META-ANALYSIS

Prognostic role of the systemic immune-inflammation in patients with non-small cell lung cancer: A meta-analysis

Guomin Zhao, Hui Zhang, Pucong Ye, Wei Chen

Abstract

Objective: To explore the prognostic value of systemic immune-inflammation in assessing patients with non-small cell lung cancer.

Method: The meta-analysis was conducted from May to July 2023, and comprised a comprehensive search PubMed, Excerpta Medica Database and Cochrane Library databases up to March 21, 2023, for relevant peer-reviewed articles evaluating the prognostic value of systemic immune-inflammation in patients with non-small cell lung cancer. Hazard ratio and 95% confidence interval were calculated to assess systemic immune-inflammation's relationship with overall survival and progression-free survival. Data was analysed using STATA 17.0.

Results: Of the 135 studies initially identified, 32(23.7%) were analysed in detail, involving 12,040 patients. Increased systemic immune-inflammation was significantly associated with poor overall survival (hazard ratio: 1.31; 95% confidence interval: 1.21-1.41; $p<0.001$) and progression-free survival (hazard ratio: 1.48; 95% confidence interval: 1.12-1.94; $p<0.001$) in non-small cell lung cancer patients. Subgroup analysis confirmed these findings, with significant associations observed across various subgroups (country, sample size, cut-off value, survival analysis type, and TNM stage). Sensitivity analysis showed that the pooled hazard ratios remained stable, with no significant changes upon the exclusion of individual studies ($p=0.75$ for OS and p=0.83 for PFS). Publication bias was assessed and no significant bias was observed for either OS or PFS (Egger's test $p=0.12$ for OS and $p=0.18$ for PFS).

Conclusions: High systemic immune-inflammation was found to be a significant predictor of poor overall survival and progression-free survival in non-small cell lung cancer patients.

Keywords: Systemic immune-inflammation index, Non-small cell lung cancer, Meta-analysis, Prognosis.

(JPMA 76: 749; 2026) **DOI: https://doi.org/10.47391/JPMA.20416**

Introduction

Non-small cell lung cancer NSCLC represents the predominant form of lung malignancy, constituting an estimated 85% of total lung cancer diagnoses.[1] Despite advancements in early detection methods and therapeutic strategies, NSCLC remains a major contributor to global cancer-related deaths due to its high prevalence and tendency to progress rapidly.[2] The disease often recurs locally or metastasises distantly, and the prognosis for NSCLC patients is generally poor.[3] To enhance patient outcomes, identifying reliable prognostic indicators is critical for predicting survival and informing the development of effective treatment strategies in NSCLC patients. This approach can significantly improve both survival rates and quality of life (QOL) for this population.

The systemic inflammatory response is a critical factor in tumour development, local immunosuppression, and cancer progression. Recent investigations have revealed that a range of biomarkers indicative of inflammation, encompassing the neutrophil-to-lymphocyte ratio (NLR),[4] platelet-to-lymphocyte ratio (PLR)[5] and systemic immune-inflammation (SII),[6-8] exhibit significant correlations with the prognosis of malignancies. The SII index is an emerging biomarker used to assess inflammation. It is calculated by multiplying the platelet and neutrophil counts, and then dividing the result by the lymphocyte count.[9] This convenient and easily available indicator has been shown to independently predict overall survival (OS) in patients with different types of malignant tumours, including pancreatic cancer,[10] colorectal cancer,[11] NSCLC[12] and hepatocellular carcinoma (HCC).[13]

A multitude of research has delved into the predictive importance of the SII concerning NSCLC, but the findings have varied across studies.[12,14-39] While some studies have identified SII as a crucial prognostic factor for NSCLC, others have not supported this view.[40-43] For example, a study demonstrated that elevated SII levels functioned as a significant independent predictor of OS in NSCLC patients treated with chemoradiotherapy (hazard ratio [HR]: 1.63; 95% confidence interval [CI]: 1.18–2.04, $p<0.001$).[35] However, a recent study using multivariate analysis

Department of Intensive Care Unit, Beijing Shijitan Hospital, Capital Medical University, Beijing, China.

Correspondence: Wei Chen. e-mail: zhaoguomin3363@bjsjth.cn

ORCID ID: 0000-0003-4737-5208

Submission completed: 24-07-2024 **1st Revision received:** 16-05-2025

Acceptance: 24-01-2026 **Last Revision received:** 23-01-2026

concluded that the SII did not emerge as a separate predictor of OS in patients afflicted with advanced stages of NSCLC (HR: 1.140; 95% CI: 0.808-1.610; *p*=0.445).[40] The current systematic review and meta-analysis was planned to furnish a more holistic and precise assessment of the prognostic significance of the SII among NSCLC patients.

Materials and Methods

The systematic review and meta-analysis was conducted from May to July 2023 in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[44] The methodology was registered in the international prospective register of systematic reviews (PROSPERO)[45] (CRD42023428555).

The study comprised search on PubMed, Excerpta Medica Database (EMBASE) and Cochrane Library databases (from their inception through March 21, 2023). Search terms included "Systemic immune inflammation index", "SII", "non-small cell lung cancer", "NSCLC", "squamous cell carcinoma", "adenocarcinoma", and "lung cancer". The strategy combined medical subject heading (MeSH) terms and key words to maximise retrieval of relevant peer-reviewed studies.

The criteria for study eligibility encompassed: research examining the correlation of SII with patient survival data (OS and/or progression-free survival [PFS]) in NSCLC patients; NSCLC diagnosis confirmed by pathological examination; provision of SII cut-off value and HRs with 95% CIs for prognostic factors; publication in English language; Newcastle-Ottawa Scale (NOS) score of at least 646. Non-human studies, articles of a review nature, correspondence, editorials, case studies and abstracts from conferences or meetings, and research featuring redundant or overlapping participant cohorts were excluded.

Two researchers extracted data from the eligible studies independently, with discrepancies being addressed through collaborative discussion. The collected data included variables, such as the lead author's name, publication year, study duration, geographical location, sample size, gender distribution, tumour-node-metastasis (TNM) staging, follow-up period, threshold value for SII, survival outcomes measured, type of survival analysis performed, source of the HR, and the HR with its 95% CI. The quality of the studies was assessed using the NOS criteria[45] and NOS score >6 was deemed to mean high quality.

