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Impact and Predictive Value of Systemic Immune-Inflammation Index (SII) on Immunotherapy in Patients with Extensive-Stage Small Cell Lung Cancer

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Research Article

Keywords: Extensive-stage small cell lung cancer, Systemic immune-inflammation index, Survival, Prognosis

Posted Date: June 18th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9527196/v1

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Additional Declarations: No competing interests reported.

Abstract

Objective

This study aims to explore the impact of the systemic immune-inflammation index (SII) on immunotherapy and its predictive value for prognosis in patients with extensive-stage small cell lung cancer (ES-SCLC) who receive first-line chemotherapy combined with immunotherapy.

Methods

The clinical data of 274 patients were retrospectively collected, and the impact of SII on immunotherapy in different patients was analyzed. Propensity score matching (PSM) was used to balance the differences between groups to further identify the influencing factors of immunotherapy efficacy.

Results

The median overall survival (OS) of all patients was 14.4 months (95%CI: 13.2–15.6), and the median progression-free survival (PFS) was 8.1 months (95%CI: 7.3–8.9). The optimal cutoff value of SII was 626.3, based on which all patients were divided into the high SII group (178 cases) and the low SII group (96 cases). Compared with the high SII group, the low SII group showed improved OS (20.3 months vs 12.2 months) and PFS (10.6 months vs 6.9 months).

Conclusion

The SII can serve as a potential predictive indicator for extensive-stage small cell lung cancer, and patients with low SII can benefit more from immunotherapy.

Introduction

The incidence and mortality of lung cancer continue to increase. According to the latest global cancer statistics released by the International Agency for Research on Cancer [1-2], by the end of 2020, approximately 1.8 million deaths worldwide were attributed to lung cancer, ranking first among all cancer-related deaths. Studies [1] have shown that in 2020, there were about 820,000 new cases of lung cancer and 710,000 deaths from lung cancer in China. Small cell lung cancer (SCLC) accounts for only 15% of lung cancer cases, characterized by strong invasiveness and early occurrence of distant metastasis. SCLC is sensitive to treatment in the early stage but is prone to drug resistance and recurrence. The systemic treatment of SCLC has remained largely unchanged in recent years. With the emergence of immune checkpoint inhibitors (ICIs), clinical studies have been conducted on extensive-stage small cell lung cancer (ES-SCLC). According to the results of the IMpower133 [3] and CASPIAN [4] studies, the median OS and median PFS of ES-SCLC patients have been improved, bringing new

opportunities and challenges to the treatment of ES-SCLC. At present, a variety of ICIs have been included in the Chinese Society of Clinical Oncology (CSCO) Small Cell Lung Cancer Clinical Practice Guidelines for the first-line treatment of ES-SCLC. However, the population that can benefit from ICIs combined therapy for ES-SCLC has not been clearly defined, and there is an urgent need to find economical and reliable prognostic indicators.

Accumulating evidence indicates that local and systemic immune responses play a crucial role in the occurrence and development of tumors and affect the survival of patients. Currently, some common clinical indicators, such as the platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII), have been proven to predict the survival outcomes of various malignant tumors to some extent. Therefore, hematological indicators related to inflammatory responses may become predictive indicators for ICIs treatment. These indicators are not only easy to operate and obtain but also can objectively reflect the immune status of the body. This study intends to explore the impact of SII on immunotherapy in ES-SCLC patients and its predictive value.

Materials and Methods

1. Clinical Information

This study retrospectively collected clinical data of ES-SCLC patients who were initially treated in the Fourth Hospital of Hebei Medical University from January 2016 to December 2021. Inclusion criteria: age ≥ 18 years; diagnosis of ES-SCLC confirmed by pathology and imaging; presence of at least 1 measurable lesion; complete clinical medical records; no second primary cancer. Exclusion criteria: having received surgical treatment; clinically diagnosed with acute or chronic inflammation, including those receiving antibiotic treatment currently or for a long time; those requiring long-term use of glucocorticoids.

2. Methods

The relevant clinical data of the enrolled patients were retrospectively collected, including laboratory examinations, histopathology, imaging, clinical, and treatment-related data. Clinical staging was performed according to the AJCC staging system and the VALG two-stage classification. Among the results of hematological examinations, the following parameters were analyzed: white blood cell count, lymphocyte count, neutrophil count, and platelet count. SII was calculated as (neutrophil count × platelet count) / lymphocyte count.

3. Follow-up

Follow-up was conducted through information from hospitalization records, telephone calls, and outpatient re-examinations, with the follow-up cutoff date being December 31, 2023. The follow-up rate was 96.4%, with 10 cases lost to follow-up (3.4%). The median follow-up time was 14.4 months (range: 1.5-82.8 months).

4. Statistical Methods

SPSS 25.0 was used for data analysis. Univariate analysis was performed using the Log-Rank test. The Kaplan-Meier method was used for comparing survival curves between groups. Variables showing significant differences in univariate analysis were subjected to multivariate COX proportional hazards regression model analysis. The χ^2 test was used for comparisons between groups. Propensity score matching (PSM) was used to balance differences between groups and reduce selection bias. A P value < 0.05 was considered statistically significant.

Results

1. Baseline Characteristics

A total of 274 patients were analyzed, including 225 males (82.1%) and 49 females (17.9%). The median age at onset was 63 years (range: 30-79 years). There were 167 patients (60.9%) with a smoking index ≥ 400, 225 patients (82.1%) with an ECOG score of 0-1, 246 patients (89.8%) with central lung cancer, and 221 patients (80.7%) who received chemoradiotherapy. The clinical characteristics are shown in Table 1.

