Heliyon 10 (2024) e23441

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Meta-analysis of the systemic immune-inflammatory index and in-hospital mortality of COVID-19 patients

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ARTICLE INFO

Keywords:
Coronavirus disease 2019
Systemic immune-inflammatory index
Prognosis
Mortality
Meta-analysis

ABSTRACT

Background: The potential significance of immunoinflammatory factors in the prognosis of individuals afflicted with coronavirus disease 2019 (COVID-19) is worthy of examination. The systemic immune-inflammatory index (SII), a recently developed immunoinflammatory metric based on the enumeration of neutrophils, platelets, and lymphocytes in blood samples, holds promise for elucidating this relationship. Consequently, in order to explore any possible correlation between the SII levels at admission and the in-hospital mortality of patients with COVID-19, we undertook a thorough systematic review and meta-analysis.

Methods: In pursuit of accomplishing the aim of this meta-analysis, an extensive search was conducted to seek out pertinent observational studies featuring longitudinal follow-up across PubMed, Cochrane Library, Embase and the Web of Science databases. The I^2 statistic was utilized to estimate the extent of heterogeneity and the Cochrane Q test was employed to evaluate heterogeneity between studies. The synthesis of outcomes involved the use of random-effects models, accounting for the possible influence of heterogeneity.

Results: Our analysis included sixteen studies, encompassing 10,007 hospitalized COVID-19 patients. Among them, 1801 patients (18.0 %) succumbed during hospitalization. The pooled results indicated that a high SII at admission was substantially linked to a higher risk of all-cause mortality (risk ratio [RR]: 2.41, 95 % confidence interval: 1.78 to 3.24, $p < 0.001$; $I^2 = 86$ %). Meta-regression analysis demonstrated a negative correlation between mean SII at baseline and patient mortality in individual studies (coefficients = −0.00023 and −0.030, $p < 0.05$), effectively explaining the observed heterogeneity. Furthermore, in patients with lower baseline SII (<1300) and a lower risk of mortality (<20 %), we observed a more pronounced association between high SII levels and the risk of all-cause mortality.

Conclusion: The results of our study indicate that a high SII upon admission could potentially function as a prognostic indicator for mortality during hospitalization in patients diagnosed with COVID-19, particularly in individuals categorized as low risk.

1. Introduction

The coronavirus disease pandemic of 2019 (COVID-19) has significantly harmed the overall health of the worldwide populace [1,

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https://doi.org/10.1016/j.heliyon.2023.e23441
Received 7 August 2023; Received in revised form 2 December 2023; Accepted 4 December 2023
Available online 8 December 2023

2]. COVID-19, being a viral-induced systemic infectious disorder, is distinguished by systemic inflammation and associated dysregulation of the immune and hemostatic systems [3–5]. Given the persistent and recurrent nature of COVID-19 infections, it is imperative to identify a dependable, cost-effective, and easily accessible parameter that can prognosticate the outcomes for patients afflicted with COVID-19 [6].

Using neutrophil, platelet, and lymphocyte counts, the systemic immune-inflammatory index (SII) can be calculated based on immunoinflammatory parameters [7,8]. Considering the cellular functions of the individual components of SII, the index may reflect systematic inflammation and immune and hemostatic status [7]. Accumulating evidence suggests that a high SII at baseline may predict poor survival in patients with cancer [9] and cardiovascular diseases [10]. It has been suggested that a high SII may potentially indicate the severity of COVID-19 [11]. Considerable pilot studies have been conducted to examine the correlation between SII and mortality in COVID-19 patients. However, the findings of these studies have not consistently aligned [12–27]. Consequently, in our request to explore the connection between SII upon admission and in-hospital mortality among individuals diagnosed with COVID-19, we performed a systematic review and meta-analysis.

2. Materials and methods

During the planning, execution, and reporting phases of the study, The Cochrane Handbook [30] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [28,29] were adhered to.

2.1. Criteria for study inclusion and exclusion

The inclusion criteria were established based on The PICOS recommendations [31] and aligned with the objective of the meta-analysis. The patient group (P) consisted of adults (18 years or above) who were hospitalized and had a confirmed COVID-19 diagnosis. The exposure group (I) comprised patients with a high SII upon admission, with methods and thresholds for identifying high SII aligning with those utilized in the original research. The control group (C) consisted of patients with a low SII upon admission. The outcome (O) of interest was the frequency of all-cause mortality throughout hospitalization, which was contrasted between patients with high and low SII at baseline. The study's design (S) involved observational approaches, specifically studies with longitudinal follow-up like cohort studies, nested case-control studies, and post-hoc analyses. The following types, including preclinical studies, reviews, editorials, and studies lacking COVID-19 diagnoses, initial SII assessment upon admission, data on in-hospital mortality, or relevant outcome measures, were excluded from this meta-analysis. The meta-analysis incorporated the research with the most extensive sample size when there was an overlap in patient populations.

2.2. Literature search

We performed an exhaustive search of electronic databases, namely Web of Science, Embase, Cochrane Library, and PubMed, spanning from their inception until June 11, 2023, to identify relevant published studies up to that date. The search strategy employed terms pertinent to our research, encompassing (1) "systemic immune-inflammation index" OR "SII" and (2) "severe acute respiratory syndrome coronavirus 2″ OR "coronavirus" OR "SARS-CoV-2″ OR "nCoV" OR ″2019-nCoV" OR "novel coronavirus" OR "COVID-19″ OR "COVID". Only articles published in English peer-reviewed journals and meeting the criteria full-length were incorporated into our analysis. Additionally, during our manual screening process, we also examined references of pertinent original and review articles to identify any potentially relevant studies.

2.3. Data extraction and quality evaluation

Two authors (HY and JT) separately performed comprehensive literature searches, collected data, and assessed the quality of the incorporated studies. If there was any disagreement, a third author (LW) was engaged to facilitate consensus between the two authors. The following information was collected, including author and country of study, type and design of the study, detailed diagnosis of the patients, age, sex, mean SII at baseline, the cutoff used to define high SII, the length of follow-up, the number of patients who passed away while hospitalized, and the variables that were adjusted for assessing the connection between SII and in-hospital mortality of COVID-19 patients. We employed the Newcastle–Ottawa Scale (NOS) [32] in evaluating the studies' quality via three aspects including the validity of the results, comparability of the study groups, and participant selection. The NOS scoring system comprises nine stars, with more stars indicating a higher quality study.