Data was analysed using STATA 17.0. The predictive significance of the SII concerning clinical endpoints was assessed by HRs and 95% CIs. The chi-square Q test, along with the I2 statistic, was deployed to scrutinise the heterogeneity in study outcomes. When minimal heterogeneity was detected, indicated by *p*>0.10 and I2 <50%, a fixed-effects model was used for analysis. In instances of significant heterogeneity, a random-effects model was employed. Heterogeneity was ascertained by conducting a stratified subgroup analysis across diverse observational metrics. Sensitivity analysis assessed the influence of each study on the collective outcomes by successively removing one study at a time. Begg's test and Egger's test[47,48] were used to assess the possibility of publication bias, with *p*<0.05 being the threshold for statistical significance.

Results

Of the 135 studies initially identified, 32(23.7%) were analysed in detail[12,14-43,48] (Figure 1), involving 12,040 patients.

The studies analysed, hailing from 2017 to 2023, were retrospective in nature and spanned a range of sample sizes, from 34 to 3,984 participants. Overall, 9(28.12%) studies[16,21,26,29,32,34,35,41,49] were conducted outside of Asia, with the remainder being conducted in China.[12,14,15,17-20,22-25,27,28,30,31,33,36-40,42,43] The SII cut-off values ranged from 395.4 to 1,270 (Table 1).

The association between SII and OS in patients with NSCLC was reported in 31 (96.87%) studies.[12,14-43] A random-effects model was used due to high heterogeneity (I2=88.5%, *p*<0.001). A high SII was significantly associated with poor OS in NSCLC (HR: 1.31; 95% CI: 1.21-1.41;

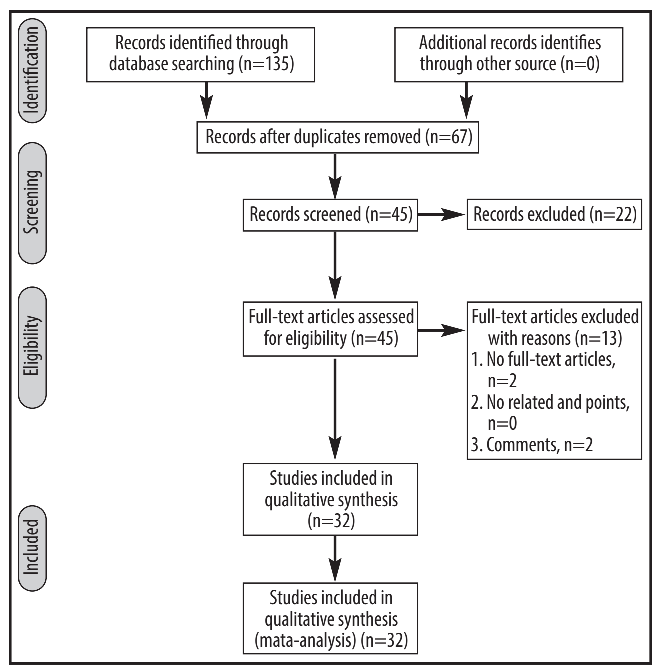

Figure-1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Table-1: Characteristics of the studies subjected to meta-analysis.

Study	Country	Sample size	Age median (range)	Gender (M/F)	TNM stage	Study period follow-up (months) median (range)	Follow-up (months) median (range)	Cut-off value of SII ($\times 10^9$/L)	Group size (high/low)	Survival endpoints	Survival analysis	NOS score
Tong Y 2017[14]	China	332	61(34-79)	206/126	III	January 2006 to May 2012	NR	660	149/183	OS	Multivariate	7
Guo D 2018[15]	China	140	62(33-83)	95/45	III-IV	August 2013 to January 2016	NR	521	72/68	OS, PFS	Multivariate	7
Berardi 2019[16]	taly	311	68(25-86)	216/95	III-IV	1st May 2006 to 30th June 2015	NR	1270	179/132	OS, PFS	Univariable	7
Deng C 2019[17]	China	203	59(28-79)	89/114	IV	Jan 2013 to Nov 2018	NR	1066.935	63/140	OS, PFS	Multivariate	7
Guo W 2019[18]	China	569	60(27-80)	425/114	I-III	July 2006 to May 2012	60.3(0.9-146.7)	419.6	307/262	OS	Multivariate	7
Li H 2019[19]	China	310	57(28-80)	162/148	IV	May 2013 to May 2016	NR	1218.81	83/227	OS	Multivariate	6
Liu J 2019[20]	China	44	60(43-74)	33/11	III-IV	March 2016 to July 2018	6.9(0.6-28.5)	603.5	22/22	OS, PFS	Multivariate	6
Bilgetekin 2020[21]	Turkey	123	60(55-66)	96/27	NR	January 2010 to March 2020	NR	730	NR	OS, PFS	Multivariate	6
Li A 2020[22]	China	252	58(24-84)	145/107	IV	October 2013 to January 2018	25.9(1-63)	630.85	154/98	OS	Multivariate	8
Li X 2020[23]	China	345	64(25-93)	255/90	III-IV	December 2012 to December 2018	NR	555.59	221/124	OS	Multivariate	7
Yan X 2020[24]	China	538	60(24-82)	343/195	I-III	January 2009 to December 2011	54(3-108)	402.37	339/199	OS	Multivariate	8
Fu F 2021[25]	China	3984	60	2139/1845	I-III	April 2008 to December 2015	45.1	479	1643/2341	OS	Multivariate	8
Ju Q 2021[43]	China	102	59.5(30-80)	41/61	III-IV	January 2014 to December 2016	NR	841.03	NR	OS, PFS	Multivariate	7
Keit 2021[26]	USA	125	67(45-86)	64/61	III	January 1st, 2010, to December 31st, 2019	12.2	1266	55/70	OS, PFS	Multivariate	8
Li W 2021[27]	China	214	60(33-80)	120/94	I-IV	January 2009 to December 2018	NR	696.52	100/114	OS	Multivariate	8
Takeda 2021[48]	Japan	42	67(29-85)	22/20	NR	1 September 2015, and 31 March 2021	NR	1000	15/27	PFS	Univariable	7
Yang H 2021[42]	China	34	56.4(38-73)	20/14	III	January 2015 to December 2019	26.4(12.4-55.4)	918.63	NR	OS	Univariable	7
Yucel 2021[29]	Turkey	136	62(21-93)	81/55	III-IV	2014-2018	17.6	640	89/47	OS, PFS	Multivariate	7
Zeng Q 2021[30]	China	253	NR	NR	II-III	January 2003 to December 2018	40	430.8	NR	OS	Multivariate	7
Zhang Y 2021[31]	China	124	60(38-73)	56/68	I-III	May 2015 to June 2018	20(6-38)	480	66/58	OS, PFS	Multivariate	7
Xu S 2021[28]	China	234	57(28-86)	137/97	IV	January 2008 to May 2010	NR	618.3	151/83	OS	Multivariate	8
Coutu 2022[34]	USA	81	63(39-80)	45/36	III	July 2004 to September 2019	NR	1260	36/45	OS	Multivariate	8
Soykut 2022[35]	Turkey	392	NR	363/29	III	January 2012 to December 2017	15(2-76)	817	212/180	OS, PFS	Multivariate	8
Abravan 2022[32]	UK	1582	68(32-91)	874/708	NR	2005–2020	14.1(1-149.1)	1218	NR	OS	Univariable	6
Gao 2018[12]	China	410	60(35-82)	267/143	I-III	2009–2011	NR	395.4	270/140	OS	Multivariate	7
Chen X 2022[33]	China	94	48 (18–76)	55/39	III-IV	January 2014 to January 2019	NR	842	47/47	OS, PFS	Univariable	8
Yang J 2022[38]	China	119	61(36-80)	67/52	III-IV	January 2017 to April 2021	NR	775.2	63/56	OS, PFS	Multivariate	7
Wang Q 2022[37]	China	202	54(24-81)	73/129	IV	November 2011 to April 2021	NR	859.79	93/109	OS	Univariable	8
Olmez 2022[41]	Turkey	82	52.5(20-77)	47/35	I-IV	January 2013 to August 2019	19.3	934.7	NR	OS, PFS	Multivariate	7
Guo D 2022[36]	China	118	59(52-71)	54/64	I-III	January 2014 to December 2017	25(12-49)	480	NR	OS, PFS	Multivariate	7
Fang Q 2023[40]	China	223	64	189/34	III-IV	NR	20.4	792.07	NR	OS, PFS	Univariable	6
Chen D 2023[39]	China	111	53(32-82)	40/71	IV	2018-2019	NR	620.2	51/60	OS	Multivariate	7