2. Optimal Cutoff Value of SII

The receiver operating characteristic (ROC) curve and the corresponding area under the curve (AUC) were plotted using SPSS 25.0 to determine the optimal cutoff value of SII (see Figure 1). The optimal cutoff value of SII was 626.3. Based on this, all patients were divided into the low SII group (96 cases, 35.0%) and the high SII group (178 cases, 65.0%).

3. Long-term Efficacy

The median OS of the entire group was 14.4 months (95%CI: 13.2-15.6), and the median PFS was 8.1 months (95%CI: 7.3-8.9). The 1-year, 2-year, and 3-year OS rates were 61.0%, 22.0%, and 14.0%, respectively, while the 1-year, 2-year, and 3-year PFS rates were 22.5%, 5.0%, and 0.5%, respectively.

4. Univariate Analysis

The results showed that SII was an influencing factor for both OS and PFS, and other results are shown in Table 2.

5. Multivariate Analysis

The results showed that SII was an independent prognostic factor for both OS and PFS, and other results are shown in Table 3 (survival curves are shown in Figures 2 and 3).

6. Impact of SII on Efficacy of Immunotherapy in ES-SCLC and Survival Analysis of ES-SCLC after PSM

6.1 To further verify the impact of immunotherapy on the survival of ES-SCLC patients, the entire group was divided into the combined treatment group (receiving immunotherapy) and the non-combined treatment group (not receiving immunotherapy) based on whether they received combined immunotherapy. The χ^2 test was used to determine differences between groups, and 1:1 propensity score matching was performed for factors with significant differences using a caliper value of 0.05. After matching, 82 pairs (164 patients) were generated (see Table 4).

6.2 Univariate prognostic analysis of 164 patients after PSM showed that SII remained an influencing factor for OS and PFS, as shown in Table 5. Multivariate prognostic analysis of 164 patients after PSM showed in Table 6.The OS and PFS curves showed in Figure 4 and Figure 5.

Discussion

Tumor-related inflammation is considered one of the main characteristics of cancer [5]. Systemic inflammatory responses are associated with the survival of tumor patients. Masjedi et al. [6] found that tumor-related inflammatory factors affect the occurrence and development of tumors, promote tumor growth and angiogenesis, and induce resistance to radiotherapy and chemotherapy. Numerous studies have shown that the prognosis of tumor patients is significantly correlated with inflammatory factors and some new biological indicators such as SII. The systemic immune-inflammation index (SII) is defined as (neutrophil count × platelet count) / lymphocyte count. This comprehensive indicator is considered a good indicator reflecting the balance between inflammation and immune status in cancer patients [7], but the mechanism underlying its impact on survival prognosis remains incompletely clear. The mechanism by which SII affects the survival of tumor patients can be explained through the roles of platelets, neutrophils, and lymphocytes in tumor development.

Platelets play an important role in tumor activities. On the one hand, platelets can deliver various pro-angiogenic factors to tumors, stimulating tumor angiogenesis. An increase in platelet count is associated with chemotherapy resistance in tumors [8]. According to studies by Bambace et al. and Lim et al. [9-10], platelets can promote the migration and metastasis of tumor cells by secreting vascular endothelial growth factor (VEGF), transforming growth factor-β (TGF-β), and platelet-derived growth factor (PDGF). On the other hand, platelet aggregation enables tumor cells to evade immune surveillance [11], facilitating the proliferation and spread of cancer cells. Tumor cells can also release cytokines to stimulate the production and activation of platelets, further promoting tumor growth and angiogenesis [12].

Neutrophils play a complex role in tumor occurrence and development, with both anti-tumor and pro-tumor effects. The anti-tumor effect is mainly exerted by releasing reactive oxygen species (ROS) and tumor necrosis factor-α (TNF-α), and they can also release soluble neutrophil granule proteins to promote tumor progression and metastasis. Previous studies have suggested that neutrophils participate in tumor angiogenesis by releasing cytokines, promoting tumor growth, and protecting

tumors from immune surveillance [13]. An increase in neutrophil count may be associated with shortened survival in tumor patients [8].

Lymphocytes in the body play a key role in the recognition and elimination of tumors, and their reduction indicates a decline in immune function. Studies have found that a reduction in lymphocytes is significantly associated with shortened survival in tumor patients [8]. Tumor-specific CD8+ T lymphocytes are the main effector cells of the body's immunity, which can infiltrate the tumor bed of immunogenic tumors and enhance the therapeutic response to ICIs [14]. Meanwhile, lymphocytes can release various cytokines, such as tumor necrosis factor-α (TNF-α) and interferon-γ (IFN-γ), which help control tumor growth and prolong the survival time of tumor patients. In addition, lymphocytes are immune cells of the body, which can inhibit the proliferation and migration of tumor cells through the immune system and play a key role in immune surveillance, which can prolong the survival of patients to a certain extent [15].

An increase in pre-treatment SII is associated with an increase in platelets, an increase in neutrophils, or a decrease in lymphocytes, which indicates an enhancement of the body's systemic inflammatory response or a decline in immune function [7]. During inflammation, the number of lymphocytes will relatively decrease while the number of neutrophils will relatively increase. Both play a key role in tumor occurrence and development; specifically, on the one hand, a decrease in lymphocyte count will weaken the body's immune function, reduce the resistance to tumors, and facilitate the growth and metastasis of tumor cells; on the other hand, enhanced body inflammation and the massive release of inflammatory mediators by neutrophils can promote the release of vascular endothelial growth factors, stimulate the formation of new tumor blood vessels, and provide sufficient nutrients for tumor growth and spread. The roles of platelets, neutrophils, and lymphocytes and their interactions involve multiple mechanisms affecting tumor growth and metastasis, which confirm that SII is a good comprehensive indicator. Our study concluded that the level of SII has a significant impact on both OS and PFS in ES-SCLC patients. Hong et al. [16] pointed out that an increase in SII indicates a poor prognosis in SCLC patients; a meta-analysis [17] showed that a high SII may be a potential prognostic marker for patients with various cancers and is associated with poor overall outcomes; Wang et al. [18] found that the pre-treatment SII level has a significant impact on the survival outcomes of SCLC patients, and these research conclusions are consistent with those of this study.

