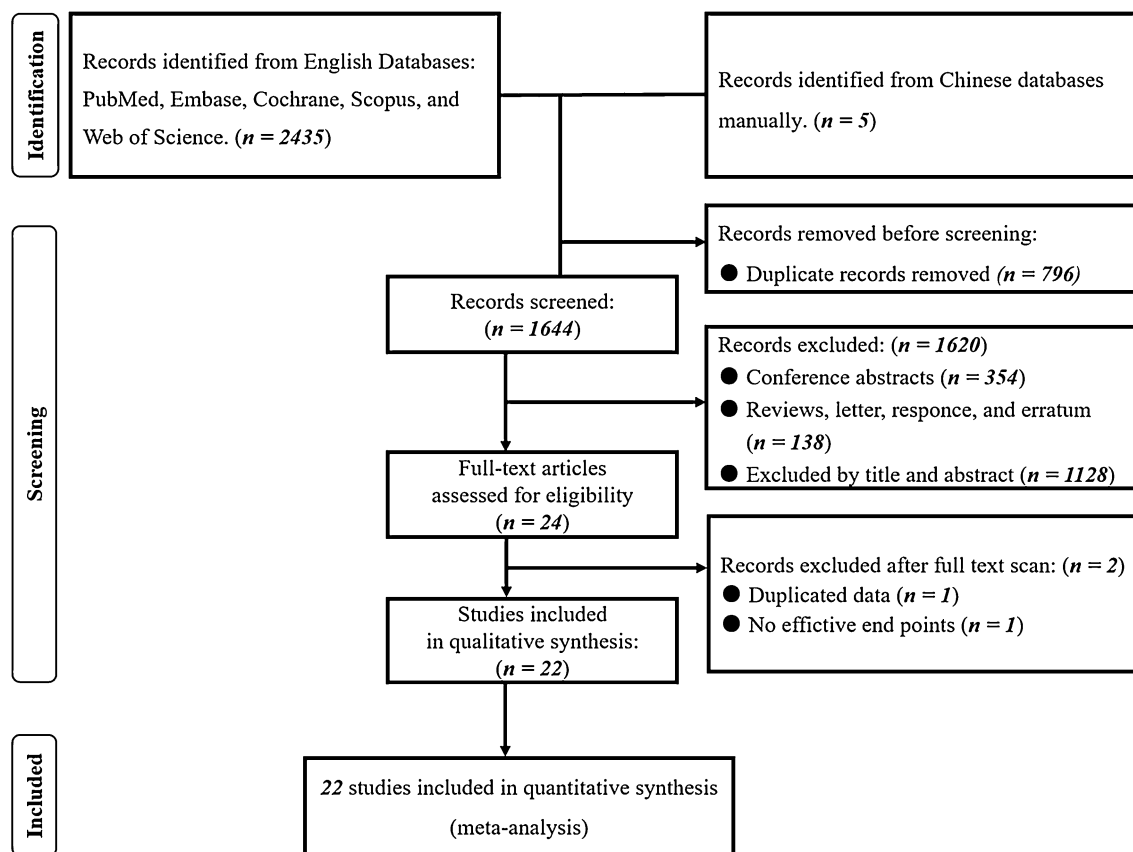


Fig. 1 PRISMA flowchart of included studies

study. The exclusion of a study [35] was based on the absence of sufficient endpoints. In this systematic review and meta-analysis (Fig. 1), a total of 22 studies [9, 10, 14–16, 24–34, 36–39, 41, 42] were ultimately incorporated.

Characteristics of the included studies

The 22 studies included in this systematic review and meta-analysis were published between 2020 and 2023. Among them, 5 articles were prospective studies [25, 29, 31, 33, 42], and the remaining 17 articles [9, 10, 14–16, 24, 26–28, 30, 32, 34, 36–39, 41] were retrospective studies. The studies were conducted in China ($n=19$, two studies were from the MIMIC database), Italy ($n=1$), and Korea ($n=2$), with a total of 12,931 patients included. Two research studies employed a 1:1 propensity score matching (PSM) technique to equalize the impact of potential confounders, leading to the incorporation of 12,737 individuals in the analysis. 11 studies [10, 16, 24–26, 28–30, 32, 34, 39] focused on AIS, 11 studies focused on HS including 5 studies [9, 31, 33, 36, 42] focused on ICH, and 6 studies [14, 15, 27, 37, 38, 41] focused on SAH. The SIRI cutoff range was between 0.77 and 6.48 ($\times 10^9/L$), while the duration of follow-up varied from hospitalization to

one year post-discharge. Table 1 provides a summary of the findings from the studies that were included.

Functional outcomes assessed by the GOS or mRS

Two studies [15, 38] reported functional outcomes assessed by GOS. The meta-analysis showed that individuals with high SIRI had a 3.17-fold higher risk of poor outcomes compared to those with low SIRI (odds ratio [OR] 3.17, 95% confidence interval [CI] 1.51–6.65, $P=0.002$, $I^2=0\%$, Fig. 2A), and the SIRI value was 0.72 higher in those with poor outcomes compared to those with good outcomes (standard mean difference [SMD] 0.72, 95%CI 0.47–0.97, $P<0.00001$, $I^2=42\%$, Fig. 2B). The predictive value of SIRI for poor outcome was 0.72 with a 95%CI of 0.63 to 0.82, $P<0.00001$, and $I^2=54\%$ (Fig. 2C). After combining with clinical data, the predictive value for poor outcome was 0.88 with a 95%CI of 0.83 to 0.94, $P<0.0001$, and $I^2=55\%$ (Fig. 2D), indicating that SIRI had a reasonably good predictive accuracy and a potential predictive ability. The results are summarized in Table 2.