2.4. Statistics

Risk ratios (RRs) and their corresponding 95 % confidence intervals (CIs) were employed as the variables to assess the relationship between the systemic SII at admission and the overall mortality rate of patients diagnosed with COVID-19 during their hospital stay. In instances where hazard ratios (HRs) were reported, these were converted to RRs. Similarly, for studies reporting odds ratios (ORs), the RRs were calculated by the formula RR═OR/([1−pRef]+[pRef × OR]), with pRef representing the prevalence of the outcome in the reference group (i.e., the group with low SII) [33]. To stabilize and normalize the variance, a logarithmic transformation was applied to each study's RR and associated standard error [34]. The Cochrane Q test and the I^2 statistic [35] were utilized to estimate between-study heterogeneity. Considerable heterogeneity between the studies is present when the I^2 value is higher than 50 %. To

account for potential heterogeneity, the results were combined by a random-effects model, as it is recognized to encompass its impact [30]. A forest plot has been used to display the main statistical values [36]. In order to determine the cause of heterogeneity, a univariate meta-regression analysis was also performed to assess how study characteristics affected the outcomes, such as patient number, mean age, male proportion, baseline mean SII, cutoff of SII, patient mortality in individual study, and quality scores. Subgroup analyses were also carried out to evaluate how study characteristics, including mean age, proportion of men, follow-up duration, and region of the study, influenced the outcomes. Furthermore, we conducted an examination to determine the consistency of the association among the entire cohort of critically ill patients, hospitalized patients with COVID-19, and chronic kidney disease (CKD) patients with COVID-19. Additionally, we assessed studies that employed both univariate and multivariate regression analyses. To evaluate publication bias, we utilized Egger's regression asymmetry test, a funnel plot, and Begg's test, relying on visual symmetry judgments [37]. For statistical significance, a two-sided p-value of less than 0.05 was considered significant. The meta-analyses were conducted with the RevMan (Version 5.1; Cochrane Collaboration, Oxford, UK) and Stata software (version 12.0; Stata Corporation, College Station, TX).

3. Results

3.1. Database search and study retrieval

Fig. 1 depicts the sequential procedure employed for conducting the literature search and study retrieval. Initially, a comprehensive search across various databases yielded a total of 404 records. No supplementary studies were discovered through the manual examination of references in pertinent original and review articles. Following the elimination of 89 duplicate entries, 315 distinct records remained. Subsequently, during the preliminary screening of titles and abstracts, 272 studies were excluded due to their lack of alignment with the objectives of the meta-analysis. After this initial screening, 43 studies were selected for further assessment through full-text reviews. Following the rigorous review process, 27 studies were excluded for specific reasons detailed in Fig. 1. Consequently,

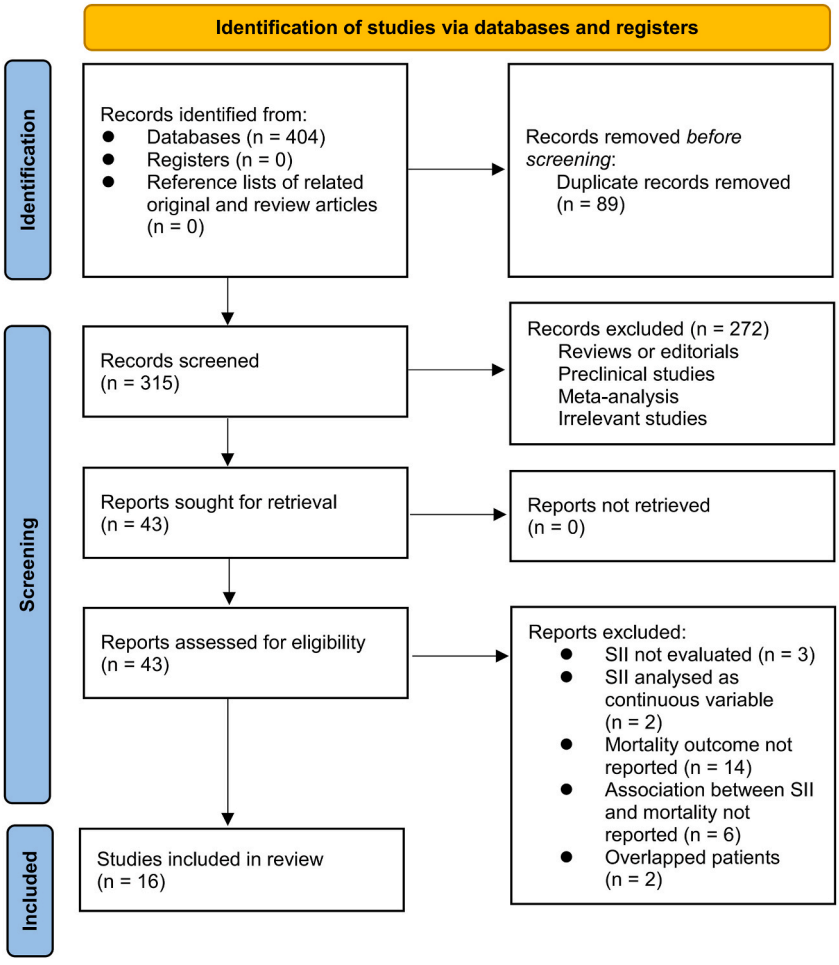

Fig. 1. Flowchart of database search and study inclusion.

Table 1
Characteristics of the included studies.