Currently, the impact of SII level on the efficacy of ICIs remains controversial. This study found that among patients receiving combined treatment, those with a high pre-treatment SII level had poor efficacy with ICIs. Some studies believe that a high SII level is associated with poor survival outcomes. The results of a meta-analysis [19] pointed out that among patients receiving ICIs, a higher SII level is significantly associated with poor survival outcomes; Fornarini et al. [20] found that in patients with advanced urinary tract cancer receiving ICIs, a lower SII level prolonged the OS of patients; a meta-analysis by Kou et al. [21] pointed out that a high SII level is associated with shortened OS and PFS; these are consistent with the results of this study. Other scholars believe that there is no correlation between SII and survival time. Chen et al. [22] revealed that there was no statistically significant

difference between a high pre-treatment SII level and a better PFS in patients with advanced gastric cancer receiving immunotherapy. This may be due to the lack of a clear standard for the optimal cutoff value of SII; some studies use the median, some follow previous research results, and others plot ROC curves to obtain the optimal cutoff value. To balance the clinical baseline characteristics and make the conclusions more convincing, this study performed 1:1 propensity score matching based on whether ICIs were received, and conducted survival analysis on the data after PSM. The results showed that in ES-SCLC patients receiving combined treatment, a high SII level is an independent and unfavorable prognostic factor for OS and PFS, which is similar to the conclusion of a meta-analysis [22]. SII is related to peripheral blood indicators, which is cheap, convenient, and easy to obtain, and has the potential to become a reliable and cheap prognostic biomarker for clinical patients with extensive-stage small cell lung cancer receiving ICIs. In conclusion, the correlation between pre-treatment SII level and the survival outcomes of patients receiving ICIs treatment needs to be further verified by prospective large-scale multi-center clinical studies.

In summary, patients with low SII have better efficacy and can benefit more from immunotherapy. However, this study has certain limitations, and the research conclusions need to be confirmed by prospective randomized controlled studies in the future.

Abbreviations

Full name	Abbreviation
Systemic immune-inflammation index	SII
Small cell lung cancer	SCLC
Extensive-stage small cell lung cancer	ES-SCLC
Propensity score matching	PSM
Overall survival	OS
Progression-free survival	PFS
Immune checkpoint inhibitors	ICIs
Chinese Society of Clinical Oncology	CSCO
Platelet-to-lymphocyte ratio	PLR
Neutrophil-to-lymphocyte ratio	NLR
Receiver operating characteristic	ROC
Area under the curve	AUC
Vascular endothelial growth factor	VEGF
Transforming growth factor-β	TGF-β
Platelet-derived growth factor	PDGF
Reactive oxygen species	ROS
Tumor necrosis factor-α	TNF-α
Interferon-γ	IFN-γ
Complete response	CR
Partial response	PR
Stable disease	SD
Progressive disease	PD
Phylactic cranial irradiation	PCI
Eastern Cooperative Oncology Group	ECOG
Neuron specific enolase	NSE
Serum progastrin releasing peptide	Pro-GRP

Declarations

Ethics approval and consent to participate:

This retrospective study was approved by Medical Ethics Committee of the Fourth Hospital of Hebei Medical University(approval :2021ky103).Individual written informed consent was waived due to the retrospective nature of the study and anonymization of all data.The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication:

Not applicable.

Availability of data and materials:

All data generated or analysed during this study are included in this published article.

Competing interests:

The authors declare that they have no competing interests.

Funding:

This research did not receive any specific grant from funding agencies in the public,commercial,or not-for-profit sectors.

Authors' contributions:

Ff.J.andZl.Z.wrote the main manuscript text and proposed the research concepts.Y.Z.gathered data of the study.Jp.W.designed the procedures.Yf,H.made the statistical analysis.Yx.W.made graphs and tables.Ch.D.and)J.L.supervised and managed this study.All authors reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

Acknowledgements:

Not applicable.

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Tables

Table 1 Clinical baseline charateristics of 274 patients with ES-SCLC

Characteristic	category	patients	proportion□%□
sex	male	225	82.1
	female	49	17.9
age	≥65	114	41.6
	<65	160	58.4
Smoking Index	<400	107	39.1
	≥400	167	60.9
ECOG score	0	108	39.4
	1	117	42.7
	2	39	14.2
	3	10	3.6
Tumor location	Central	246	89.8
	Peripheral	28	10.2
T staging	T_1	16	5.8
	T_2	47	17.2
	T_3	104	38.0
	T_4	107	39.1
N staging	N_0	16	5.8
	N_1	7	2.6
	N_2	138	50.4
	N_3	113	41.1
TNM staging	□$_A$	216	78.8
	□$_B$	58	21.2
Treatment	Chemoradiotherapy	221	80.7
	Chemotherapy	44	16.1
	Radiotherapy	9	3.3
Cycles of chemotherapy	<4	80	29.2

	≥4	194	70.8
Immunotherapy	yes	87	31.8
	no	187	68.2
PCI	yes	19	6.9
	no	255	93.1
Response	CR	1	0.36
	PR	122	44.5
	SD	145	52.9
	PD	6	2.2
SII	low	96	35.0
	high	178	65.0