Eight studies [9, 14, 16, 24, 25, 29, 39, 41] reported the SIRI values between good and poor outcome group, and the SIRI values were found to be 0.61 higher than that in

Table 1 The baseline characteristics of included studies

Author	Year	Nation	Study design	Participants (n)	Male (%)	Age (y)	Type of stroke	Type of intervention	Cutoff ($\times 10^9/L$)	Primary endpoints	Secondary endpoints	Follow-up	NOS
Fei et al.	2020	China	Retrospective cohort study	146	63.01	60.21 $\pm$ 13.84	ICH in basal ganglia	–	5.4	END (assessed by NIHSS and GCS)	Predictive value of SIRI	3	5
Zhang et al.	2020	China	Retrospective cohort study	178	34.83	57.64 $\pm$ 10.23	aSAH	Coiling or Clipping	4.105	Functional outcome (assessed by GOS)	Predictive value of SIRI	90 d	7
Zhang et al.	2020	China	Retrospective cohort study	125	36	56.00 $\pm$ 12.00	aSAH	Coiling or Clipping	3.63	Vasospasm	Predictive value of SIRI	–	5
Lattanzi et al.	2021	Italy	Retrospective cohort study	184	47.28	75 (61–81)	AIS	EVT	3.8	Futile Recanalization (assessed by mRS)	Predictive value of SIRI	90 d	8
Li et al.	2021	China	Retrospective study based on a prospectively collected database	403 in original cohort 262 in PSM cohort	68.48 in original cohort 67.55 in PSM cohort	58.56 $\pm$ 13.28 in original cohort 58.77 $\pm$ 13.56 in PSM cohort	ICH	Surgical intervention or conservative treatment	2.76	Functional outcomes (assessed by mRS) mortality	Predictive value of SIRI	90 d for functional outcomes 30 d for mortality	8
Shi et al.	2021	China	Retrospective cohort study	135	40.74	57.03 $\pm$ 2.15	aSAH	–	5.91	Poor outcome (assessed by GOS)	HHS, mFS, DCI, Pneumonia, AHC; Predictive value of SIRI	90 d	8
Yi et al.	2021	Korea	Retrospective study based on a prospectively collected database	440	59.09	70.34 $\pm$ 12.87	AIS	MT	2.9	Functional outcome (assessed by mRS)	Predictive value of SIRI	90 d	8
Yun et al.	2021	Korea	Retrospective multi-center	680	68.24	56.43 $\pm$ 12.96	aSAH	Surgery or Intervention	3.2	Functional outcome (assessed by mRS)	HHS, mFS, DCI, Vasospasm, AHC	90 d	8
Zhang et al.	2021	China	Retrospective cohort	2450 (MIMIC-III database)	52.29	68.17 $\pm$ 15.68	Stroke	–	3.8	Mortality	Predictive value of SIRI	In-hospital, 30 d, 90 d, 1 year	7
Li et al.	2022	China	Retrospective single-center	303	58.75	69 (60–78)	AIS	IVT	–	Functional outcome (assessed by mRS)	Predictive value of SIRI	90 d	8

Table 1 (continued)

Author	Year	Nation	Study design	Participants (n)	Male (%)	Age (y)	Type of stroke	Type of intervention	Cutoff ($\times 10^9/L$)	Primary endpoints	Secondary endpoints	Follow-up	NOS
Ma et al.	2022	China	Prospective single-center	63	68.84	65.35 $\pm$ 11.33	AIS	IVT with alteplase	1.01	Functional outcome (assessed by mRS)	Severity of AIS (NIHSS) Predictive value of SIRS	90 d	9
Wang et al.	2022	China	Retrospective single-center cohort study	375	65.87	61.9 $\pm$ 11.3	AIS	–	0.767	END (assessed by NIHSS)	–	every day for 7 days after admission	7
Yu et al.	2022	China	Retrospective single-center	111	66.67	58.49 $\pm$ 15.01	SAH	–	6.478	Functional outcome (assessed by mRS)	HHS, mFS, WFNS, DCI, Vasospasm, AHC, Rebleeding; Predictive value of SIRS	90 d	8
Zhou et al.	2022	China	Prospective single-center	287	68.99	61.55 $\pm$ 13.08	AIS	–	1.349	Functional outcome (assessed by mRS)	Predictive value of SIRS	90 d	9
Dang et al.	2023	China	Retrospective cohort	2043 in original cohort 888 in PSM cohort (MIMIC-IV database)	50.37 in original cohort 51.16 in PSM cohort	70.4 (57.9–81.8) in original cohort 71.5 (58.6–82.8) in PSM cohort	AIS	Thrombolysis or thrombectomy	4.57	LOS ICU, LOS hospital, 90 d all-cause mortality	30 d all-cause mortality 1-year all-cause mortality	In-hospital, 30 d, 90 d, 1-year	7
Huang et al.	2023	China	Retrospective single-center cross-sectional study	234	50.43	69 (57–78)	AIS	Thrombolysis or antiplatelet or anticoagulation	1.79	Functional outcome (assessed by mRS)	Severity of AIS (NIHSS) Predictive value of SIRS	–	7
Wang JJ et al.	2023	China	Prospective single-center	640	71.41	56.0 (48.0–64.0)	ICH	–	5.03	Functional outcome (assessed by mRS)	Complicated infections mortality	30 d, 90 d, 1-year	8
Yan et al.	2023	China	Retrospective single-center	2802	61.67	68.02 $\pm$ 11.53	AIS	–	2.74	SAP	Predictive value of SIRS	7 days after admission	6
Yu et al.	2023	China	Prospective single-center observational study	378	66.93	63.54 $\pm$ 13.72	ICH	–	–	SAP	Predictive value of SIRS	–	7

Table 1 (continued)

Author	Year	Nation	Study design	Participants (n)	Male (%)	Age (y)	Type of stroke	Type of intervention	Cutoff ($\times 10^9/L$)	Primary endpoints	Secondary endpoints	Follow-up	NOS
Chu et al.	2023	China	Retrospective single-center	240	33.75	66.00 (60.00–73.35)	AIS	IVT	1.00	Functional outcome (assessed by mRS)	Predictive value of SIRS	90 d	8
Hou et al.	2023	China	Retrospective cohort	394 in original cohort 200 in PSM cohort	44.87	55.6±9.8	aSAH	Coiling or Clipping	5.36	Functional outcome (assessed by mRS)	Predictive value of SIRS	90 d	9
Wang RH et al.	2023	China	Prospective multi-center observational	320	66.56	62.5 (51.3–73)	ICH	Nasogastric tube surgery	2.291	SAP	Predictive value of SIRS	7 days after admission	9