Study	Country	Design	Diagnosis	Patient number	Mean age (years)	Male (%)	Mean SII at admission	Cutoff of SII	Follow-up duration	Number of patients died	Variables adjusted
Rokni 2020	Iran	RC	Patients with COVID-19	233	52.3	63.9	1279	500	During hospitalization	28	None
Fois 2020	Italy	RC	Patients with COVID-19	119	72	64.7	1137	1835 (ROC analysis derived)	During hospitalization	29	Age, PaO2/FiO2, intensity of care, and CCI
Moisa 2021	Romania	RC	Critically ill patients with COVID-19	272	62.7	68.4	5055	3700 (ROC analysis derived)	During ICU stay	142	Age, hospital acquired infection, PaO2/FiO2, and higher respiratory support
Acar 2021	Turkey	RC	Patients with COVID-19	148	59.5	37.8	2445	2699 (ROC analysis derived)	During hospitalization	19	Age, CRP, ICU stay, and comorbidities
López-Escobar 2021	Spain	RC	Patients with COVID-19	2088	69	59.6	1422	1387 (ROC analysis derived)	During hospitalization	321	Age, diastolic BP, NLR rate of change >10 % per day, creatinine, urea and glucose
Sevinc 2021	Turkey	RC	HD patients with COVID-19	117	61.2	48.7	1382	1145 (ROC analysis derived)	During hospitalization	29	None
Muresan 2022	Romania	RC	Patients with COVID-19	899	70.5	53.3	1463	2209 (ROC analysis derived)	During hospitalization	143	Age, obesity, comorbidities, and nutritional status
Kudlinski 2022	Poland	RC	Critically ill patients with COVID-19	285	59.3	66.3	3922	2058 (ROC analysis derived)	During ICU stay	108	Age, CRP, and PCT
Qiu 2022	China	RC	Patients with COVID-19	2347	72.2	41.7	429	999 (ROC analysis derived)	During hospitalization	57	Age, sex, disease severity, and comorbidities
Gutierrez-Perez 2022	Mexico	RC	Patients with COVID-19	807	59	65.4	3233	2892 (ROC analysis derived)	During hospitalization	316	Age and sex
Ghobadi 2022	Iran	RC	Patients with COVID-19	1792	59.5	55.1	1103	1994 (ROC analysis derived)	During hospitalization	353	Age, disease severity, and CCI
Oguz 2022	Turkey	RC	HD patients with COVID-19	123	61.1	61	1267	726 (ROC analysis derived)	During hospitalization	28	Age, CRP, ferritin, DM, and CAD
Karaaslan 2022	Turkey	RC	HD patients with COVID-19	191	54.3	49.2	586	619 (ROC analysis derived)	During hospitalization	35	None
Ozdemir 2022	Turkey	RC	CKD patients with COVID-19	93	70	50.5	958	1180 (ROC analysis derived)	During hospitalization	34	None
Kalejaiye 2023	Nigeria	RC	Patients with COVID-19	48	54.4	55.2	933	813 (ROC analysis derived)	During hospitalization	6	None
Haryati 2023	Indonesia	RC	Patients with COVID-19	445	50	54.8	1816	2504 (ROC analysis derived)	During hospitalization	153	None

RC, retrospective cohort; COVID-19, Coronavirus disease 2019; HD, hemodialysis; CKD, chronic kidney disease; SII, systemic immune-inflammatory index; ROC, receiver operating characteristic; ICU, intensive care unit; CCI, Charlson Comorbidity Index; CRP, *C*-reactive protein; BP, blood pressure; NLR, neutrophil-to-lymphocyte ratio; PCT, procalcitonin; CAD, coronary artery disease; DM, diabetes mellitus.

Table 2
Study quality evaluation via the Newcastle-Ottawa Scale.

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at baseline	Control for age	Control for other confounding factors	Assessment of outcome	Enough long follow-up duration	Adequacy of follow-up of cohorts	Total
Rokni 2020	0	1	1	1	0	0	1	1	1	6
Fois 2020	0	1	1	1	1	1	1	1	1	8
Moisa 2021	0	1	1	1	1	1	1	1	1	8
Acar 2021	1	1	1	1	1	1	1	1	1	9
López-Escobar 2021	0	1	1	1	1	1	1	1	1	8
Sevinc 2021	0	1	1	1	0	0	1	1	1	6
Muresan 2022	0	1	1	1	1	1	1	1	1	8
Kudlinski 2022	1	1	1	1	1	1	1	1	1	9
Qiu 2022	0	1	1	1	1	1	1	1	1	8
Gutierrez-Perez 2022	0	1	1	1	1	0	1	1	1	7
Ghobadi 2022	1	1	1	1	1	1	1	1	1	9
Oguz 2022	0	1	1	1	1	1	1	1	1	8
Karaaslan 2022	0	1	1	1	0	0	1	1	1	6
Ozdemir 2022	0	1	1	1	0	0	1	1	1	6
Kalejaiye 2023	0	1	1	1	0	0	1	1	1	6
Haryati 2023	0	1	1	1	0	0	1	1	1	6

16 studies were deemed suitable and were included in the subsequent meta-analysis [12–27].

3.2. Study characteristics

Overall, 16 retrospective cohort studies were identified, and Table 1 presents their summarized characteristics. These studies were conducted in Iran, Italy, Romania, Turkey, Spain, Poland, China, Mexico, Nigeria, and Indonesia and published between 2020 and 2023. Ten of them included overall adult patients hospitalized for COVID-19, while the others included critically ill patients [16,21], patients on hemodialysis [17,20,23], patients with CKD [24] and COVID-19. In total, 10,007 patients hospitalized for COVID-19 were included. Their average age were 50–72 years. The mean SII at admission in patients of each study was 586–5055. The optimal cutoff of SII was derived by the results of receiver operating characteristic curve analysis in 15 studies [12,14–27], while in one study [13], the cutoff of SII was arbitrarily determined. A total of 1801 (18.0 %) patients died in hospitalization. six studies used univariate analysis to find the connection between SII and in-hospital mortality [13,17,20,24,26,27], while the other ten studies [12,14–16,18,19,21–23,25] used multivariate analysis by adjusting age, sex, comorbidities, and other possible confounding factors. The included studies' NOS were 6–9, suggesting that their quality was moderate to good (Table 2).

3.3. Overall meta-analysis

According to pooled data, patients hospitalized for COVID-19 had a higher risk of all-cause mortality if their SII was high at admission (RR: 2.41, 95 % CI: 1.78 to 3.24, $p < 0.001$), although there was significant heterogeneity (p for Cochrane Q test <0.001; $I^2 = 86$ %; Fig. 2).

3.4. Meta-regression analysis

Meta-regression showed that mean SII at baseline and patient mortality of individual study were negatively correlated with the results (coefficients = −0.00023 and −0.030, both $p < 0.05$; Table 3 and Fig. 3), which explained the heterogeneity. Other variables, such as patient number, mean age, male proportion, cutoff of SII, or study quality scores, did not significantly influence the outcome (p all >0.10; Table 3).

