Am J Transl Res 2023;15(5):3309-3317
www.ajtr.org /ISSN:1943-8141/AJTR0149921

*Original Article*

# Correlation of systemic immune-inflammatory response index with clinical data in patients with malignant ovarian tumor

Jinhui Feng[1], Qiming Wang[2]

*[1]Third Gynecology, Ningbo Women's and Children's Hospital, 339 Liuting Street, Haishu, Ningbo, Zhejiang, China; [2]Department of Obstetrics and Gynecology, Ningbo Women's and Children's Hospital, 339 Liuting Street, Haishu, Ningbo, Zhejiang, China*

Received March 1, 2023; Accepted April 13, 2023; Epub May 15, 2023; Published May 30, 2023

**Abstract:** Objective: To determine the correlation of the systemic immune-inflammatory response index (SIRI) with clinical data in patients with malignant ovarian tumor. Methods: The clinical data of 118 patients with ovarian cancer (OC) treated in Ningbo Women's and Children's Hospital from February 2016 to January 2018 were retrospectively studied. Patients were divided into high and low SIRI expression groups according to the receiver operator curve (ROC) optimal cut-off (Cut-off) value, and the association of SIRI with the patient's clinical data was analyzed. Cox regression was adopted for the analysis of prognostic factors impacting the patients' 5-year survival. The associations of SIRI with tumor markers were also analyzed. A risk prediction model was constructed based on the Cox regression coefficient. Results: The group of patients who died showed notably higher neutrophil (NEUT) and SIRI levels than the surviving group, and also showed a significantly lower lymphocyte (LYM) level than the surviving group ($P < 0.001$). The areas under the ROC curves (AUC) for CA125, NEUT, LYM, and SIRI for predicting death from OC were 0.779, 0.754, 0.776, and 0.848, respectively. In addition, the AUC of each index was ranked CA125 > SIRI > LYM > NEUT. The high-expression group had a higher proportion of patients with stage III-IV and lymph node metastasis (LNM) than the low-expression group ($P < 0.05$). SIRI showed a positive correlation with serum carbohydrate antigen 125 (CA125), CA153, and HE4 (all $P < 0.05$), but had no correlation with CA199, AFP, or CEA (all $P > 0.05$). According to multivariate Cox regression analysis, age, FIGO stage, SIRI, and therapeutic regimen were independent prognostic factors for the 5-year survival of OC patients (all $P < 0.05$). The risk score was significantly higher in the death group than that in the surviving group ($P < 0.001$), and the AUC of this risk score for predicting 5-year survival was 0.876. Conclusion: Patients with an increased SIRI level account for a large proportion of OC patients with a high FIGO stage and LNM. The 5-year survival rate of patients with a high SIRI level is unfavorable, suggesting the use of SIRI as an observation index for the prognosis of OC.

**Keywords:** Systemic immune-inflammatory response index, ovarian cancer, 5-year survival, prognosis, Cox regression

## Introduction

Ovarian cancer (OC) is a frequent female malignant tumor, ranking the eighth most common cancer and the fifth leading cause of cancer-associated death among women worldwide [1]. According to data from the World Health Organization [2], in 2020, there were approximately 313,959 new cases of OC and 207,252 deaths from OC. Although the incidence of OC varies by region and population, most cases are diagnosed among women over 50 years old [3]. There are several different types of OC, but the most frequent is epithelial OC, which begins with cells arranged on the surface of the ovary, accounting for 85-90% of all OCs [4]. Some common symptoms of OC include abdominal or pelvic pain, abdominal distension, changes in bowel or bladder habits, and a quick sense of fullness after eating [5]. These symptoms may also be triggered by other diseases, such as irritable bowel syndrome, which challenges doctors to identify OC.

The prognosis of OC is bound up with the cancer stage at diagnosis, the type of OC, and the overall health status of the patient [6]. Because of the occult symptoms, OC usually has entered a late clinical stage at the time of diagnosis, which makes the treatment more challenging

and prognosis poor [7]. According to statistics, the five-year survival rate of OC patients is approximately 49%, which means that about half of the women diagnosed with OC survive for at least five years after diagnosis [8]. However, the survival rate may vary greatly due to the different stages of cancer at diagnosis [9]. The systemic immune-inflammatory response index (SIRI) is a marker to measure the host's immune response to a tumor [10]. It is calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, which reflects a balance between pro-inflammatory and anti-inflammatory processes *in vivo* [11]. Increasing SIRI levels were found to be associated with poor prognosis in multiple cancers [12]. A high SIRI level may represent a weakened immune response and a more aggressive cancer phenotype, which probably results in an unfavorable prognosis [13]. Additionally, as a simple and cost-effective marker, SIRI shows good prospects in various clinical environments including cancer, autoimmune disease, and infectious disease [14]. However, whether SIRI has prognostic value in OC is still controversial.