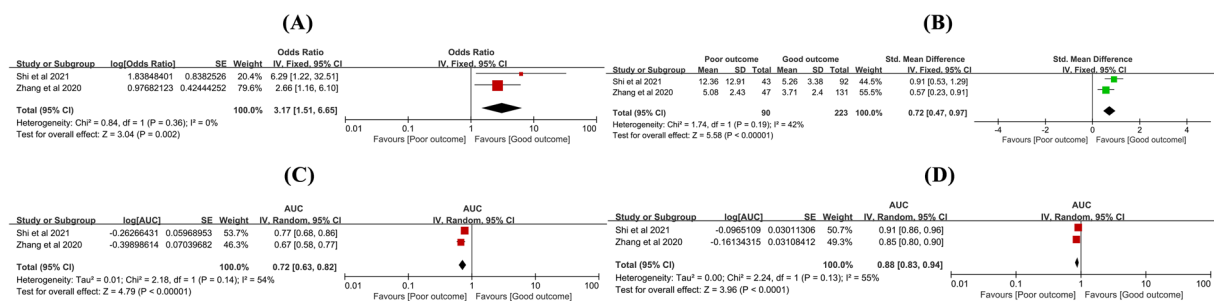


Fig. 2 The relationship of SIRS and functional outcomes (assessed by GOS). **A** SIRS for predicting poor outcome; **B** The difference of SIRS values between poor outcome and good outcome; **C** The predictive value of SIRS for poor outcome; **D** The predictive value of SIRS combined with clinical data for poor outcome

good outcome with a 95% CI of 0.52 to 0.69, $P < 0.00001$, and $I^2 = 60\%$ (Fig. 3A). 12 studies [9, 14, 16, 24, 25, 27–29, 31, 34, 39, 41] assessed functional outcomes using the mRS scale and reported the ORs and 95% CIs for SIRS and poor outcome, with 2 studies [24, 41] considering SIRS as both a continuous and dichotomous variable. The meta-analysis of 7 studies [9, 24, 25, 27, 29, 39, 41] considering SIRS as a continuous variable showed that for each standard deviation increase in SIRS, the risk of poor outcome increased by 20% (OR 1.20, 95% CI 1.07–1.34, $P = 0.001$, $I^2 = 66\%$, Fig. 3B). The meta-analysis of 7 studies [14, 16, 24, 28, 31, 34, 41] considering SIRS as a dichotomous variable showed that high SIRS was associated with a higher risk of poor outcome compared to low SIRS (OR 3.01, 95% CI 2.00–4.54, $P < 0.0001$, $I^2 = 74\%$, Fig. 3C). The predictive value of SIRS for poor outcome was 0.72 with a 95% CI 0.69 to 0.76, $P < 0.00001$, and $I^2 = 78\%$ (Fig. 3D). The results are summarized in Table 2.

In summary, despite the use of different assessment tools for poor outcome, it was consistently found that high SIRS was strongly associated with poor outcomes. In other words, there was a significant correlation between high SIRS and poor outcome.

SIRS and mortality

Four studies [9, 10, 30, 31] reported mortality rates ranging from in-hospital to 1 year after discharge. The meta-analysis showed that a high SIRS was associated with a 1.68-fold increased risk for in-hospital mortality (OR 1.68, 95% CI 1.43–1.97, $P < 0.00001$, $I^2 = 0\%$, Fig. 4A), a 1.50-fold increased risk for 1-month mortality (OR 1.50, 95% CI 1.14–1.98, $P = 0.004$, $I^2 = 85\%$, Fig. 4B), a 1.77-fold increased risk for 3-month mortality (OR 1.77, 95% CI 1.53–2.04, $P < 0.00001$, $I^2 = 0\%$, Fig. 4C), and a 1.65-fold increased risk for 1-year mortality (OR 1.65, 95% CI 1.43–1.92, $P < 0.00001$, $I^2 = 1\%$, Fig. 4D) when compared to those with low SIRS. The results are summarized in Table 2.

SIRS and SAP

Three studies [32, 33, 42] reported the SAP. The SIRS value of SAP was increased by 3.24 than non-SAP with 95% CI 1.56 to 4.91, $P = 0.0002$ and $I^2 = 88\%$ (Fig. 5A). 4 studies [32, 33, 38, 42] reported the ORs and 95CIs for SAP, in which one study [32] regarded the SIRS values as continuous variable and dichotomous variable. Three studies [32, 33, 42] regarded the SIRS value as continuous variable and the meta-analysis showed that for each standard deviation increase in SIRS, the risk of SAP increased by 11% (OR 1.11, 95% CI 1.05–1.18, $P = 0.0006$, $I^2 = 66\%$, Fig. 5B). Two studies [32, 38] regarded the SIRS value as dichotomous variable and the meta-analysis showed that high SIRS had 2.89-folds risk for SAP comparing low SIRS (OR 2.89, 95% CI 2.23–3.75, $P < 0.00001$, $I^2 = 0\%$, Fig. 5C). One study [33] randomized patients into the training and validation cohorts, and the two cohorts were regarded as two independent studies. The predictive value of SIRS for SAP was 0.81 with 95%CI ranged from 0.74 to 0.89, $P < 0.00001$, $I^2 = 90\%$ (Fig. 5D). The results are summarized in Table 2.

SIRS and END after stroke

Two studies [26, 36] provided data on END. The SIRS value of END was found to be 0.37 higher than that of non-END with a 95% CI of 0.34 to 0.40, $P < 0.00001$ and $I^2 = 0\%$ (Fig. 6A). However, the meta-analysis revealed that high SIRS did not significantly increase the risk of END compared to low SIRS (OR 1.78, 95% CI 0.95–3.34, $P = 0.07$, $I^2 = 85\%$, Fig. 6B). The results are summarized in Table 2.