3.5. Subgroup analysis

Subsequent subgroup analysis suggested that the correlation between high SII and the risk of all-cause mortality was more remarkable in patients with lower baseline SII (<1300, RR: 3.25, 95 % CI: 2.58 to 4.09) as compared to those with higher baseline SII (≥1300, RR: 1.95, 95 % CI: 1.38 to 2.75; p for subgroup difference = 0.02; Fig. 4A), and the association was stronger in low-risk patients (mortality <20 %, RR: 3.60, 95 % CI: 3.07 to 4.23) as compared to high-risk patients (mortality ≥20 %, RR: 1.52, 95 % CI: 1.23 to 1.89; p for subgroup difference <0.001; Fig. 4B). Moreover, consistent results were obtained from subgroup analysis based on the mean age and percentage of men in each study (p for subgroup difference = 0.80 and 0.38, Fig. 5A and B). A stronger correlation between high SII and mortality of patients with COVID-19 was observed for studies reporting mortality during hospitalization

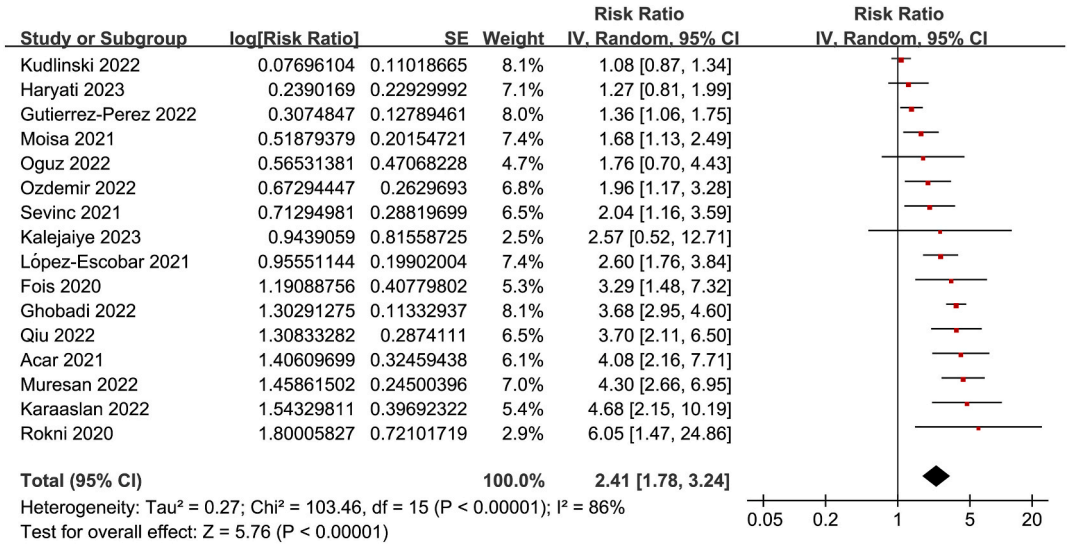

Fig. 2. Forest plots for the overall meta-analyses regarding the correlation between SII at admission and risk of in-hospital mortality of patients with COVID-19.

Table 3
Univariate meta-regression analysis.

	RR for the association between SII and mortality of patients with COVID-19		
Covariate	Coefficient	95 % CI	*p*
Patient number	0.0002	−0.0016 to 0.0056	0.26
Mean age (years)	0.022	−0.021 to 0.064	0.29
Proportion of men (%)	−0.032	−0.079 to 0.015	0.33
Mean SII at admission	−0.00023	−0.00041 to −0.00005	0.01
Cutoff of SII	−0.00022	−0.00054 to 0.00010	0.16
Mortality (%)	−0.030	−0.045 to −0.015	0.001
NOS	0.049	−0.210 to 0.308	0.69

RR risk ratio; CI, confidence interval; SII, systemic immune-inflammatory index; COVID-19, Coronavirus disease 2019.
NOS, Newcastle-Ottawa Scale.