Table 2 Univariate survival analysis for OS and PFS

Characteristic	category	OS		PFS	
		mOS(95%CI)	P value	mPFS （95%CI）	P value
sex	male	13.8(12.5-15.1)	0.004	7.9(7.1-8.7)	0.005
	female	18.3(12.3-24.3)		9.6(6.9-12.2)	
age	≥65	13.6(12.4-14.8)	0.536	8.3(7.3-9.3)	0.373
	<65	15.4(13.8-17.0)		7.9(6.7-9.1)	
Smoking Index	<400	15.4(13.6-17.1)	0.041	8.8(7.4-10.2)	0.032
	≥400	13.3(11.6-15.0)		7.9(7.0-8.8)	
ECOG score	≤1	15.5(14.6-16.4)	<0.001	8.7(7.9-9.5)	0.027
	≥2	10.7(9.5-11.9)		6.7(4.9-8.4)	
Tumor location	Central	14.7(13.5-15.8)	0.475	8.2(7.5-9.0)	0.817
	Peripheral	12.2(9.2-13.9)		7.8(4.6-11.0)	
T stage	T_{1-2}	14.9(12.2-17.6)	0.916	7.8(5.8-9.7)	0.281
	T_{3-4}	14.3(12.9-15.6)		8.3(7.6-9.0)	
N stage	N_{0-1}	21.2(15.3-27.2)	0.030	10.9(9.5-12.3)	0.027
	N_{2-3}	14.0(12.7-15.4)		7.9(7.0-8.7)	
Treatment	Chemoradiotherapy	14.2(12.8-15.6)	0.844	8.6(7.8-9.4)	0.101
	Single treatment	14.9(12.5-17.3)		7.1(5.7-8.5)	
Cycles of chemotherapy	<4	11.3(9.6-13.0)	<0.001	5.4(4.2-6.6)	<0.001
	≥4	15.4(14.4-16.5)		8.9(8.3-9.5)	

Immunotherapy	yes	17.2(12.9-21.5)	<0.001	9.2(8.0-10.4)	0.049
	no	13.0(11.6-14.4)		7.7(6.7-8.7)	
PCI	yes	16.7(10.5-22.9)	0.041	12.4(9.9-14.9)	0.008
	no	14.0(12.6-15.4)		7.9(7.1-8.7)	
Response	CR+PR	15.4(14.4-16.4)	0.128	8.6(7.4-9.7)	0.516
	SD+PD	12.3(10.6-14.0)		7.8(6.6-9.1)	
SII	low	20.3(16.4-24.1)	<0.001	10.6(9.6-11.5)	<0.001
	high	12.2(11.1-13.3)		6.9(6.1-7.7)	

Table 3 Univariate survival analysis for OS and PFS

Characteristic	category	OS		PFS	
		mOS(95%CI)	Pvalue	mPFS （95%CI）	Pvalue
sex	male	13.8(12.5-15.1)	0.004	7.9(7.1-8.7)	0.005
	female	18.3(12.3-24.3)		9.6(6.9-12.2)	
age	≥65	13.6(12.4-14.8)	0.536	8.3(7.3-9.3)	0.373
	<65	15.4(13.8-17.0)		7.9(6.7-9.1)	
Smoking Index	<400	15.4(13.6-17.1)	0.041	8.8(7.4-10.2)	0.032
	≥400	13.3(11.6-15.0)		7.9(7.0-8.8)	
ECOGscore	≤1	15.5(14.6-16.4)	<0.001	8.7(7.9-9.5)	0.027
	≥2	10.7(9.5-11.9)		6.7(4.9-8.4)	
Tumor location	Central	14.7(13.5-15.8)	0.475	8.2(7.5-9.0)	0.817
	Peripheral	12.2(9.2-13.9)		7.8(4.6-11.0)	
T stage	T_{1-2}	14.9(12.2-17.6)	0.916	7.8(5.8-9.7)	0.281
	T_{3-4}	14.3(12.9-15.6)		8.3(7.6-9.0)	
N stage	N_{0-1}	21.2(15.3-27.2)	0.030	10.9(9.5-12.3)	0.027
	N_{2-3}	14.0(12.7-15.4)		7.9(7.0-8.7)	
Treatment	Chemoradiotherapy	14.2(12.8-15.6)	0.844	8.6(7.8-9.4)	0.101
	Single treatment	14.9(12.5-17.3)		7.1(5.7-8.5)	
Cycles of chemotherapy	<4	11.3(9.6-13.0)	<0.001	5.4(4.2-6.6)	<0.001
	≥4	15.4(14.4-16.5)		8.9(8.3-9.5)	

Immunotherapy	yes	17.2(12.9-21.5)	<0.001	9.2(8.0-10.4)	0.049
	no	13.0(11.6-14.4)		7.7(6.7-8.7)	
PCI	yes	16.7(10.5-22.9)	0.041	12.4(9.9-14.9)	0.008
	no	14.0(12.6-15.4)		7.9(7.1-8.7)	
Response	CR+PR	15.4(14.4-16.4)	0.128	8.6(7.4-9.7)	0.516
	SD+PD	12.3(10.6-14.0)		7.8(6.6-9.1)	
SII	low	20.3(16.4-24.1)	<0.001	10.6(9.6-11.5)	<0.001
	high	12.2(11.1-13.3)		6.9(6.1-7.7)	

Table 4 Relationship between clinical features before and after PSM

Characteristic	category	□□	□□□	P	□□	□□□	P
		N=87	N=187	(before)	N=82	N=82	(after)
sex	male	68	157	0.244	63	72	0.065
	female	19	30		19	10	
age	≥65	27	87	0.015	27	37	0.109
	<65	60	100		55	45	
Smoking Index	<400	35	72	0.785	33	36	0.635
	≥400	52	115		49	46	
ECOGscore	≤1	84	141	<0.001	79	79	1.000
	≥2	3	46		3	3	
Tumor location	Central	81	165	0.216	76	70	0.134
	Peripheral	6	22		6	12	
T stage	T_{1-2}	24	39	0.218	23	18	0.367
	T_{3-4}	63	148		59	64	
N stage	N_{0-1}	10	13	0.207	9	11	0.633
	N_{2-3}	77	174		73	71	
Treatment	Chemoradiotherapy	67	154	0.297	65	68	0.550
	Single treatment	20	33		17	14	
Cycles of chemotherapy	<4	17	70	0.016	17	11	0.213
	≥4	63	124		65	71	
Response	CR+PR	46	77	0.070	41	49	0.209
	PD+SD	41	110		41	33	
SII	low	36	60	0.133	36	35	0.875

	high	51	127		46	47	
PCI	yes	7	12	0.621	7	6	0.773
	no	80	175		75	76	

Table 5 Kaplan-Meier univariate survival analysis for OS and PFS in 164 patients with ES-SCLC after PSM