M: Male, F: Female, OS: Overall survival, PFS: Progression-free survival, NOS: Newcastle-Ottawa Scale, TNM: Tumour-node-metastasis, NR: Not reported.

$p<0.001$). Subgroup analysis indicated that the prognostic value of SII for OS was significant regardless of country, sample size, cut-off value, survival analysis type, or TNM stage. Subgroup analyses demonstrated that the sources of the significant heterogeneity were country, sample size, cut-off value, survival analysis type, or TNM stage (Table 2, Figure 2).

There were 16 studies[15-17,20,21,26,29,31,33,35,36,38,40,41,43,49] showing the association between SII and PFS. Heterogeneity was significant (I2=83.1%, $p<0.001$), and a random-effects model was used. An elevated SII was associated with poor PFS in NSCLC by the combined results (HR: 1.48; 95% CI: 1.12-1.94; $p<0.001$) (Figure 3). Subgroup analysis showed that the association between SII and PFS remained significant across all subgroups, including country, sample size, cut-off value, survival analysis type and TNM stage (Table 3). Subgroup analyses revealed that the significant heterogeneity could be attributed to factors, such as country, sample size, cut-off value, survival analysis type, or TNM stage. (Table 3).

Sensitivity analysis showed that the pooled HRs and corresponding 95% CIs remained stable regardless of the exclusion of any single study (Figures 4-5).

There was no evidence of significant publication bias for OS or PFS (Figurer 6-7).

Discussion

The current systematic review

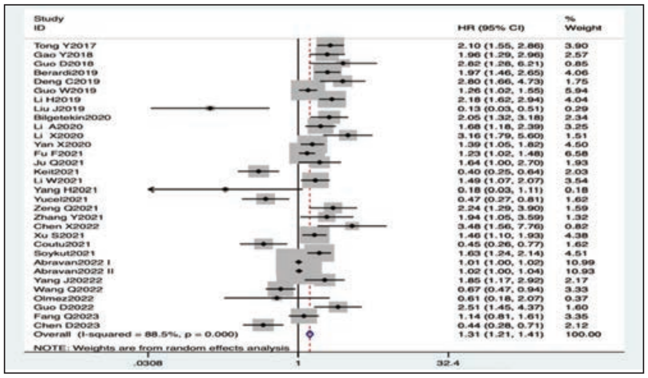

Figure-2: Forest plot for the relationship between SII and OS in NSCLC patients.

SII: Systemic immune-inflammation, NSCLC: Non-small cell lung cancer, OS: Overall survival.

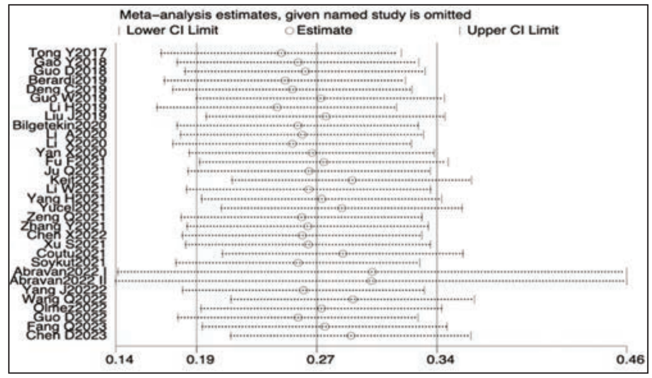

Figure-4: Sensitivity analysis of the association between pre-treatment SII and OS.

SII: Systemic immune-inflammation, OS: Overall survival.

Table-2: Subgroup analysis of the prognostic effect of SII for overall survival (OS) in patients with NSCLC.

Subgroups	No. of comparisons	No. of patients	HR (95%CI)	*p*-value	Effects model	Heterogeneity I2(%)	Heterogeneity *p*-value
Total	32	119988	1.31(1.21-1.41)	<0.001	Random	88.5	<0.001
Countries							
Asian	23	8955	1.50(1.25-1.80)	<0.001	Random	88	<0.001
Non-Asian	9	3043	1.01(0.74-1.37)	0.972	Random	89.8	<0.001
Sample size							
≤200	14	1433	1.05(0.78-1.42)	0.748	Random	86.2	<0.001
>200	18	10565	1.52(1.26-1.83)	<0.001	Random	90.3	<0.001
Cutoff value							
≤660	16	7801	1.43(1.15-1.78)	0.001	Random	88.8	<0.001
>660	16	4197	1.25(1.00-1.56)	0.053	Random	88.7	<0.001
Survival analysis							
Multivariate	25	9341	1.41(1.15-1.74)	0.001	Random	84.2	<0.001
Univariate	7	2657	1.05(0.99-1.12)	0.106	Random	85.4	<0.001
TNM stage							
I-III	11	6835	1.46(1.16-1.82)	0.001	Random	76.1	<0.001
III-IV	16	2951	1.25(0.96,1.64)	0.099	Random	90.3	<0.001
I-IV	3	296	1.17(0.54-2.54)	0.108	Fixed	47.4	0.168
NR	2	1916	1.45(0.92-2.27)	0.700	Random	90.8	<0.001

SII: Systemic immune-inflammation, NSCLC: Non-small cell lung cancer, HR: Hazard ratio, CI: Confidence interval, TNM: Tumour-node-metastasis, NR: Not reported.