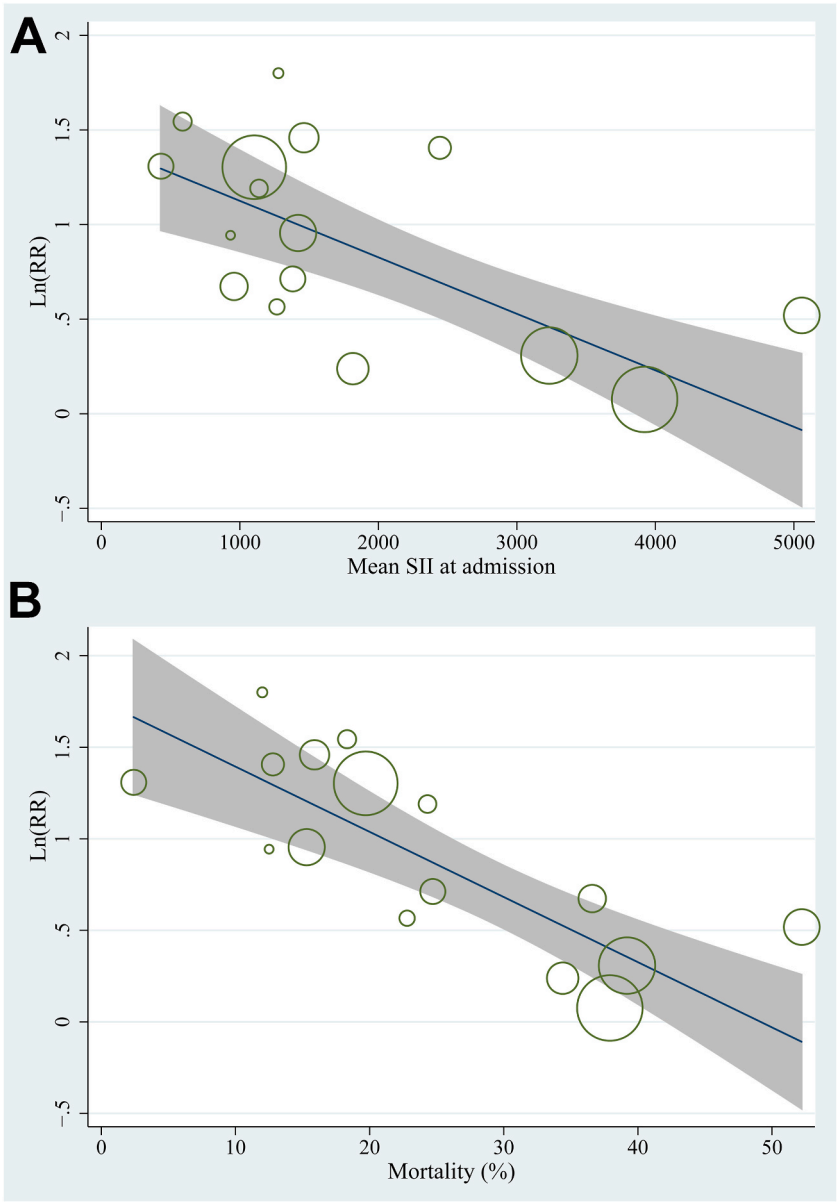

Fig. 3. Meta-regression analyses to evaluate the influence of mean SII at baseline and patient mortality in individual studies on the outcome of the meta-analysis; A, meta-regression analysis for the influence of mean SII at baseline; and B, meta-regression analysis for the influence of patient mortality in individual study.

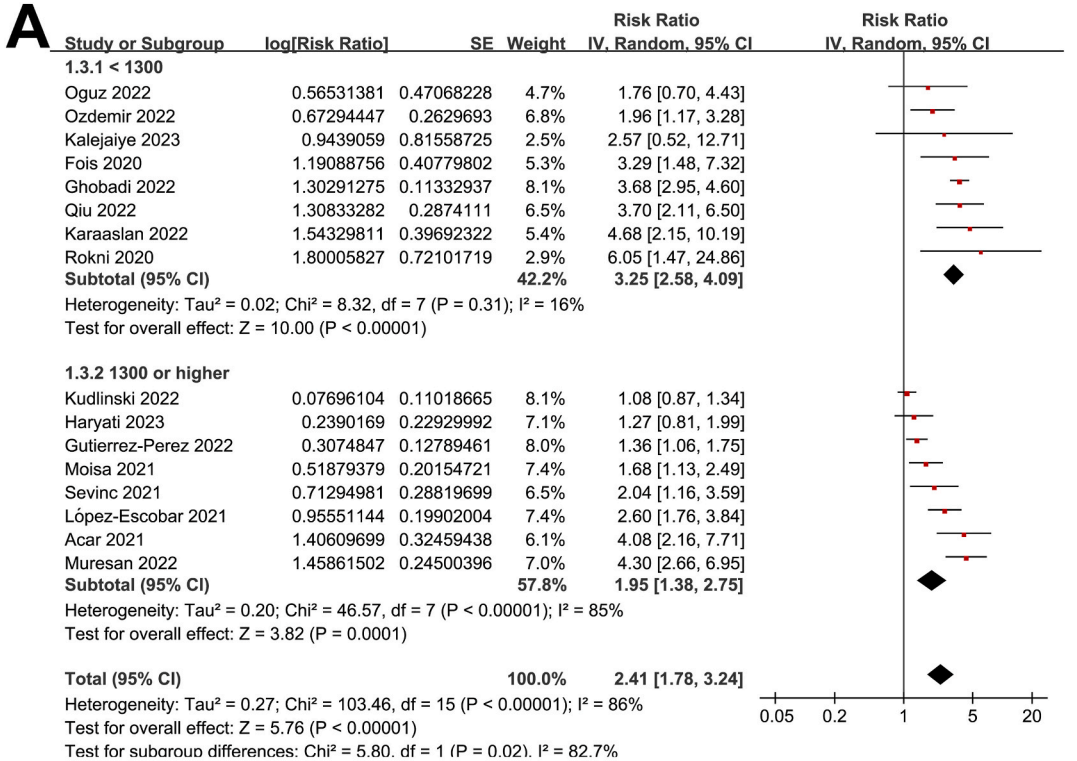

Fig. 4. Forest plots depicting the subgroup analyses for the association between SII at admission and risk of in-hospital mortality of patients with COVID-19; A, subgroup analysis according to the mean SII at baseline of each study; and B, subgroup analysis according to patient mortality in the individual study.