Characteristic	category	OS		PFS	
		mOS (95%CI)	Pvalue	mPFS （95%CI）	Pvalue
sex	male	16.5(14.5-18.5)	0.03	9.2(8.4-9.9)	0.004
	female	23.3(12.9-33.7)		11.5(9.1-13.9)	
age	≤65	15.9(14.2-17.5)	0.976	9.3(7.8-10.8)	0.383
	>65	18.7(16.1-21.2)		9.3(8.3-10.4)	
Smoking Index	<400	17.5(14.5-20.4)	0.371	10.7(8.8-12.7)	0.069
	≥400	16.7(13.8-19.6)		9.2(8.5-9.8)	
ECOGscore	≤1	8.5(16.3-20.7)	<0.001	9.4(8.4-10.3)	0.004
	≥2	9.8(5.0-14.5)		5.4(2.4-8.4)	
Tumor location	Central	16.7(14.5-18.9)	0.904	9.2(8.5-9.9)	0.504
	Peripheral	19.2(8.0-30.4)		10.2(8.0-12.5)	
T stage	T_{1-2}	20.8(13.5-28.1)	0.905	9.6(7.0-12.2)	0.498
	T_{3-4}	16.7(14.6-18.8)		9.3(8.4-10.3)	
N stage	N_{0-1}	15.9(8.5-23.4)	0.749	10.9(9.6-12.2)	0.098
	N_{2-3}	17.5(15.1-19.8)		9.2(8.4-10.0)	
Treatment	Chemoradiotherapy	16.6(14.2-19.0)	0.337	9.4(8.4-10.3)	0.877
	Single treatment	22.1(14.9-29.3)		8.8(6.7-10.8)	
Cycles of chemotherapy	<4	19.3(10.6-28.1)	0.345	5.4(2.4-8.3)	0.008
	≥4	16.7(14.6-18.8)		9.5(8.6-10.4)	

Immunotherapy	yes	22.2(16.4-28.1)	0.024	9.4(8.3-10.5)	0.562
	no	15.9(14.4-17.5)		9.2(7.5-10.9)	
PCI	yes	29.0(0-63.2)	0.062	13.0(10.4-15.6)	0.142
	no	16.7(14.5-18.9)		9.2(8.4-9.9)	
Response	CR+PR	17.5(14.2-20.7)	0.781	9.4(8.0-10.8)	0.781
	PD+SD	16.7(13.9-19.5)		9.0(8.0-10.0)	
SII	low	19.2(14.6-23.8)	0.003	10.9(9.9-11.9)	<0.001
	high	15.9(14.8-16.9)		7.9(6.7-9.0)	

Table 6 Multivariate prognostic for OS and PFS in patients with ES-SCLC after PSM

Characteristic	OS		PFS	
	Sig	Exp(B)	Sig	Exp(B)
SII	0.021	1.548	0.003	1.658
Sex	0.075	0.632	0.007	0.549
ECOG score	<0.001	8.534	0.012	2.955
Immunotherapy	0.002	1.749	--	--
Cycles of chemotherapy	0.353	0.798	0.030	0.619
PCI	--	--	0.440	1.236