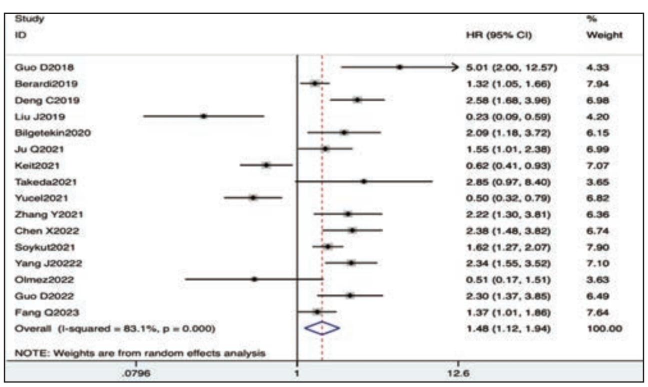

Figure-3: Forest plot for the relationship between SII and PFS in NSCLC patients.

SII: Systemic immune-inflammation, NSCLC: Non-small cell lung cancer, PFS: Progression-free survival.

and meta-analysis was planned to assess the prognostic value of the SII in patients with NSCLC. To our knowledge, the meta-analysis comprises the largest number of studies and cases to date. The primary outcome analysis showed a significant association between an elevated SII and worse OS and PFS in NSCLC patients. Subgroup analyses based on country, sample size, cut-off value, survival analysis type, and TNM stage suggested that the prognostic value of the SII was not influenced by these factors, although they may contribute to the observed heterogeneity. The sensitivity analysis and publication bias tests confirmed the reliability of the findings. The findings propose that the SII can serve as an effective prognostic index for poor OS or PFS in NSCLC patients.

Studies have provided strong evidence of a significant relationship between the prognosis of malignant tumours and various inflammatory cells, including platelets, neutrophils and lymphocytes.[50-53] The SII, a composite parameter derived from platelet, neutrophil and lymphocyte counts, has been identified as an independent predictor of malignancy.[14,21,29,54-56] SII has been proposed

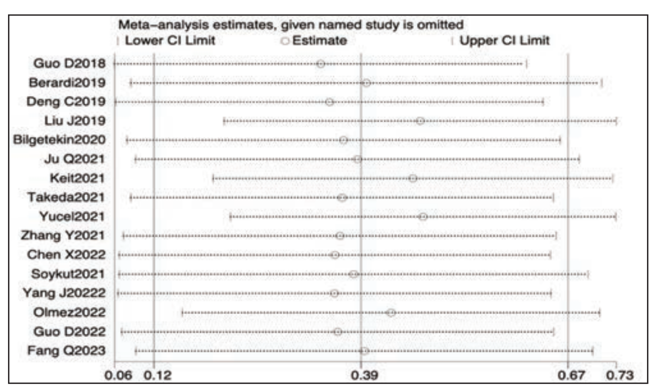

Figure-5: Sensitivity analysis of the association between pre-treatment SII and PFS.

SII: Systemic immune-inflammation, PFS: Progression-free survival.

Table-3: Subgroup analysis of the prognostic effect of SII for PFS in patients with NSCLC.

Subgroups	No. of studies	No. of patients	HR (95%CI)	*p*-value	Effects model	Heterogeneity	
						I^2(%)	*p*-value
Total	16	2378	1.48(1.12-1.94)	<0.001	Random	83.1	<0.001
Countries							
Asian	7	1167	1.87(1.34-2.61)	<0.001	Random	75.9	<0.001
Non-Asian	9	1211	1.09(0.72-1.66)	0.681	Random	84.6	<0.001
Sample size							
≤200	12	2378	1.40(0.90-2.18)	<0.001	Random	86.3	<0.001
>200	4	1129	1.59(1.25-2.01)	0.134	Random	62.2	0.047
Cutoff value							
≤660	5	562	1.25(0.49-3.20)	0.642	Random	91.3	<0.001
>660	111	1816	1.57(1.23-2.02)	<0.001	Random	75.2	<0.001
Survival analysis							
Multivariate	12	670	1.38(0.94-2.03)	0.101	Random	84.2	<0.001
Univariate	4	1708	1.60(1.19-2.14)	0.002	Fixed	85.4	0.091
TNM stage							
I-III	4	759	1.48(0.85-2.60)	0.057	Random	86.8	<0.001
III-IV	9	1372	1.46(0.99-2.15)	0.002	Random	86.5	<0.001
I-IV	1	82	0.51(0.17-1.51)	0.170	/	/	/
NR	2	165	2.24(1.35-3.72)	0.700	Fixed	0	0.620

SII: Systemic immune-inflammation, NSCLC: Non-small cell lung cancer, PFS: Progression-free survival, HR: Hazard ratio, CI: Confidence interval, TNM: Tumour-node-metastasis, NR: Not reported.

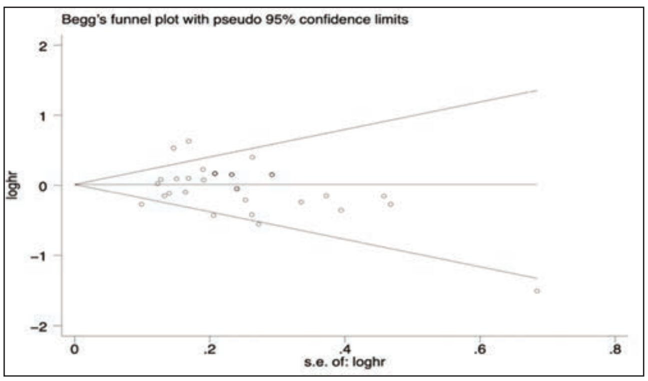

Figure-6A: Begg's test for publication bias regarding overall survival (OS) (p=0.158).