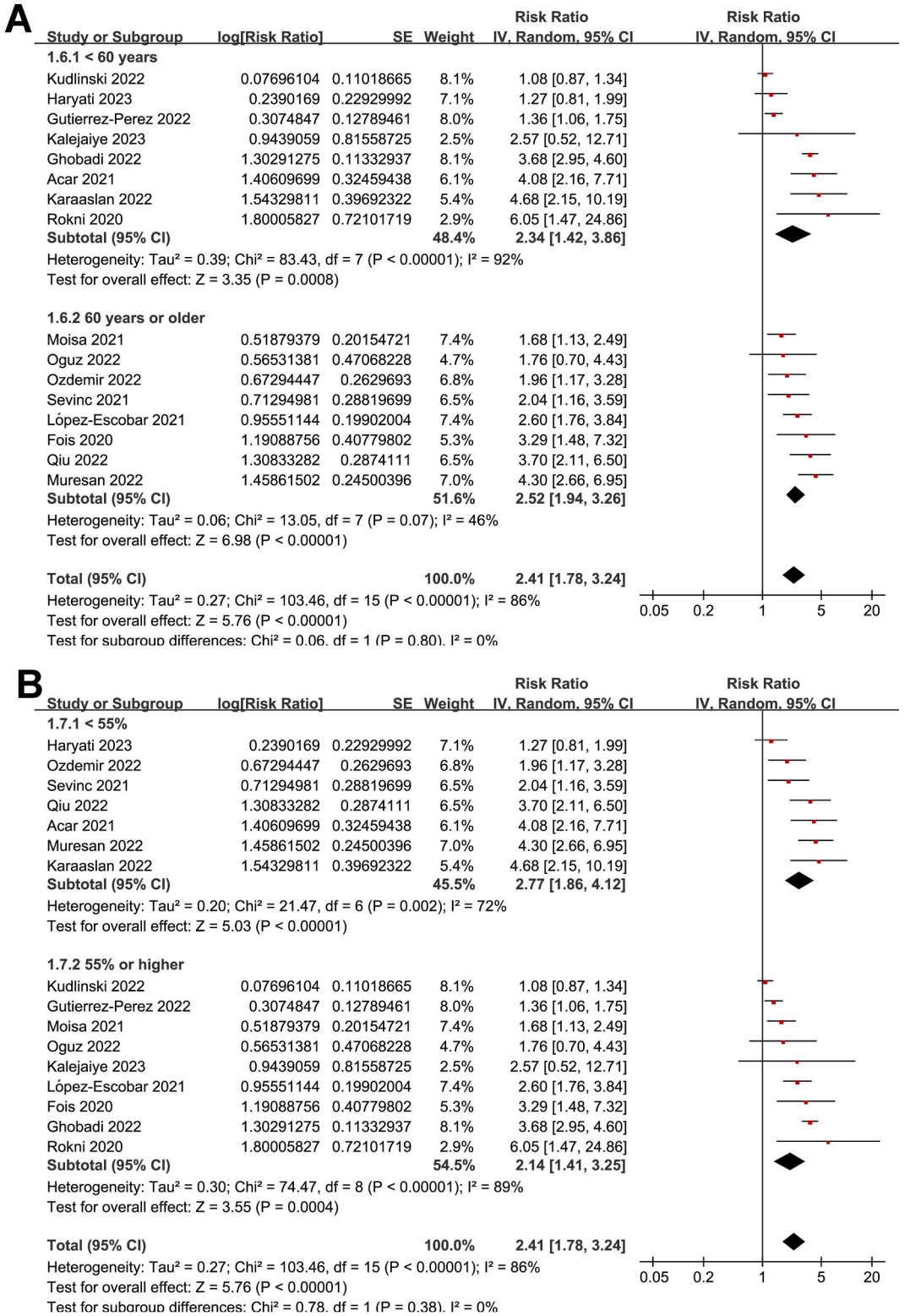

Fig. 5. Forest plots depicting the subgroup analyses for the association between SII at admission and risk of in-hospital mortality of patients with COVID-19; A, subgroup analysis according to the mean age of the patients; and B, subgroup analysis according to the proportion of men of each study.

compared to that during ICU stay (RR: 2.66 versus 1.30, p for subgroup difference = 0.007; Fig. 6A). In addition, the correlation between high SII and mortality of patients with COVID-19 was similar in studies from Asian and European countries (p for subgroup difference = 0.62; Fig. 6B). Finally, Similar findings were observed in studies with overall patients with COVID-19 and CKD patients

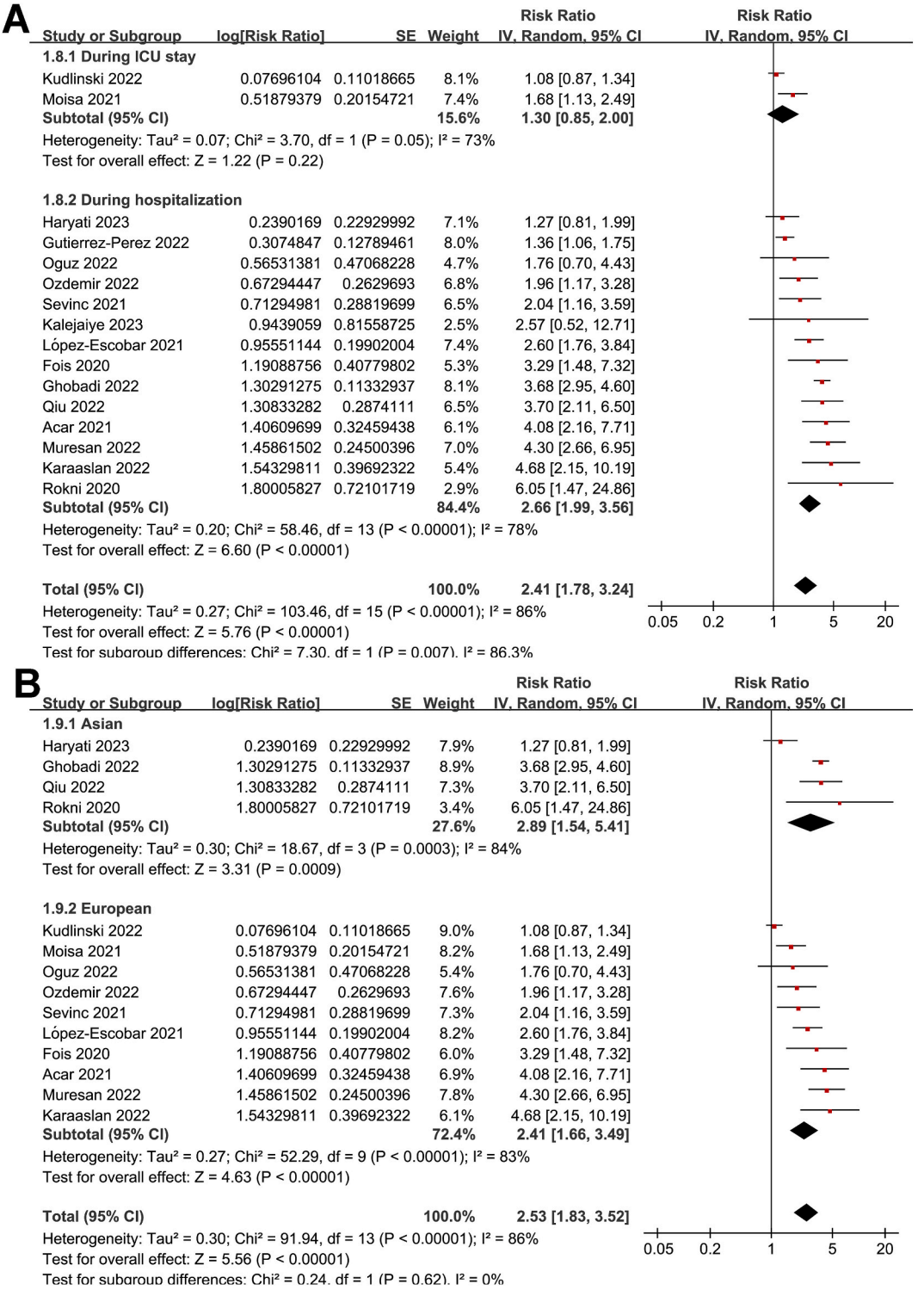

Fig. 6. Forest plots depicting the subgroup analyses for the association between SII at admission and risk of in-hospital mortality of patients with COVID-19; A, subgroup analysis according to follow-up duration; and B, subgroup analysis according to region of the study.