SIRS and SAH-related clinical parameters

Five studies [14, 15, 27, 38, 41] investigated the association between SIRS and SAH-related clinical parameters. The meta-analysis indicated that high SIRS was usually associated with higher scores for HHS (OR 2.70, 95% CI 1.45–5.01, $P = 0.002$, $I^2 = 67\%$, Fig. 7A), mFS (OR 2.99,

Table 2 Meta-analysis of different outcomes

Items	Results		
	Studies, <i>n</i>	OR (95% CI)	<i>P</i> -value (Heterogeneity, <i>I</i> ² and <i>P</i> for Cochran <i>Q</i>)
Functional outcomes (assessed by GOS)	2	3.17 (1.51–6.65)	<i>P</i> = 0.002 (<i>I</i> ² = 0%, <i>P</i> = 0.36)
Functional outcomes (assessed by mRS)			
Continuous variable	7	1.20 (1.07–1.34)	<i>P</i> = 0.001 (<i>I</i> ² = 66%, <i>P</i> = 0.008)
Dichotomous variable	7	3.01 (2.00–4.54)	<i>P</i> < 0.0001 (<i>I</i> ² = 74%, <i>P</i> = 0.0007)
Mortality			
In-hospital	3	1.68 (1.43–1.97)	<i>P</i> < 0.00001 (<i>I</i> ² = 0%, <i>P</i> = 0.37)
1 month	4	1.50 (1.14–1.98)	<i>P</i> = 0.004 (<i>I</i> ² = 85%, <i>P</i> = 0.0002)
3 months	3	1.77 (1.53–2.04)	<i>P</i> < 0.00001 (<i>I</i> ² = 0%, <i>P</i> = 0.77)
1 year	2	1.65 (1.43–1.92)	<i>P</i> < 0.00001 (<i>I</i> ² = 1%, <i>P</i> = 0.31)
SAP			
Continuous variable	3	1.11 (1.05–1.18)	<i>P</i> = 0.0006 (<i>I</i> ² = 66%, <i>P</i> = 0.05)
Dichotomous variable	2	2.89 (2.23–3.75)	<i>P</i> < 0.00001 (<i>I</i> ² = 0%, <i>P</i> = 0.60)
END	2	1.78 (0.95–3.34)	<i>P</i> = 0.07 (<i>I</i> ² = 85%, <i>P</i> = 0.01)
SAH-related clinical parameters			
HHS	4	2.70 (1.45–5.01)	<i>P</i> = 0.002 (<i>I</i> ² = 67%, <i>P</i> = 0.03)
mFS	4	2.99 (1.57–5.70)	<i>P</i> = 0.0009 (<i>I</i> ² = 77%, <i>P</i> = 0.005)
DCI	3	3.09 (2.16–4.43)	<i>P</i> < 0.00001 (<i>I</i> ² = 0%, <i>P</i> = 0.89)
Vasospasm	3	1.67 (1.28–2.17)	<i>P</i> = 0.0001 (<i>I</i> ² = 79%, <i>P</i> = 0.008)
AHC	4	1.90 (0.84–4.29)	<i>P</i> = 0.12 (<i>I</i> ² = 81%, <i>P</i> = 0.001)
Predictive value of SIRS for poor outcome (assessed by GOS)			
SIRS	2	0.72 (0.63–0.82)	<i>P</i> < 0.00001 (<i>I</i> ² = 54%, <i>P</i> = 0.14)
SIRS combining with clinical data	2	0.88 (0.83–0.94)	<i>P</i> < 0.0001 (<i>I</i> ² = 55%, <i>P</i> = 0.13)
Predictive value of SIRS for poor outcome (assessed by mRS)	12	0.72 (0.69–0.76)	<i>P</i> < 0.00001 (<i>I</i> ² = 78%, <i>P</i> < 0.00001)
Predictive value of SIRS for SAP	4	0.81 (0.74–0.89)	<i>P</i> < 0.00001 (<i>I</i> ² = 90%, <i>P</i> < 0.00001)
Items	Results		
	Studies, <i>n</i>	SMD or MD (95% CI)	<i>P</i> value heterogeneity (<i>I</i> ² , <i>P</i> for Cochran <i>Q</i>)
SIRS values between different endpoints			
Poor/good outcome (assessed by GOS)	2	0.72 (0.47–0.97)	<i>P</i> < 0.00001 (<i>I</i> ² = 42%, <i>P</i> = 0.19)
Poor/good outcome (assessed by mRS)	8	0.61 (0.52–0.69)	<i>P</i> < 0.00001 (<i>I</i> ² = 60%, <i>P</i> = 0.01)
SAP and Non-SAP	3	3.24 (1.56–4.91)	<i>P</i> = 0.0002 (<i>I</i> ² = 88%, <i>P</i> = 0.0002)
END and Non-END	2	0.37 (0.34–0.40)	<i>P</i> < 0.00001 (<i>I</i> ² = 0%, <i>P</i> = 0.79)

95% CI 1.57–5.70, *P* = 0.0009, *I*² = 77%, Fig. 7B), increased risk of DCI (OR 3.09, 95% CI 2.16–4.43, *P* < 0.00001, *I*² = 0%, Fig. 7C), and vasospasm (OR 1.67, 95% CI 1.28–2.17, *P* = 0.0001, *I*² = 79%, Fig. 7D) compared to low SIRS. However, the risk of AHC (OR 1.90, 95% CI 0.84–4.29, *P* = 0.12, *I*² = 81%, Fig. 7E) was not statistically significant between the two groups. It is noteworthy that HHS, mFS, DCI, vasospasm, and AHC are all indicators of SAH severity, indicating that high SIRS was associated with more severe SAH. In regions with limited medical resources and where CT scans are not readily available, this simple index may prove valuable in predicting SAH

severity and patient stratification. The results are summarized in Table 2.