This study analyzed the influence of SIRI, clinical data, and prognosis of patients with malignant ovarian tumor, with the purpose of providing markers for clinical diagnosis and prognosis.

## Methods and materials

### *Patient information*

A total of 118 patients with OC treated in Ningbo Women's and Children's Hospital from February 2016 to January 2018 were retrospectively enrolled. This study was conducted with permission from the Ethics Committee of Ningbo Women's and Children's Hospital (EC2022-008).

### *Inclusion and exclusion criteria*

Inclusion criteria: Patients diagnosed and confirmed with primary OC by pathologic examination; patients whose pathologic staging met the International Federation of Gynecology and Obstetrics (FIGO) staging criteria [5], patients without a history of ovarian surgery, radiotherapy, or chemotherapy before admission; patients with detailed case data; and patients with estimated survival > 6 months.

Exclusion criteria: Patients who had undergone a blood transfusion recently or had received antibiotics within 2 weeks before the operation; patients with diseases associated with pregnancy or the blood system, patients with thrombotic disease, immune disease, severe liver or kidney damage, or malignant tumors in other parts.

### *Collection of clinical data*

The following case information of each patient was collected: neutrophil percentage (NEUT%), lymphocyte percentage (LYM%), serum carbohydrate antigen 125 (CA125), CA153, CA199, alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), human epididymal protein 4 (He4), and patient's age, FIGO staging, histological classification, tumor diameter, lymph node metastasis (LNM), and ascites. The SIRI condition of each patient was calculated by Eq.

### *Collection of follow-up data*

Each patient was followed up since the patient was discharged from the hospital after surgery, once every three months for the first two years, and once every six months or one year after two years, until the termination date of follow-up (January 30, 2023) or the death date of the patient. The main follow-up methods included outpatient service and telephone follow-up.

### *Outcome measures*

*Primary outcome measures:* The SIRI in surviving patients was determined. According to the cut-off value of the receiver operating characteristic (ROC), the patients were assigned to high and low SIRI groups to understand the association of SIRI with the patient's clinical data.

*Secondary outcome measures:* Cox regression was used for analysis of the prognostic factors impacting the patients' 5-year survival. The association of SIRI with tumor markers was also analyzed. The difference in the area under the ROC curve for each index was compared. A risk prediction model was constructed based on the Cox regression coefficient.

### *Statistical analyses*

This study used SPSS 26.0 and GraphPad Prism 8 software for data analyses. The optimal cut-off of SIRI was determined based on

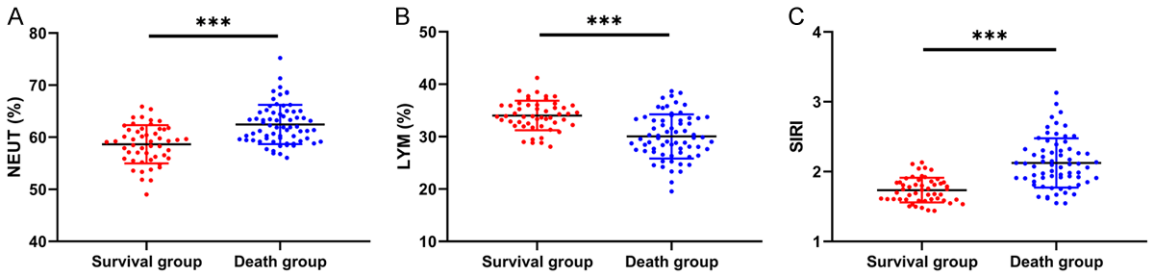


**Figure 1.** NEUT, LYM, and SIRI levels of surviving OC patients and dead patients. A. Comparison of NEUT level between surviving OC patients and dead patients. B. Comparison of LYM level between surviving OC patients and dead patients. C. Comparison of SIRI level between surviving OC patients and dead patients. Note NEUT%: Neutrophil percentage; LYM%: Lymphocyte percentage; SIRI: Systemic immune-inflammatory response index. ***P < 0.001.