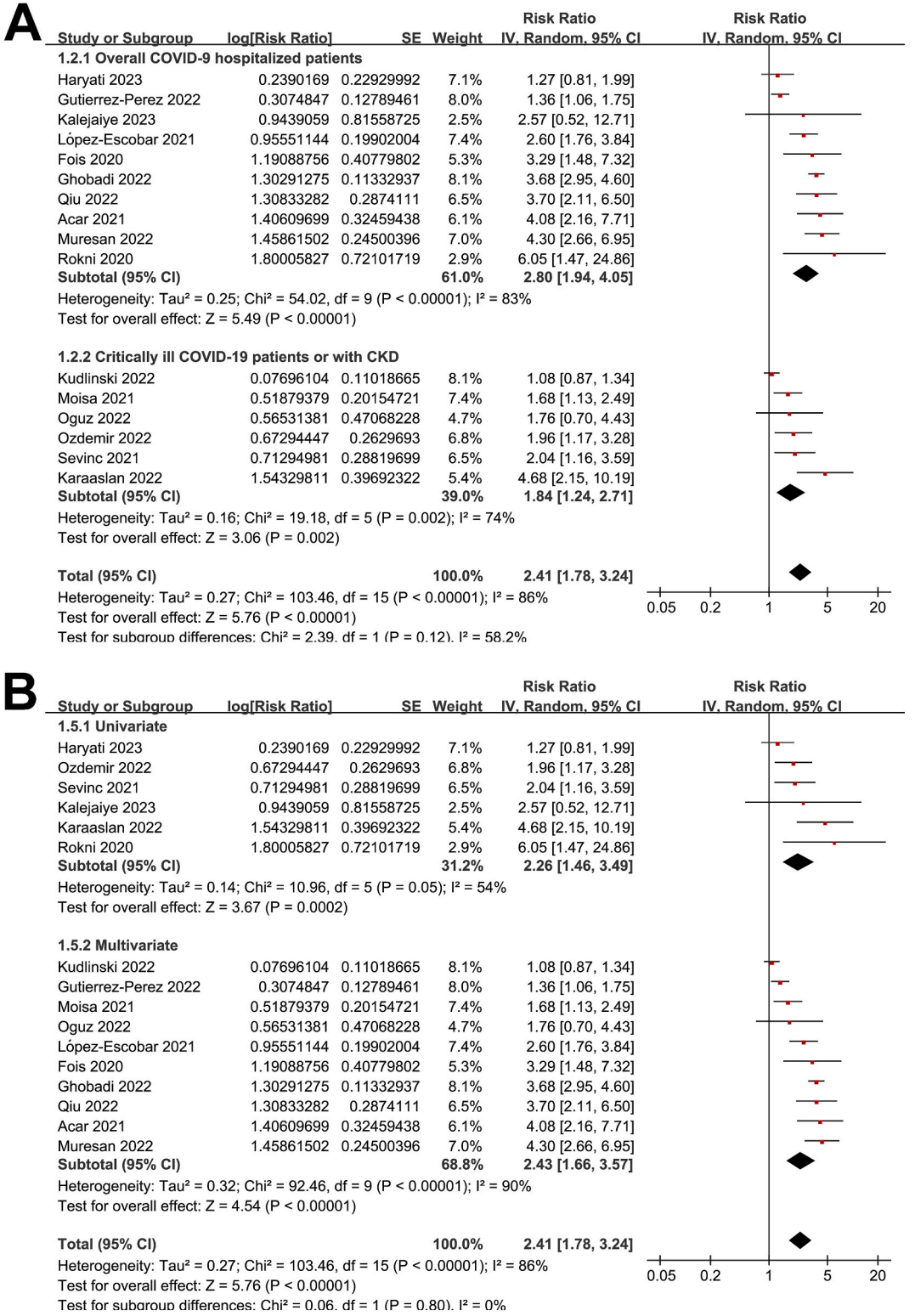

Fig. 7. Forest plots depicting the subgroup analyses for the association between SII at admission and risk of in-hospital mortality of patients with COVID-19; A, subgroup analysis according to the diagnosis of the patients; and B, subgroup analysis according to the NOS of each study.

with COVID-19 (p for subgroup difference = 0.12, Fig. 7A) and studies with univariate and multivariate analyses (p for subgroup difference = 0.80, Fig. 7B).

3.6. Estimation of publication bias

The funnel plots presented in Fig. 8 depict the meta-analysis results concerning the correlation between SII at admission and the in-hospital mortality risk among patients diagnosed with COVID-19. Upon visual inspection, the plots exhibit symmetrical patterns, implying a minimal presence of publication bias. Furthermore, the statistical analyses conducted, including Begg's test ($p = 0.49$) and Egger's regression tests ($p = 0.33$), provide further evidence supporting the notion of a low probability of publication bias.

4. Discussion

This study investigates the correlation between SII at admission and the risk of in-hospital mortality among patients diagnosed with COVID-19 through systematic review and meta-analysis based on 16 cohort studies. According to our research, hospitalized COVID-19 patients may have a higher risk of all-cause mortality if their baseline SII is high. Meta-regression and subgroup analyses further indicated that the mean SII and patient mortality in individual studies significantly influenced the results. These analyses revealed a more pronounced connection between high SII and mortality in patients with lower baseline SII (<1300), while indicating a reduced risk of mortality (<20 %). These findings were consistent across studies involving overall patients with COVID-19, those with CKD, and those with both univariate and multivariate analyses. Moreover, other study characteristics, including age, sex, and region of the study country, were not found to have a significant effect on the results. Collectively, these results emphasize the potential significance of SII as a determinant of short-term mortality in hospitalized patients diagnosed with COVID-19.

To the best of our understanding, there is limited research in the form of meta-analyses that have examined the connection between SII and the prognosis of individuals diagnosed with COVID-19. Several notable methodological strengths are incorporated in our meta-analysis. Firstly, we conducted an extensive search of literature across four widely recognized databases, ensuring the inclusion of up-to-date evidence regarding the correlation between SII and in-hospital mortality among patients diagnosed with COVID-19. Furthermore, we conducted multiple meta-regression and subgroup analyses to investigate potential factors contributing to heterogeneity, thereby revealing the influence of mean SII and patient characteristics. Furthermore, consistent findings were observed in subgroups of studies with both univariate and multivariate regression analyses, suggesting that the connection between high SII and in-hospital mortality appears to be unaffected by potential confounding variables like age and comorbidities. The ease and convenience of obtaining SII through routine complete blood count, a fast and inexpensive procedure, further support its potential as a prognostic biomarker for patients hospitalized with COVID-19.