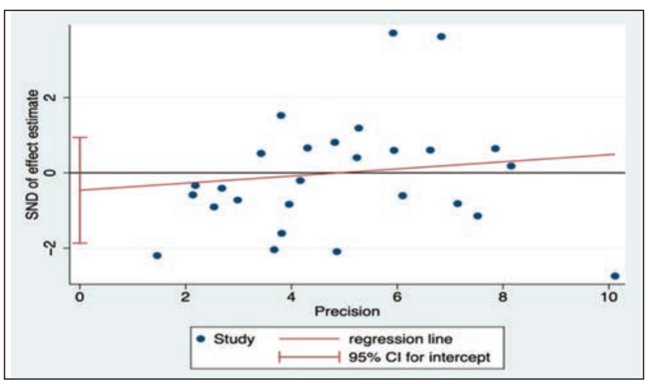

Figure-6B: Figure 6B: Egger's test for publication bias regarding overall survival (OS) (*p*=0.506).

as a useful parameter for predicting clinical outcomes in cancer patients, and its prognostic value may be attributed to the function of platelets, neutrophils and lymphocytes. A high SII value may be driven by an elevated neutrophil count, an increased platelet count, or a decreased lymphocyte count. The exact mechanism underlying the prognostic value of SII in NSCLC remains unclear, but several possible explanations can be considered. First, neutrophils can play a role in promoting tumour growth and metastasis by secreting various cytokines and chemokines that inhibit the host's immune response to cancer cells. Tumours often exploit neutrophils to evade immune detection by suppressing cytotoxic immune cells, such as T cells and natural killer (NK) cells, which are critical for identifying and eliminating cancer cells. Additionally, neutrophils release extracellular structures based on deoxyribonucleic acid (DNA) known as neuroendocrine tumours (NETs), which promote tumour progression by facilitating angiogenesis — the formation of new blood vessels. This process supports tumour growth and enhances the likelihood of metastasis. Thus, high levels of neutrophils, as reflected in a high SII, may be associated

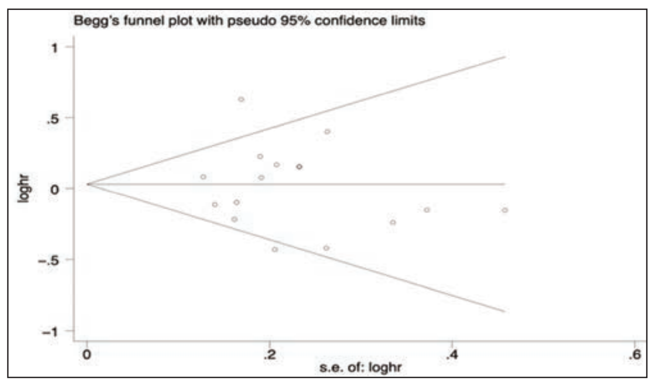

Figure-7A: Begg's test for publication bias regarding progression-free survival (PFS) or PFS (*p*=0.928).

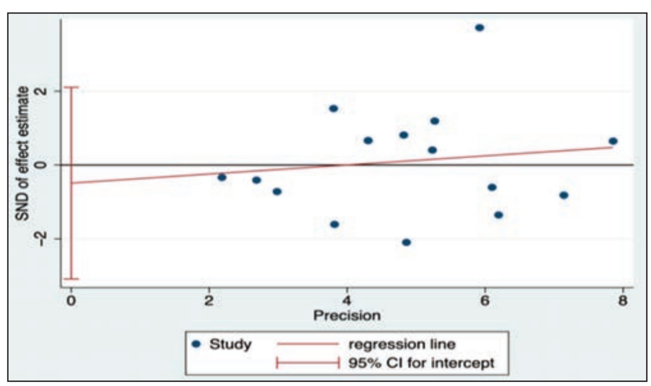

Figure-7B: Egger's test for publication bias regarding progression-free survival (PFS) (*p*=0.692).

with poor clinical outcomes in NSCLC patients.[57] Secondly, platelets have been shown to play a role in promoting tumour cell proliferation and metastasis by inhibiting tumour cell exosmosis. They do this by enhancing the contraction of endothelial cells induced by tumour cells, which helps to promote tumour cell retention and growth. This process is thought to be mediated by the release of various factors from platelets, such as transforming growth factor beta (TGF-β), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF), which are known to be involved in promoting angiogenesis, cell survival and migration. Therefore, elevated platelet levels can be associated with increased tumour angiogenesis, as well as a decreased likelihood of tumour cell lysis.[58,59] Third, lymphocytes play a critical role in T-cell-mediated antitumor immune responses. Their presence within the tumour microenvironment is consistently linked to improved prognoses in cancer patients. These cells can migrate into and infiltrate tumours, where they identify and eliminate cancer cells. Additionally, lymphocytes can activate other immune cells and produce cytokines that enhance the immune response against cancer. Therefore, a low lymphocyte count, as reflected by an elevated SII, may indicate an impaired immune response against cancer and a poorer prognosis in NSCLC.[60]

SII is considered to be a more objective and effective indicator compared to other systemic immuno-inflammatory scores as it reflects the balance between host immune and inflammatory states. SII has been shown to have prognostic value in a variety of tumours.61-65 For example, Li Q et al. demonstrated that preoperative SII can be used as a predictive factor for the prognosis of patients with thymoma who underwent radical resection.[61] Cesur et al. pointed out that the SII index may predict mortality in neuroblastoma patients, suggesting that the immune system's inflammatory response may be associated with prognosis in neuroblastoma patients.[62] In addition, Nicolò et al. demonstrated that ovarian cancer patients with a high SII had worse OS, suggesting that inflammation and immune response may play a crucial role in the progression and prognosis of ovarian cancer.[63] A recent meta-analysis of 12 studies with 8,083 patients showed that a high pre-treatment SII was associated with poor OS and PFS in patients with prostate cancer.[64] Li et al. revealed that elevated pre-treatment SII was associated with poor OS, inferior cancer-specific survival (CSS), disease-free survival (DFS), and PFS.[65]

Recent studies[10,18] have shown that SII is closely related to the OS and DFS of patients with clear cell renal cell carcinoma (the 5-year OS rate in the high SII group decreased by 12.7%, $p<0.001$), and the combination of SII and prognostic nutritional index (PNI) can further improve the predictive efficacy. SII demonstrates stable prognostic predictive ability in multiple cancer types, such as HCC, prostate cancer and colorectal cancer, by reflecting the inflammation-immune balance in the tumour microenvironment, suggesting that it may serve as an immune-inflammatory marker for pan-cancer types.