Figures

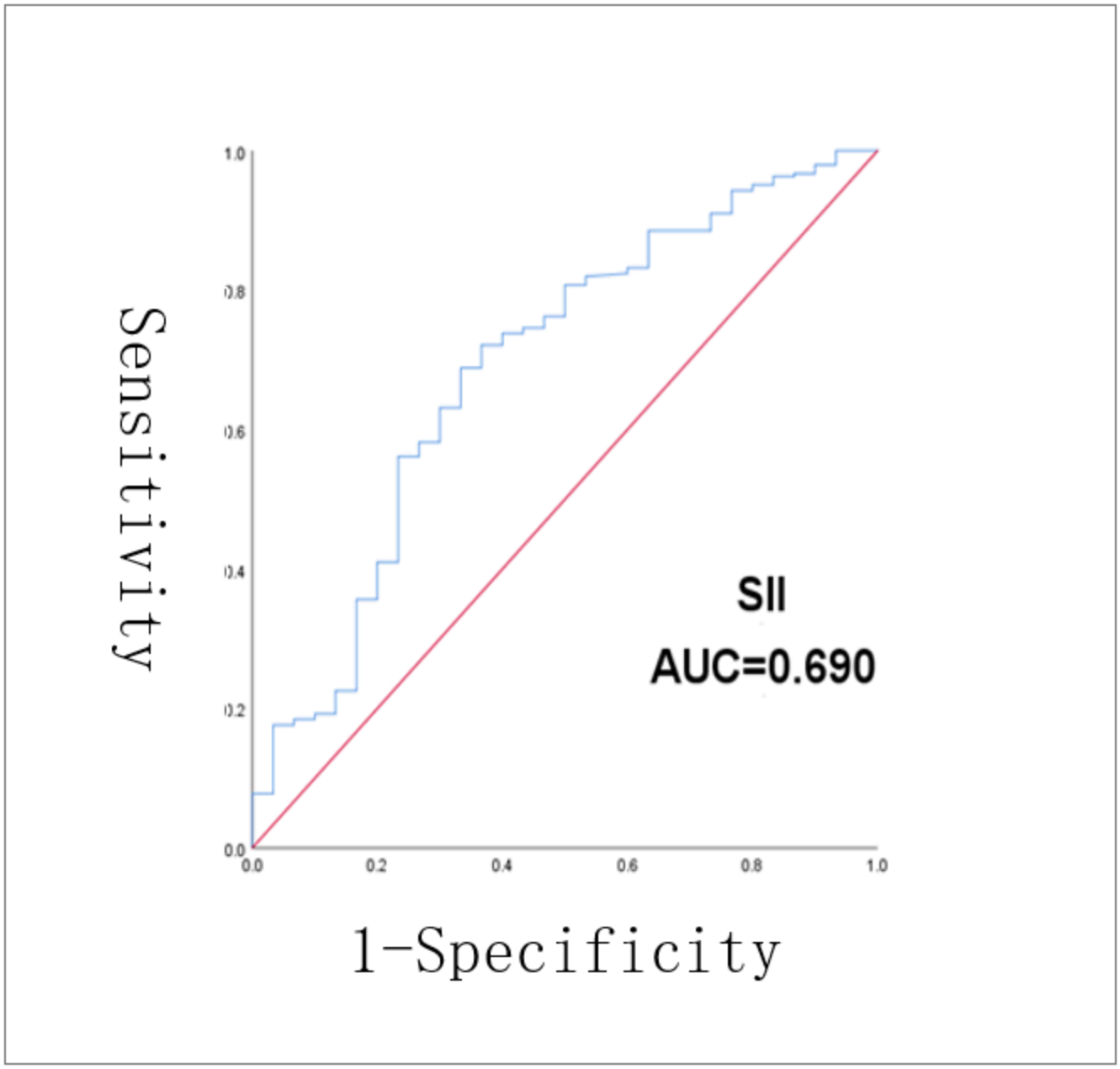


Figure 1

The ROC curve of SII

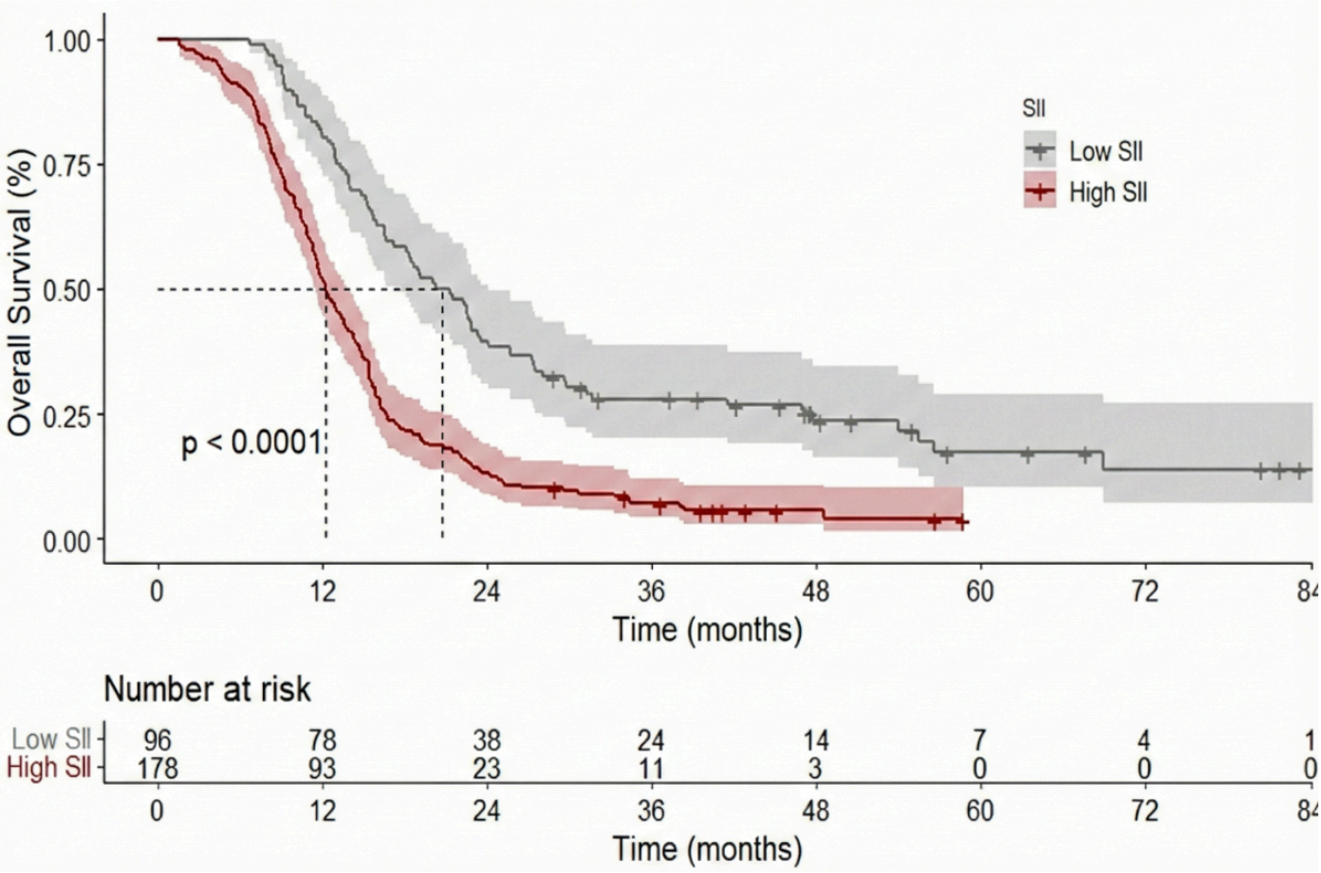


Figure 2