Analyses of subgroups based on sub-type of stroke

Subgroup analyses were conducted based on the sub-type of stroke (IS and HS) for (i) the difference in SIRS values between the poor outcome group and the good outcome group, (ii) predicting poor outcome when SIRS was regarded as a continuous variable or dichotomous variable, and (iii) the predictive value of SIRS for poor outcome. Subgroup analysis demonstrated that the SIRS values were higher in the poor outcome group than in

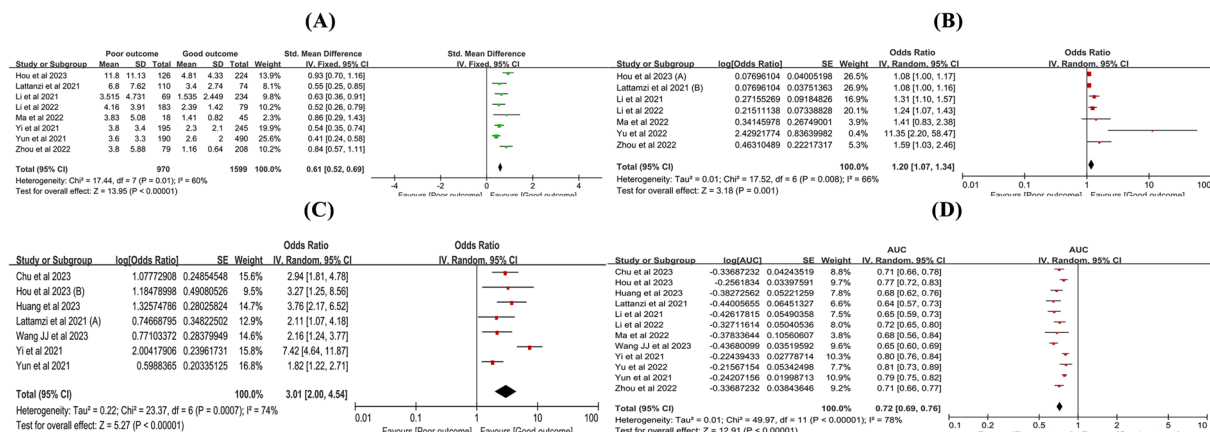


Fig. 3 The relationship of SIRI and functional outcomes (assessed by mRS). **A** The difference of SIRI values between poor outcome and good outcome; **B** SIRI for predicting poor outcome (continuous); **C** SIRI for predicting poor outcome (dichotomous); **D** The predictive value of SIRI for poor outcome

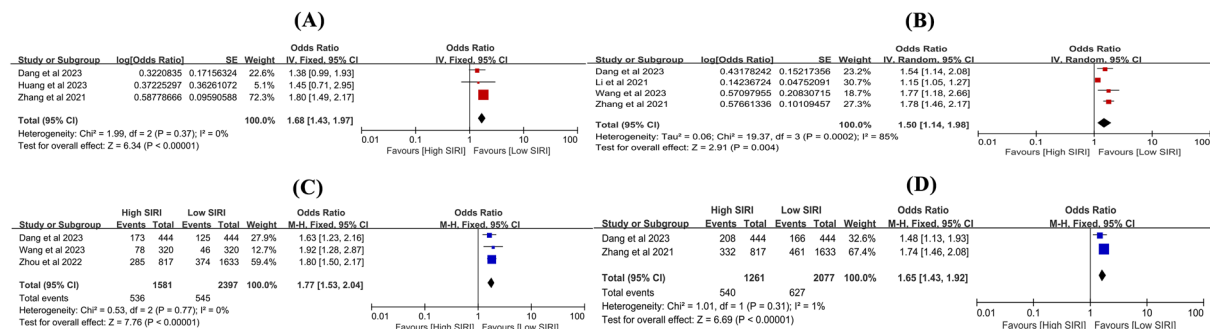


Fig. 4 The relationship of SIRI and mortality. **A** SIRI for predicting in-hospital mortality; **B** SIRI for predicting 1-month mortality; **C** SIRI for predicting 3-month mortality; **D** SIRI for predicting 1 year mortality

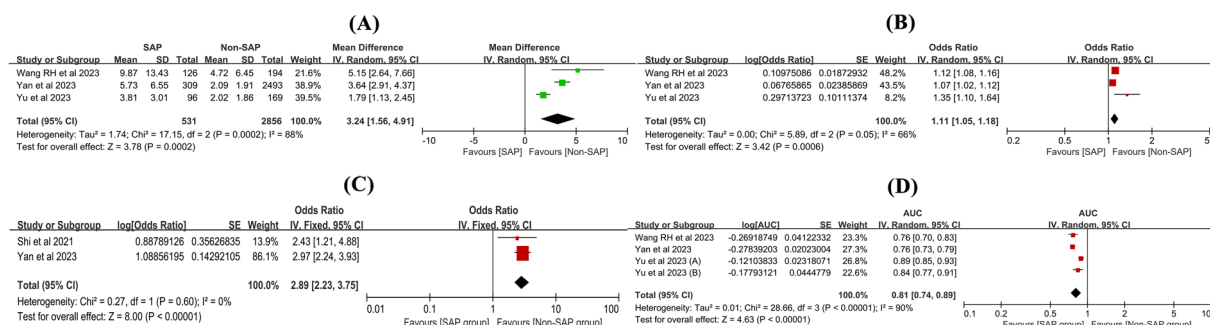


Fig. 5 The relationship of SIRI and SAP. **A** The difference of SIRI values between SAP and Non-SAP; **B** SIRI for predicting SAP (continuous); **C** SIRI for predicting SAP (dichotomous); **D** The predictive value of SIRI for SAP

the good outcome group for both IS (SMD: 0.62; 95% CI 0.49–0.75, $P < 0.00001$, $I^2 = 14\%$) and HS (SMD: 0.65; 95% CI 0.33–0.67, $P < 0.00001$, $I^2 = 84\%$) (Fig. 8A). When SIRI was regarded as a continuous variable, subgroup analysis demonstrated that for each standard deviation

increase in SIRI, the risk of poor outcome increased by 19% for IS (OR: 1.19; 95% CI 1.04–1.37, $P = 0.01$, and $I^2 = 50\%$), whereas no statistically significant difference was found for HS (OR: 1.28; 95% CI 0.94–1.74, $P = 0.12$, and $I^2 = 83\%$) (Fig. 8B). Similarly, when SIRI was regarded