While the results of the current meta-analysis are promising, it does have several limitations that may influence the interpretation of the findings. First, the majority of participants were from China, potentially increasing heterogeneity and limiting the generalisability of the results to broader populations. Second, inherent heterogeneity exists within the meta-analysis due to variations in study methodologies and cut-off values used to define the SII across different studies. However, sensitivity analysis showed that the results were not influenced by any single study, and there was no evidence of publication bias. Thirdly, all the included studies were retrospective in nature, which may have led to selection bias. Fourthly, the variation in the cut-off values for SII across the included studies may introduce heterogeneity in the meta-analysis. Lastly, the differences in follow-up time and outcome indicators across studies may also be a source of heterogeneity. Large-scale, prospective trials involving different populations are needed to validate the current results and provide more robust evidence for the use of SII as a prognostic indicator in cancer patients. Also, future studies shall incorporate the immune checkpoint inhibitors (ICIs) targeted therapy subgroup, analyse the interaction between SII and treatment response, and explore a composite prognostic model combining SII with indicators, such as programmed cell death-ligand 1 (PD-L1) expression and tumour mutational burden (TMB).

Conclusions

Elevated pre-treatment SII was found to be associated with worse OS or PFS in patients with NSCLC, indicating that SII could be a useful and cost-effective prognostic parameter in the treatment of NSCLC patients.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: The study was financially supported by the National Key Research and Development Programme of China (Grant No. 2020YFC2005403) and the Beijing Major Epidemic Prevention and Control Key Specialty Intensive Care Medical Construction Project (Grant No. ZDYQFZZDZK).

References

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin 2017;67:7-30. doi: 10.3322/caac.21387
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424. doi: 10.3322/caac.21492
3. Yu Y, Qian L, Cui J. Value of neutrophil-to-lymphocyte ratio for predicting lung cancer prognosis: A meta-analysis of 7,219 patients. Mol Clin Oncol 2017;7:498-506. doi: 10.3892/mco.2017.1342
4. McNamara MG, Templeton AJ, Maganti M, Walter T, Horgan AM, McKeever L, et al. Neutrophil/lymphocyte ratio as a prognostic factor in biliary tract cancer. Eur J Cancer 2014;50:1581-9. doi: 10.1016/j.ejca.2014.02.015
5. Cho KM, Park H, Oh DY, Kim TY, Lee KH, Han SW, et al. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and their dynamic changes during chemotherapy is useful to predict a more accurate prognosis of advanced biliary tract cancer. Oncotarget 2017;8:2329-41. doi: 10.18632/oncotarget.13731
6. Ha H, Nam AR, Bang JH, Park JE, Kim TY, Lee KH, et al. Soluble programmed death-ligand 1 (sPDL1) and neutrophil-to-lymphocyte ratio (NLR) predicts survival in advanced biliary tract cancer patients treated with palliative chemotherapy. Oncotarget 2016;7:76604-12. doi: 10.18632/oncotarget.12810
7. Hu X, Pang Q, Liu H, Qian Z, Jin H, Zhou L, et al. Inflammation-based prognostic scores in patients with extrahepatic bile duct lesions treated by percutaneous transhepatic biliary stenting combined with (125)I seeds intracavitary irradiation. Clin Transl Oncol 2019;21:665-73. doi: 10.1007/s12094-018-1969-2
8. Sellers CM, Uhlig J, Ludwig JM, Stein SM, Kim HS. Inflammatory markers in intrahepatic cholangiocarcinoma: Effects of advanced liver disease. Cancer Med 2019;8:5916-29. doi: 10.1002/cam4.2373
9. Zhong JH, Huang DH, Chen ZY. Prognostic role of systemic immune-inflammation index in solid tumors: a systematic review and meta-analysis. Oncotarget 2017;8:75381-8. doi: 10.18632/oncotarget.18856
10. Murthy P, Zenati MS, Al Abbas AI, Rieser CJ, Bahary N, Lotze MT, et al. Prognostic Value of the Systemic Immune-Inflammation Index (SII) After Neoadjuvant Therapy for Patients with Resected Pancreatic Cancer. Ann Surg Oncol 2020;27:898-906. doi: 10.1245/s10434-019-08094-0
11. Chen JH, Zhai ET, Yuan YJ, Wu KM, Xu JB, Peng JJ, et al. Systemic immune-inflammation index for predicting prognosis of colorectal cancer. World J Gastroenterol 2017;23:6261-72. doi: 10.3748/wjg.v23.i34.6261
12. Gao Y, Zhang H, Li Y, Wang D, Ma Y, Chen Q. Preoperative increased systemic immune-inflammation index predicts poor prognosis in patients with operable non-small cell lung cancer. Clin Chim Acta 2018;484:272-7. doi: 10.1016/j.cca.2018.05.059
13. Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res 2014;20:6212-22. doi: 10.1158/1078-0432.Ccr-14-0442
14. Tong YS, Tan J, Zhou XL, Song YQ, Song YJ. Systemic immune-inflammation index predicting chemoradiation resistance and poor outcome in patients with stage III non-small cell lung cancer. J Transl Med 2017;15:221. doi: 10.1186/s12967-017-1326-1
15. Guo D, Zhang J, Jing W, Liu J, Zhu H, Fu L, et al. Prognostic value of systemic immune-inflammation index in patients with advanced non-small-cell lung cancer. Future oncol 2018;14:2643-50. doi: 10.2217/fon-2018-0285
16. Berardi R, Santoni M, Rinaldi S, Bower M, Tiberi M, Morgese F, et al. Pre-treatment systemic immune-inflammation represents a prognostic factor in patients with advanced non-small cell lung cancer. Ann transl med 2019;7:572. doi: 10.21037/atm.2019.09.18
17. Deng C, Zhang N, Wang Y, Jiang S, Lu M, Huang Y, et al. High systemic immune-inflammation index predicts poor prognosis in advanced lung adenocarcinoma patients treated with EGFR-TKIs. Medicine 2019;98:e16875. doi: 10.1097/MD.000000000001687
18. Guo W, Cai S, Zhang F, Shao F, Zhang G, Zhou Y, et al. Systemic immune-inflammation index (SII) is useful to predict survival outcomes in patients with surgically resected non-small cell lung cancer. Thorac cancer 2019;10:761-8. doi: 10.1111/1759-7714.12995
19. Li H, Wang G, Zhang H, Song X, Cao J, Zhang X, et al. Prognostic role of the systemic immune-inflammation index in brain metastases from lung adenocarcinoma with different EGFR mutations. Genes immun 2019;20:455-61. doi: 10.1038/s41435-018-0050-z
20. Liu J, Li S, Zhang S, Liu Y, Ma L, Zhu J, et al. Systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio can predict clinical outcomes in patients with metastatic non-small-cell lung cancer treated with nivolumab. J clin lab anal 2019;33:e22964. doi: 10.1002/jcla.22964
21. Bilgetekin I, Basal FB. Systemic Immune-inflammation Index is the Best Prognostic Factor in Patients with Advanced Stage Adenocarcinoma of the Lung Treated with Pemetrexed. Jcpsp-j coll physici 2020;30:933-9. doi: 10.29271/jcpsp.2020.09.933
22. Li A, Mu X, He K, Wang P, Wang D, Liu C, et al. Prognostic value of lymphocyte-to-monocyte ratio and systemic immune-inflammation index in non-small-cell lung cancer patients with brain metastases. Future oncol 2020;16:2433-44. doi: 10.2217/fon-2020-0423
23. Li X, Hu P, Liu J, Zhang J, Liu Q. Systemic immune-inflammation index predicted overall survival and radiosensitivity in advanced non-small-cell lung cancer. Future oncol 2020;16:103-15. doi: 10.2217/fon-2019-0761
24. Yan X, Li G. Preoperative systemic immune-inflammation index predicts prognosis and guides clinical treatment in patients with non-small cell lung cancer. Bioscience rep 2020;40:BSR20200352. doi:10.1042/BSR20200352
25. Fu F, Deng C, Wen Z, Gao Z, Zhao Y, Han H, et al. Systemic immune-inflammation index is a stage-dependent prognostic factor in patients with operable non-small cell lung cancer. Transl lung cancer 2021;10:3144-54. doi: 10.21037/tlcr-21-267
26. Keit E, Coutu B, Zhen W, Zhang C, Lin C, Bennion N, et al. Systemic inflammation is associated with inferior disease control and survival in stage III non-small cell lung cancer. Ann transl med 2021;9:227. doi: 10.21037/atm-20-6710
27. Li W, Qu Y, Wen F, Yu R, He X, Jia H, et al. Prognostic nutritional index and systemic immune-inflammation index are prognostic biomarkers for non-small-cell lung cancer brain metastases. Biomark med 2021;15:1071-84. doi: 10.2217/bmm-2020-0786
28. Xu S, Cao S, Yu Y. High systemic immune-inflammation index is a predictor of poor prognosis in patients with nonsmall cell lung cancer and bone metastasis. J cancer res ther 2021;17:1636-42. doi: 10.4103/jcrt.jcrt_176_21
29. Yucel S, Bilgin B. The prognostic values of systemic immune-inflammation index and derived neutrophil-lymphocyte ratio in EGFR-mutant advanced non-small cell lung cancer. J oncol pharm pract 2021;27:71-7. doi: 10.1177/1078155220913106
30. Zeng Q, Li J, Sun N, Xue Q, Gao Y, Zhao J, et al. Preoperative systemic immune-inflammation index predicts survival and recurrence in patients with resected primary pulmonary sarcomatoid carcinoma. Transl Lung Cancer Res 2021;10:18-31. doi: 10.21037/tlcr-20-960.
31. Zhang Y, Chen Z, Jin F, Guo D, Chen Q, Liu Z, et al. The Value of the Systemic Immune-Inflammation Index in Predicting Survival Outcomes in Patients with Brain Metastases of Non-Small-Cell Lung Cancer Treated with Stereotactic Radiotherapy. Mediat inflamm