The OS curve of SII

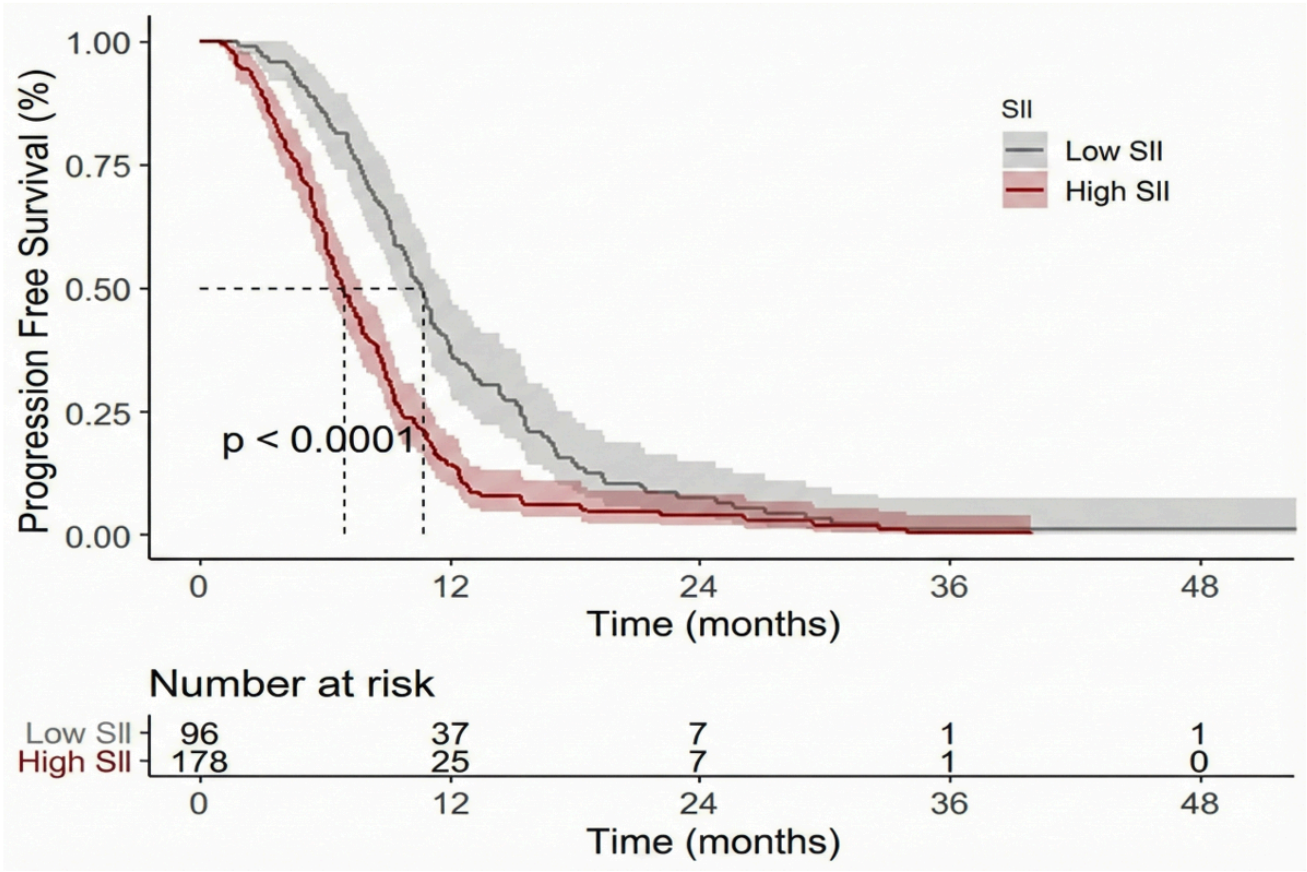


Figure 3

The PFS curve of SII

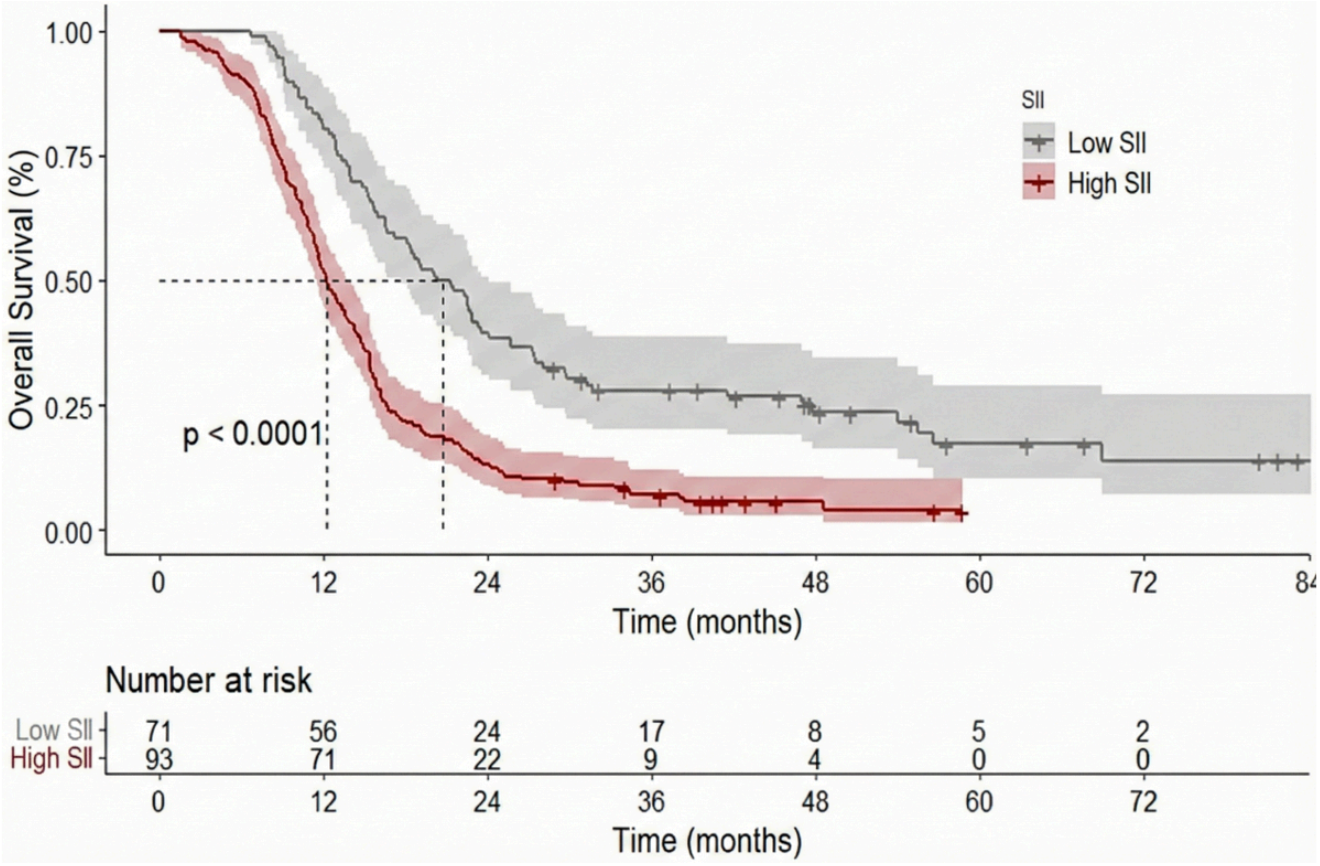