There may be several mechanisms that account for the link between a high SII and an elevated risk of all-cause mortality among patients hospitalized with COVID-19. Considering the cellular components of the SII, a high SII may reflect the increased severity of inflammatory (high neutrophils) and thrombotic (high platelets) dysfunction and compromised immune function (low lymphocytes), which has been related to the severity and the increased incidence of adverse clinical outcomes of patients diagnosed with COVID-19 [7]. An early study from China showed that a high SII may effectively predict the cases of severe COVID-19, as defined according to the National Guidelines for the Diagnostic and Treatment of COVID-19 [38]. In addition, patients with a high SII at admission were

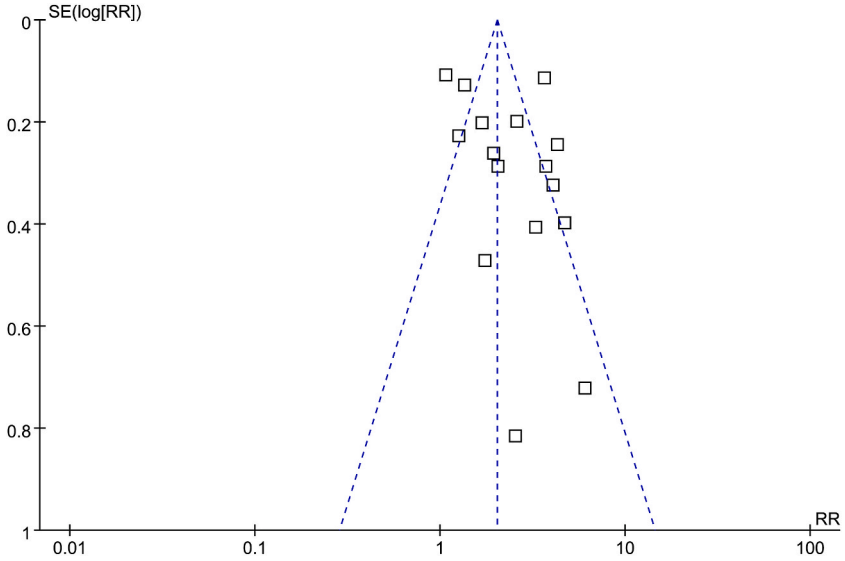

Fig. 8. Funnel plots depicting the publication bias underlying the meta-analysis of the association between SII at admission and risk of in-hospital mortality of patients with COVID-19.

confirmed to be more likely to be admitted to ICU because of the severity of the disease [39]. Finally, a high SII at admission has also been suggested to be a predictor of a few adverse in-hospital events in patients with COVID-19, such as the demand for invasive mechanical ventilation [40], acute limb ischemia [41], and acute venous thrombotic events [22], all of which may contribute to the elevated mortality risk.

Significant heterogeneity was observed across the included studies. Results of the mega-regression and subgroup-analysis revealed that the link between a high SII and the risk of all-cause mortality may be stronger in studies of patients with lower baseline SII and lower risk of mortality, which implies that the predictive efficacy of SII for poor in-hospital survival may potentially be more useful in low-risk patients. These findings may suggest that the essential source of heterogeneity in the meta-analysis may be the severity of COVID-19 infection at admission. These findings are beneficial in the current epidemic status that many patients with COVID-19 have mild or moderate symptoms. On the other hand, we found a stronger association between a high SII with hospital during hospitalization compared to ICU stay. However, caution should be exercised in interpreting these results, particularly for the subgroup related to ICU stay, given that only two studies were included. Furthermore, it is crucial to approach the interpretation of the results from the mega-regression and subgroup analyses with caution, as they were derived from data obtained at the study level. To substantiate these findings, it is essential to conduct extensive prospective studies on a large scale.

Some specific limitations constrained this study. Firstly, the inclusion of only retrospective studies introduces the potential for selection and recall biases. To establish validity, prospective studies are necessary. Secondly, owing to its nature as a meta-analysis of observational studies, these findings cannot draw a direct connection between a high SII and the heightened risk of in-hospital mortality in COVID-19 patients. As the published time of included studies spanned from 2020 to 2023, the differences in the vaccination status of the patients and the variants of COVID-19 might affect the results of the meta-analysis. However, by re-evaluating the included studies, none reported the vaccination status of the patients, and only one study [25] reported the variant of COVID-19. Therefore, we were unable to perform subgroup analysis accordingly. Studies are required in the future to ascertain if the vaccination status of the patients and the different variants of COVID-19 may significantly affect the connection between SII and mortality of COVID-19 patients. Furthermore, determining an optimal SII cutoff to predict the mortality of COVID-19 patients remains elusive, underscoring the necessity for further investigation. Finally, the correlation between SII and the long-term prognosis of COVID-19 patients is still unknown. For example, COVID-19 infection has been linked to a variety of adverse outcomes, including cardiac dysfunction [42], new-onset neurodegenerative diseases [43], and new-onset diabetes [44]. Determining whether a high SII at baseline could predict these long-term adverse outcomes after COVID-19 infection is interesting.

5. Conclusions

The findings of this meta-analysis indicate that a heightened SII upon admission is linked to an elevated likelihood of mortality from any cause among individuals admitted to the hospital with COVID-19. It is noteworthy that this association seems to be particularly prominent in patients classified as low-risk. While additional prospective studies are required to corroborate and authenticate these results, the evidence derived from this meta-analysis substantiates the potential usefulness of SII as a valuable prognostic indicator for in-hospital outcomes in patients afflicted with COVID-19. Incorporating SII assessment into clinical practice may aid in identifying patients at higher risk of adverse outcomes and facilitate more targeted and timely interventions to improve patient care and management.

Funding

None.

Data availability statement

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Hao Yuan: Writing – original draft, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Jing Tian:** Writing – review & editing, Formal analysis, Data curation. **Lu Wen:** Writing – review & editing, Supervision, Software, Project administration, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

None.

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