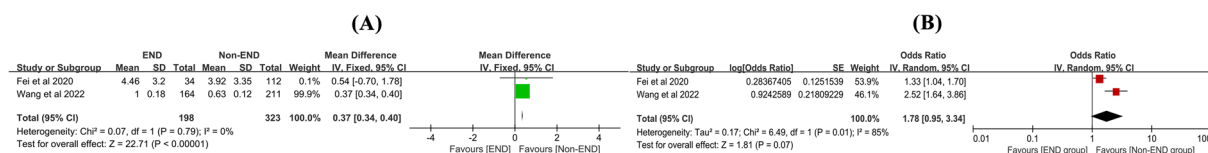


Fig. 6 The relationship of SIRI and END. **A** The difference of SIRI values between END and Non-END; **B** SIRI for predicting END

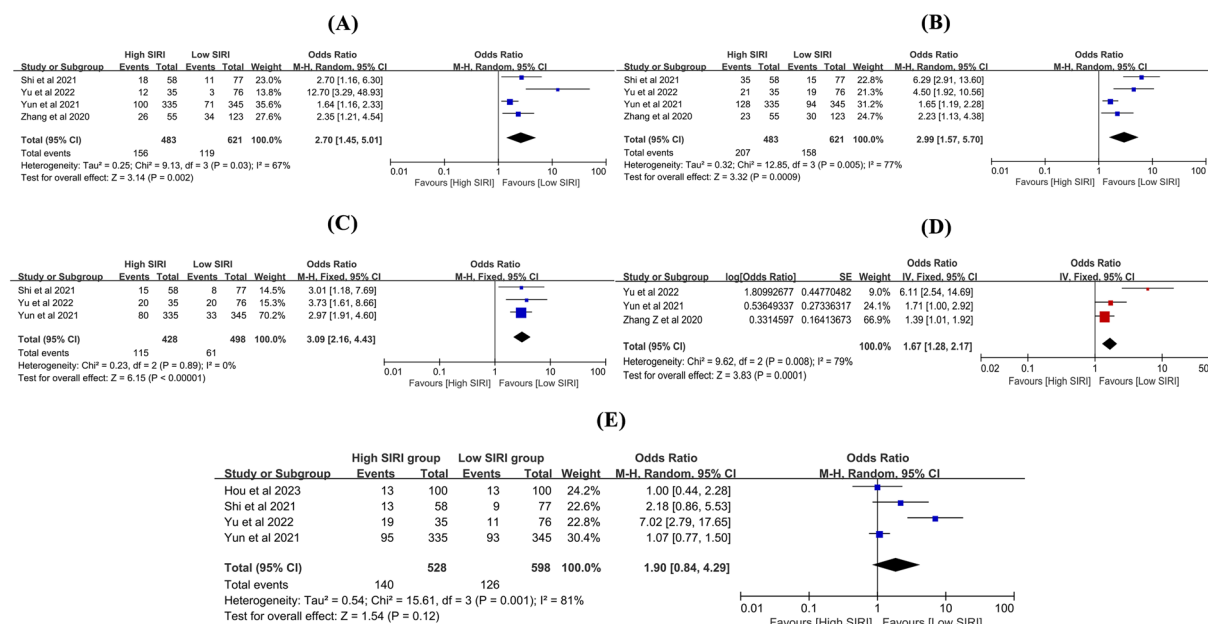


Fig. 7 The relationship of SIRI and SAH-associated clinical parameters. The **A** HHS, **B** mFS, **C** DCI, **D** vasospasm, and **E** AHC between high SIRI and low SIRI

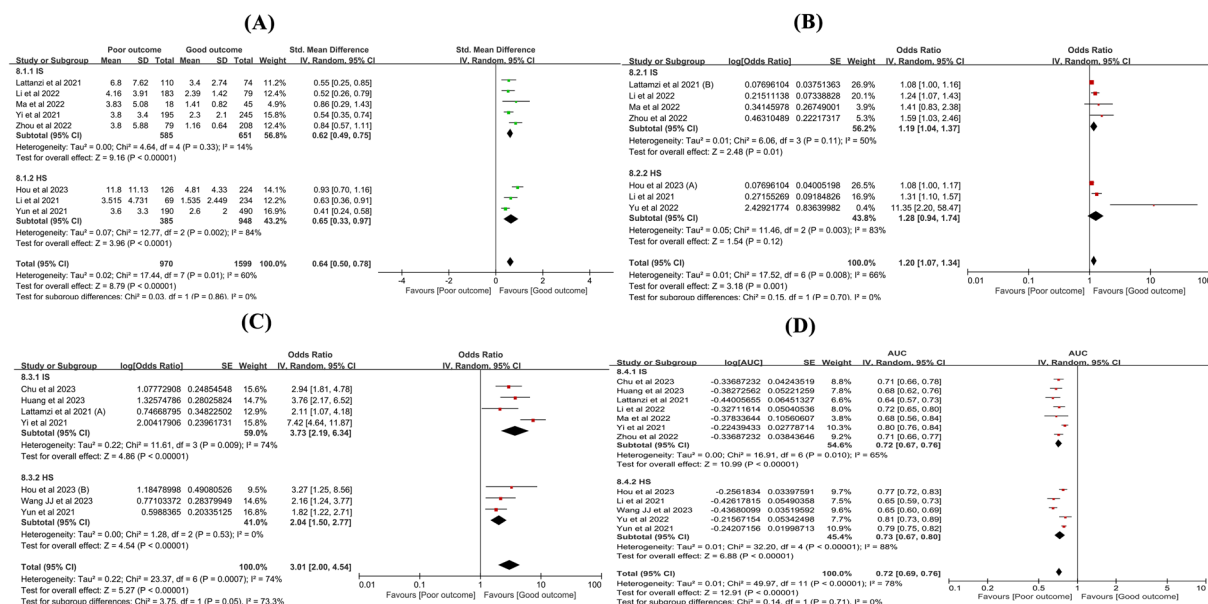


Fig. 8 Subgroup analyses based on sub-type of stroke. **A** The difference of SIRI values between poor outcome and good outcome; **B** SIRI for predicting poor outcome (continuous); **C** SIRI for predicting poor outcome (dichotomous); **D** The predictive value of SIRI for poor outcome