Figure 4

The OS curve of SII after PSM

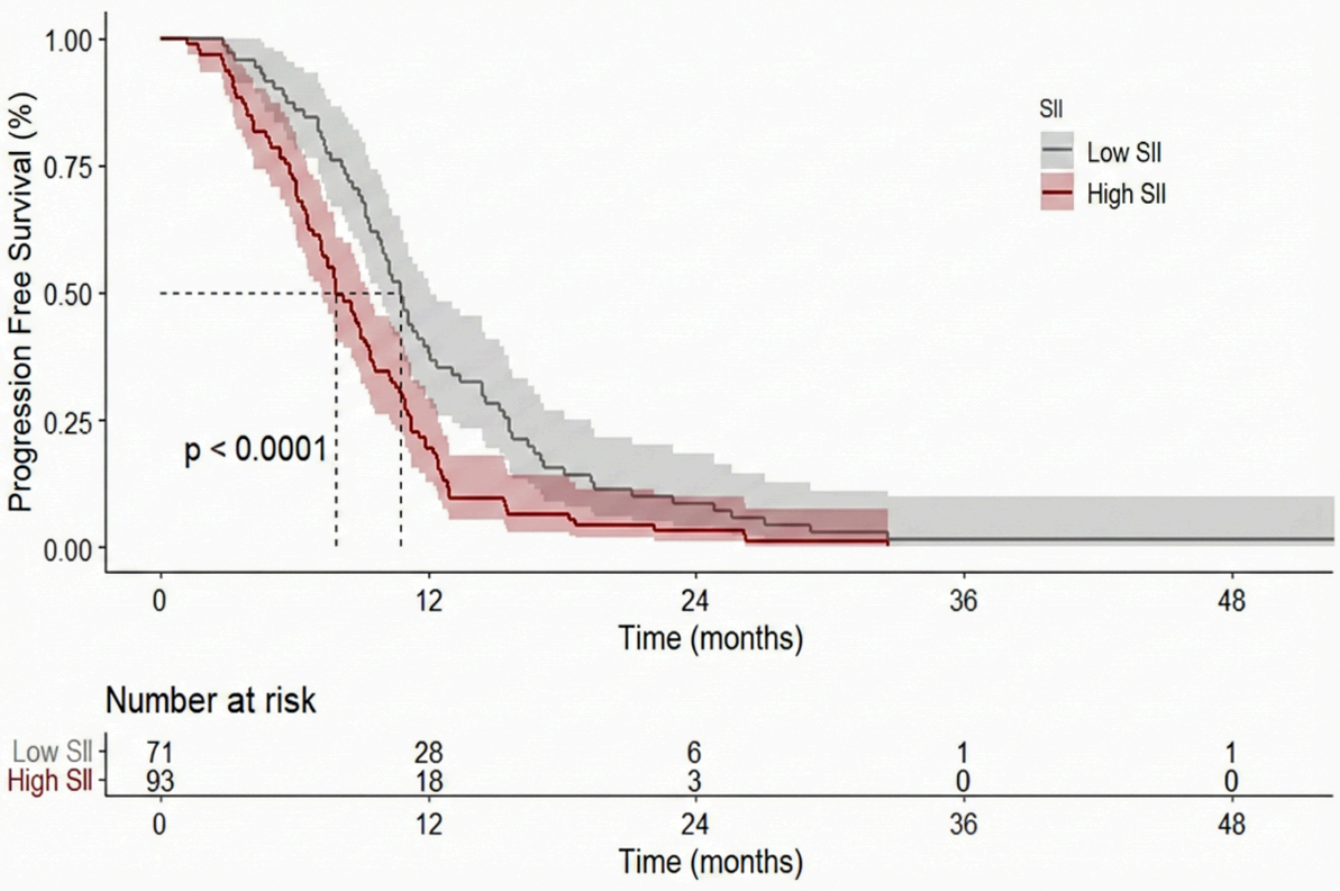


Figure 5

The PFS curve of SII after PSM