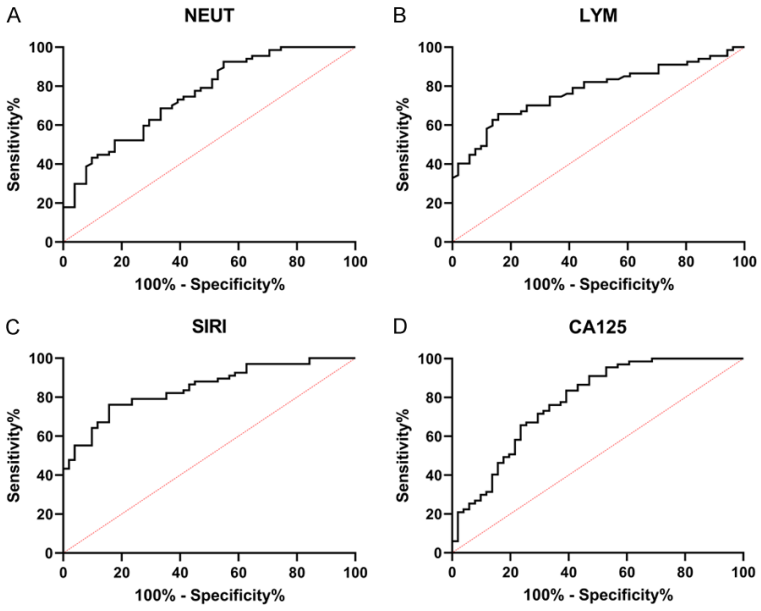


**Figure 2.** ROC curves of NEUT, LYM and SIRI for predicting the death of OC patients. A: ROC of NEUT in forecasting the death of OC patients. B: ROC of LYM in forecasting the death of OC patients. C: ROC of SIRI in forecasting the death of OC patients. D: ROC of CA125 in forecasting the death of OC patients. Note NEUT%: Neutrophil percentage; LYM%: Lymphocyte percentage; SIRI: Systemic immune-inflammatory response index; CA125: carbohydrate antigen 125; ROC: receiver operating characteristic.

the ROC curve. Based on this value, the patients were assigned to a high SIRI group or a low SIRI group. The Kaplan-Meier (K-M) method was used to draw the survival curve, and the log-rank test was adopted for inter-group comparison of the 5-year survival. Counted data were described by frequency (percentage), and their inter-group comparison was done by $\chi^2$ test. Measured data were described by mean ± SD, and their inter-group comparison was done by independent-samples t test. The Pearson test was used to test the correlation between the data. Differences in the area under the ROC curve of each index were analyzed using the pairwise test by ROC curve analysis. Cox proportional hazard regression model was used for analysis of independent risk factors affecting the OC patients' prognosis. P < 0.05 was considered significant.

## Results

### *Levels of NEUT, LYM, and SIRI in surviving OC patients*

The clinical data and vital status of the 118 patients were analyzed. Up to the end of follow-up, 51 patients survived, showing a 5-year survival rate of 43.65%. The patients were assigned to a surviving group (n=51) or a death group (n=67) on this basis. According to inter-group comparison of NEUT, LYM, and SIRI between the two groups, the death group showed significantly higher NEUT and SIRI levels but a lower LYM level than the surviving group (all P < 0.001, **Figure 1**).

### *ROC curves of NEUT, LYM, and SIRI in predicting patients' death*

The predictive values of CA125, NEUT, LYM, and SIRI for death in OC patients was analyzed by ROC curves. According to the results, the areas under the ROC curve of CA125, NEUT, LYM, and SIRI in predicting death from OC were 0.779, 0.754, 0.776, and 0.848, respectively (**Figure 2**; **Table 1**). Further analysis revealed

**Table 1.** Values of ROC curves

| Predictor variable | Area under the curve (AUC) | Confidence interval (CI) | Cut-off | Sensitivity | Specificity | Youden index |
|---|---|---|---|---|---|---|
| NEUT | 0.754 | 0.667-0.841 | 58.32 | 92.54% | 45.10% | 37.64% |
| LYM | 0.776 | 0.693-0.859 | 31.65 | 65.67% | 84.31% | 49.99% |
| SIRI | 0.848 | 0.780-0.915 | 1.900 | 76.11% | 84.31% | 60.43% |
| CA125 | 0.779 | 0.693-0.865 | 321.00 | 83.58% | 60.78% | 44.36% |

Note: NEUT%: Neutrophil percentage; LYM%: Lymphocyte percentage; SIRI: Systemic immune-inflammatory response index.