as a dichotomous variable, subgroup analysis demonstrated that the risk of a poor outcome at a high SIRI level was 3.73 times greater than that at a low SIRI level for IS (OR: 3.73; 95% CI 2.19–6.34, $P < 0.00001$, and $I^2 = 74\%$) and 2.04 times greater for HS (OR: 2.04; 95% CI 1.50–2.77, $P < 0.00001$, $I^2 = 0\%$) (Fig. 8C). Lastly, the predictive value of SIRI for poor outcomes was 0.72 for IS (AUC: 0.72; 95% CI 0.67–0.76) and 0.73 for HS (AUC: 0.73; 95% CI 0.67–0.80) (Fig. 8D). The results are summarized in Table 3.

Risk of bias assessment and publication bias assessment

The NOS has assessed and awarded a median of 8 stars to all the research, with an inter-quartile range of 5 to 9 stars. The methodological quality of the studies included can be found in Additional file 1: Table S4. Additionally, the probability of publication bias was evaluated through funnel plot results, which are displayed in Additional file 1: Figure S1.

Discussion

Secondary brain tissue damage after AIS [43, 44] is attributed to the inflammatory reaction. Inflammatory cells of the immune system secrete different substances, such as cytokines, adhesion molecules, and chemokines, which worsen the harm to tissues. Earlier research has indicated that the inflammatory reaction can be promptly initiated following a stroke and is closely associated with unfavorable consequences [45–47]. The investigation of biomarkers is focused on various inflammatory factors linked to stroke, which are emphasized by these mechanisms.

The importance of inflammation in the development of stroke has been confirmed by many research studies. In every step of atherosclerotic plaque development, inflammation plays a crucial role and leads to the occurrence of thrombotic events [48]. The beginning of early plaque formation is marked by monocyte attachment to the vascular endothelium, movement into the arterial intima, and later transformation into foamy macrophages [49, 50]. The occurrence of stroke is frequently a result of the disturbance of atherosclerotic plaques, which is linked to the infiltration of monocyte/macrophage and T-cells [51]. Furthermore, inflammation is crucial in the pathophysiological processes of brain damage. After ischemia, white blood cells escape from the bloodstream and enter the brain and meninges [52]. The brain is harmed by neutrophils when they release enzymes like metalloproteases (MMP-9), cathepsin G, reactive oxygen and nitrogen compounds, and the inflammatory IL-1 β [53]. The arrival of monocyte-derived macrophages (MDMs) in the ischemic brain may play a vital role in controlling the immune reaction following a stroke [54, 55]. Additionally, stroke can activate systemic inflammation and neurohumoral pathways, leading to immune activation, immunodepression, and functional impairment of various peripheral organs [53, 55–59]. Therefore, markers of inflammation might suggest the prognosis after a stroke.

The SIRI is an innovative and comprehensive indicator that relies on the absolute values of neutrophil, monocyte, and lymphocyte counts in the peripheral blood. During the initiation of stroke, the activation of peripheral circulating neutrophils occurs first, leading to

Table 3 Subgroup analyses based on sub-type of stroke

Items	Results		
	studies, <i>n</i>	SMD/OR/AUC (95% CI)	<i>P</i> -value (heterogeneity, I^2 and <i>P</i> for Cochran <i>Q</i>)
SIRI values between poor and good outcome [§]			
IS	5	0.62 (0.49–0.75)	$P < 0.00001$ ($I^2 = 14\%$, $P = 0.33$)
HS	3	0.65 (0.33–0.97)	$P < 0.00001$ ($I^2 = 60\%$, $P = 0.002$)
Poor outcome (continuous variable)*			
IS	4	1.19 (1.04–1.37)	$P = 0.01$ ($I^2 = 50\%$, $P = 0.11$)
HS	3	1.28 (0.94–1.74)	$P = 0.12$ ($I^2 = 83\%$, $P = 0.003$)
Poor outcome (dichotomous variable)*			
IS	4	3.73 (2.19–6.43)	$P < 0.00001$ ($I^2 = 74\%$, $P = 0.009$)
HS	3	2.04 (1.50–2.77)	$P < 0.00001$ ($I^2 = 0\%$, $P = 0.53$)
Predictive value of SIRI for poor outcome*			
IS	7	0.72 (0.67–0.76)	$P < 0.00001$ ($I^2 = 65\%$, $P = 0.010$)
HS	5	0.73 (0.67–0.80)	$P < 0.00001$ ($I^2 = 88\%$, $P < 0.00001$)

* represents the data are expressed as OR

§ represents the data are expressed as SMD

※ represents the data are expressed as AUC

the release of antimicrobial enzymes and chemical substances that worsen brain damage [60, 61]. In the initial phase of AIS, elevated neutrophil counts were linked to greater infarction size, suggesting that the rise in neutrophil levels may worsen blood–brain barrier damage by facilitating excessive matrix metalloproteinase-9 expression [62, 63]. Furthermore, following AIS, monocytes serve as another crucial category of inflammatory cells capable of infiltrating infarct locations and exacerbating cerebral harm [64–66]. Contrary to neutrophils and monocytes, certain lymphocytes have a crucial function in controlling and diminishing local inflammation during the inflammatory response after AIS, thereby providing protection [67]. Hence, a substantial SIRI ($N\uparrow \times M\uparrow/L\downarrow$) can precisely indicate the adaptive immune response and inflammation response, which play a crucial role in the occurrence of stroke and hold potential as a reliable prognostic indicator. Furthermore, these three types of blood cells symbolize distinct pathways related to inflammation and immunity within the body, thereby offering a more holistic indication of the body's inflammatory condition.