2021;2021:2910892. doi:10.1155/2021/2910892

32. Abravan A, Salem A, Price G, Faivre-Finn C, van Herk M. Effect of systemic inflammation biomarkers on overall survival after lung cancer radiotherapy: a single-center large-cohort study. Acta Oncol 2022;61:163-71. doi: 10.1080/0284186X.2021.2022201
33. Chen X, Hong X, Chen G, Xue J, Huang J, Wang F, et al. The Pan-Immune-Inflammation Value predicts the survival of patients with anaplastic lymphoma kinase-positive non-small cell lung cancer treated with first-line ALK inhibitor. Transl Oncol 2022;17:101338. doi: 10.1016/j.tranon.2021.101338
34. Coutu BG, Johnson KC, Bhirud A, Baine MJ, Zhen W, Zhang C, et al. Systemic Immune-Inflammatory Index Association with Survival in Patients Undergoing Trimodality Therapy for Lung Cancer. Oncology-basel 2022;100:247-56. doi: 10.1159/000520989
35. Delikgoz Soykut E, Kemal Y, Karacin C, Karaoglanoglu O, Kurt M, Aytac Arslan S. Prognostic impact of immune inflammation biomarkers in predicting survival and radiosensitivity in patients with non-small-cell lung cancer treated with chemoradiotherapy. J Med Imaging Radiat Oncol 2022;66:146-57. doi: 10.1111/1754-9485.13341
36. Guo D, Liu J, Li Y, Chen Q, Zhao Y, Guo X, et al. A Novel Score Combining Magnetic Resonance Spectroscopy Parameters and Systemic Immune-Inflammation Index Improves Prognosis Prediction in Non-Small Cell Lung Cancer Patients With Brain Metastases After Stereotactic Radiotherapy. Front Oncol 2022;12:762230. doi: 10.3389/fonc.2022.762230
37. Wang Q, Tan X, Deng G, Fu S, Li J, Li Z. Dynamic changes in the systemic immune-inflammation index predict the prognosis of EGFR-mutant lung adenocarcinoma patients receiving brain metastasis radiotherapy. BMC Pulm Med 2022;22:75. doi: 10.1186/s12890-022-01866-7
38. Yang J, Deng M, Bi M, Wang Y, Qiao X, Zhang S. Prognostic values of inflammatory indexes in bevacizumab-treated patients with advanced non-small-cell lung cancer. Future Sci OA 2022;8:Fso798. doi: 10.2144/fsoa-2021-0162
39. Chen D, Qin H, Deng G, Wang Q, Wang H, Liu X. Pre-radiotherapy systemic immune inflammation index associated with overall survival in patients with advanced EGFR mutant non-small cell lung cancer receiving thoracic radiotherapy. Clin transl oncol 2023;25:226-35. doi: 10.1007/s12094-022-02936-2
40. Fang Q, Yu J, Li W, Luo J, Deng Q, Chen B, et al. Prognostic value of inflammatory and nutritional indexes among advanced NSCLC patients receiving PD-1 inhibitor therapy. Clin exp pharmacol p 2023;50:178-90. doi: 10.1111/1440-1681.13740
41. Olmez OF, Bilici A, Gursoy P, Cubukcu E, Sakin A, Korkmaz T, et al. Impact of systemic inflammatory markers in patients with ALK-positive non-small cell lung cancer treated with crizotinib. Pulmonology 2023;29:478-85. doi: 10.1016/j.pulmoe.2022.11.006.
42. Yang H, Wang K, Li B, Li S, Li Y, Yuan L. The Prognostic Role of Blood Inflammatory Biomarkers and EGFR Mutation Status in Stage IIIA/N2 Non-Small Cell Lung Cancer Patients Treated With Trimodality Therapy. Front Oncol 2021;11:707041. doi: 10.3389/fonc.2021.707041
43. Ju Q, Huang T, Zhang Y, Wu L, Geng J, Mu X, et al. Systemic immune-inflammation index predicts prognosis in patients with different EGFR-mutant lung adenocarcinoma. Medicine 2021;100:e24640. doi: 10.1097/MD.0000000000024640
44. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev 2021;10:89. doi: 10.1186/s13643-021-01626-4
45. National Institute for Health and Care Research (NIHR). PROSPERO: International prospective register of systematic reviews, version 2.0.28. [Online] 2024-2025 [Cited 2026 January 24]. Available from URL: https://www.crd.york.ac.uk/prospero/
46. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25:603-5. doi: 10.1007/s10654-010-9491-z
47. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088-101. doi: 10.2307/2533446
48. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Bmj 1997;315:629-34. doi: 10.1136/bmj.315.7109.629
49. Takeda T, Yamada T, Tanimura K, Nakano T, Ishida M, Tachibana Y, et al. Prognostic Markers of Survival among Japanese Patients with Anaplastic Lymphoma Kinase-Positive Non-Small-Cell Lung Cancer Receiving First-Line Alectinib. Diagnostics (Basel) 2021;11:2170. doi:10.3390/diagnostics11122170
50. Grenader T, Nash S, Plotkin Y, Furuse J, Mizuno N, Okusaka T, et al. Derived neutrophil lymphocyte ratio may predict benefit from cisplatin in the advanced biliary cancer: the ABC-02 and BT-22 studies. Ann Oncol 2015;26:1910-6. doi: 10.1093/annonc/mdv253
51. Wang S, Yang X, Yu Z, Du P, Cao Y, Ji Y, et al. The values of systemic immune-inflammation index and neutrophil-lymphocyte ratio in predicting testicular germ cell tumors: A retrospective clinical study. Front Oncol 2022;12:e893877. doi: 10.3389/fonc.2022.893877.
52. Wu M, Yang S, Feng X, Li C, Yu F, Dong J. Prognostic value of the postoperative neutrophil-lymphocyte ratio in solid tumors: A meta-analysis. PLoS One 2021;16:e0250091. doi:10.1371/journal.pone.0250091
53. Zhang Z, Lin Q, Chen Y, Su C, Lin W, Wei D, et al. Prognostic Evaluation of Metastasis-Related Lymphocyte/Monocyte Ratio in Stage Ⅰ-Ⅲ Breast Cancer Receiving Chemotherapy. Front Oncol 2022;11:e782383. doi: 10.3389/fonc.2021.782383.
54. Zhang Y, Chen Z, Jin F, Guo D, Chen Q, Liu Z, et al. The Value of the Systemic Immune-Inflammation Index in Predicting Survival Outcomes in Patients with Brain Metastases of Non-Small-Cell Lung Cancer Treated with Stereotactic Radiotherapy. Mediators Inflamm 2021;2021:e2910892. doi: 10.1155/2021/2910892.
55. Zhou Y, Dai M, Zhang Z. Prognostic Significance of the Systemic Immune-Inflammation Index (SII) in Patients with Small Cell Lung Cancer: A Meta-Analysis. Front Oncol 2022;12:e814727. doi:10.3389/fonc.2022.814727
56. Obata Y, Kanda M, Shimizu D, Takami H, Inokawa Y, Hattori N, et al. The preoperative systemic immune-inflammation index is associated with an unfavorable prognosis for patients undergoing curative resection of esophageal squamous cell carcinoma after neoadjuvant therapy. Surg Today 2023;53:964-72. doi: 10.1007/s00595-023-02658-0.
57. Miyahara Y, Takashi S, Shimizu Y, Ohtsuka M. The prognostic impact of neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR) in patients with distal bile duct cancer. World J Surg Oncol 2020;18:78. doi: 10.1186/s12957-020-01847-2
58. Xie J, Zou Y, Ye F, Zhao W, Xie X, Ou X, et al. A Novel Platelet-Related Gene Signature for Predicting the Prognosis of Triple-Negative Breast Cancer. Front Cell Dev Biol 2022;9:e795600. doi: 10.3389/fcell.2021.795600.
59. Huong PT, Nguyen LT, Nguyen XB, Lee SK, Bach DH. The Role of Platelets in the Tumor-Microenvironment and the Drug Resistance of Cancer Cells. Cancers (Basel) 2019;11:240. doi: 10.3390/cancers11020240.
60. Roddy H, Meyer T, Roddie C. Novel Cellular Therapies for Hepatocellular Carcinoma. Cancers (Basel) 2022;14:504. doi: 10.3390/cancers14030504
61. Li Q, Pu Y, Gong Z, Yu Y, Sun W, Cheng Z, et al. Preoperative systemic

immune-inflammation index for predicting the prognosis of thymoma with radical resection. Thorac Cancer 2023;14:1192-200. doi: 10.1111/1759-7714.14854.

62. Cesur IB, Özçelik Z. Systemic Immune-Inflammation Index May Predict Mortality in Neuroblastoma. Cureus 2023;15:e35705. doi: 10.7759/cureus.35705

63. Bizzarri N, D'Indinosante M, Marchetti C, Tudisco R, Turchiano F, Scambia G, et al. The prognostic role of systemic inflammatory markers in apparent early-stage ovarian cancer. Int J Clin Oncol 2023;28:314-20. doi: 10.1007/s10147-022-02272-z

64. Meng L, Yang Y, Hu X, Zhang R, Li X. Prognostic value of the pretreatment systemic immune-inflammation index in patients with prostate cancer: a systematic review and meta-analysis. J Transl Med 2023;21:79. doi: 10.1186/s12967-023-03924-y

65. Li M, Li Z, Wang Z, Yue C, Hu W, Lu H. Prognostic value of systemic immune-inflammation index in patients with pancreatic cancer: a meta-analysis. Clin Exp Med 2022;22:637-46. doi: 10.1007/s10238-021-00785-x

Author Contribution:

GZ, HZ, PY & WC: Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.