Previous studies have demonstrated that the SIRI is an effective marker for assessing the clinical prognosis of various stroke types, including AIS, ICH, and SAH. Fei et al. [36] have shown that SIRI is closely correlated with the occurrence of END in basal ganglia ICH patients and has predictive value in improving the early identification and screening of END and patient outcomes. Wang et al. [26] have reported that SIRI can serve as a new predictor of END in a more objective and reliable manner, as well as a monitor of treatment response. However, our analysis indicates that high SIRI does not increase the risk of END compared with low SIRI. As only 2 studies have focused on the relationship between SIRI and END after stroke, further research is necessary and urgent. In another study, Lin et al. [35] investigated the association between SIRI and atrial fibrillation and found that elevated SIRI values are potential biomarkers of AF among IS patients. However, as there is limited research on the relationship between SIRI and cardiovascular disease, further exploration is warranted. Yu et al. [33] studied the relationship between SIRI and SAP and demonstrated that SIRI at admission can be used as a prognostic inflammatory biomarker in ICH patients with SAP. Yan et al. [32] also reported that SIRI has a good predictive value for SAP, and stroke patients with high SIRI levels (≥ 2.74) should be aware of the risk of SAP. Our analysis showed that although there was no dose–response relationship between SIRI and SAP, high SIRI had a 2.89-fold risk for SAP compared with low SIRI.

As we are aware, SIRI has emerged as a promising prognostic indicator for stroke patients. However, it is essential to consider potential confounding factors that

may affect SIRI values, such as infections that develop or coexist with stroke, especially in the elderly population who are susceptible to aspiration pneumonia and urine infections. Moreover, the ongoing COVID-19 pandemic has further complicated the situation, as almost all stroke patients have a compromised and diminished immune system, which could interfere with blood cell count and, consequently, affect SIRI values. Therefore, it is imperative to accurately document comorbidities, including infections and COVID-19 infection status, and pay closer attention to the basic conditions of elderly patients to make appropriate adjustments in data analysis. Future investigations should also consider the influence of stroke patients' histories of infection to obtain a more comprehensive understanding of SIRI as a prognostic marker for stroke outcomes. Overall, a more in-depth investigation into the relationship between SIRI, infection, and stroke outcomes, taking into account potential confounding factors, could provide more valuable insights for improving stroke management and patient outcomes.

To our knowledge, this is the first systematic review and meta-analysis to investigate the association between SIRI and clinical outcomes in stroke patients. Our analysis demonstrated that high SIRI values were associated with poor outcomes regardless of the assessment tools used. Furthermore, high SIRI values were related to both short-term and long-term mortality and could indicate the severity of SAH. In other words, higher SIRI values indicated more severe SAH. In places where CT scans are not available and medical conditions are poor, this simple index may play an important role in predicting the severity of SAH and stratifying patients. The predictive value of SIRI for poor outcomes and SAP was relatively high, with adverse endpoints typically having higher SIRI values.

Limitations

While our study provides important insights into the association between SIRI and stroke patient outcomes, it is important to acknowledge several limitations. Firstly, due to the nature of inflammation response in stroke, most of the existing literature on this topic comprises retrospective studies, which may introduce limitations in terms of sample size, confounding variables, and selection bias. Secondly, with the exception of four prospective studies, the majority of studies included in our analysis were retrospective, resulting in considerable heterogeneity in data reporting and follow-up protocols. Therefore, further high-quality prospective studies are needed to confirm the validity and generalizability of our findings. Thirdly, based on our systematic review, the majority of included studies (86%, 19 out of 22 studies) were carried out in China, with two studies from the

MIMIC database. As we know, the MIMIC database was established by the Beth Israel Deaconess Medical Center (Boston, MA, USA), and the population consisted mainly of US citizens. Therefore, these two studies reflected the relationship between SIRI and clinical outcomes in Americans. But the existing literature still lacks related studies in Europe or Africa. The broader applicability of SIRI as a predictive tool for stroke outcomes should be identified further in other ethnicities and countries. Fourthly, the high heterogeneity observed in some of our endpoints could influence the robustness of our results. Fifthly, some results are not mirrored to the total population of our studies selected, for each variable evaluated a different lesser number of studies were included. Hence, some findings are less robust. Despite these limitations, our meta-analysis provides valuable preliminary findings that could assist clinicians in making informed treatment decisions for stroke patients. Future research should aim to address these limitations and provide further insights into the association between SIRI and stroke outcomes.

Conclusion

This study could potentially pave the way for groundbreaking insights into the relationship between SIRI and stroke patient outcomes, as it appears to be the first meta-analysis to explore this association. Given the critical role of the inflammatory response in stroke recovery, closely monitoring patients with high SIRI levels could represent a promising strategy for mitigating brain damage post-stroke. Thus, further investigation into SIRI and its impact on clinical outcomes is essential. While our initial findings offer valuable insights into this area, continued research is necessary to fully elucidate the potential of SIRI, ideally through dynamic monitoring and large-scale, multi-center studies. Ultimately, this research has the potential to inform clinical decision-making and improve patient outcomes following stroke.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s40001-023-01446-3>.

Additional file 1: Table S1. PRISMA 2020 checklist. **Table S2.** Search strategy. **Table S3.** The definition of mRS and GOS. **Table S4.** ROB assessment for the quality of studies in meta-analysis. **Figure S1.** Funnel plot results of main end points.

Author contributions

The present study was conceived through the joint efforts of YWH, YZ, CF, YHA, ZPL and XSY. YWH developed the initial idea. ZPL and XSY subsequently devised and refined the search strategy, and YWH and YZ conducted the literature search. CF and YHA conducted data extraction. YWH and XSY formulated the study design. YWH and XSY contributed to the original draft, and ZPL was responsible for revising the manuscript. YWH, YZ, CF and YHA are co-first

authors. ZPL and XSY are co-corresponding authors. All authors have made substantial contributions to this article and have given their full approval of the submitted version.

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Availability of data and materials

The original contributions presented in the study are included in the article/ Additional Material. Any additional queries regarding the research should be directed towards the corresponding author. The additional material for this article can be found online.

Declarations

Ethics approval and consent to participate

Not applicable.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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