**Table 2.** Comparison of AUCs of each marker

| Test results | Z value | *P* value | AUC difference | Standard error difference | 95% CI | |
|---|---|---|---|---|---|---|
| | | | | | Down | Up |
| CA125 - NEUT | 2.105 | 0.035 | 0.025 | 0.291 | 0.002 | 0.048 |
| CA125 - LYM | 9.176 | < 0.001 | 0.555 | 0.294 | 0.437 | 0.674 |
| CA125 - SIRI | -1.463 | 0.144 | -0.069 | 0.279 | -0.161 | 0.023 |
| NEUT - LYM | 8.499 | < 0.001 | 0.530 | 0.295 | 0.408 | 0.653 |
| NEUT - SIRI | -2.094 | 0.036 | -0.094 | 0.279 | -0.182 | -0.006 |
| LYM - SIRI | -8.336 | < 0.001 | -0.624 | 0.282 | -0.771 | -0.477 |

Notes: SIRI: systemic immune-inflammatory response indexes; FIGO: International Federation of Gynecology and Obstetrics.

that the areas under the curve of the four indices were ranked CA125 > SIRI > LYM > NEUT (**Table 2**).

*Association of SIRI level with patients' clinical data*

According to SIRI ≥ 1.90, the patients were assigned to a high SIRI expression group (n=49) or a low SIRI expression one (n=69). Then their differences in clinical data were compared. According to analysis, the high-expression group had a significantly higher proportion of patients with stage III-IV and LNM than the other group (**Table 3**, P < 0.05).

*Association of SIRI with tumor markers*

The associations of SIRI with CA125, CA153, CA199, AFP, CEA, and HE4 were analyzed. According to the results, SIRI showed a positive correlation with CA125, CA153, and HE4 (all P < 0.05, **Figure 3**), but had no correlation with CA199, AFP, or CEA (all P > 0.05, **Figure 3**).

*Cox regression analysis of prognostic factors in OC patients*

Finally, the prognostic factors of patients' 5-year survival were analyzed based on Cox regression. According to the results, age, FIGO stage, LNM, SIRI, and therapeutic regimen were linked to the patients' 5-year survival by univariate analysis (all P < 0.01, **Table 4**). According to multivariate Cox regression analysis, age, FIGO stage, LNM, SIRI, and therapeutic regimen were independent prognostic factors for t patients' 5-year survival (all P < 0.05, **Figure 4**).

*Construction of a risk model*

According to the Cox regression coefficient, we constructed a risk prediction model. Risk score =0.654 * age + 0.795 * FIGO stage + 0.613 * LNM + (-1.301) * SIRI + 0.784 * therapeutic regimen. By comparison, it was found that the risk score in the death group was significantly higher than that of the survival group (P < 0.001, **Figure 5A**). In addition, ROC curve analysis showed that the AUC of the risk score for predicting 5-year survival was 0.876 (**Figure 5B**).

## Discussion

The application of molecularly targeted drugs has prolonged the progression-free survival of OC patients to some extent in recent years, but the mortality of the disease still ranks first among gynecologic malignant tumors [16].

As the two mediators of tumor microenvironment, immunity and inflammation play a crucial

**Table 3.** Association of SIRI expression with patients' clinical data

| Factor | SIRI | | $\chi^2$ value | *P*-value |
|---|---|---|---|---|
| | High expression group (n=60) | Low expression group (n=58) | | |
| Age (Y) | | | | |
| ≥ 50 | 33 | 28 | 0.464 | 0.534 |
| < 50 | 27 | 30 | | |
| FIGO staging | | | | |
| Stage I-II | 25 | 40 | 8.883 | 0.003 |
| Stage III-IV | 35 | 18 | | |
| Histological type | | | | |
| Low level | 31 | 25 | 0.867 | 0.351 |
| High level | 29 | 33 | | |
| Tumor size | | | | |
| ≥ 5 cm | 38 | 30 | 1.628 | 0.202 |
| < 5 cm | 22 | 28 | | |
| Lymph node metastasis | | | | |
| Yes | 33 | 20 | 5.018 | 0.025 |
| No | 27 | 38 | | |
| Ascites | | | | |
| Yes | 20 | 15 | 0.789 | 0.374 |
| No | 40 | 43 | | |
| Therapeutic regimen | | | | |
| Simple surgery | 29 | 25 | 0.325 | 0.568 |
| Surgical combination chemotherapy | 31 | 33 | | |

Notes: SIRI: systemic immune-inflammatory response indexes; FIGO: International Federation of Gynecology and Obstetrics.

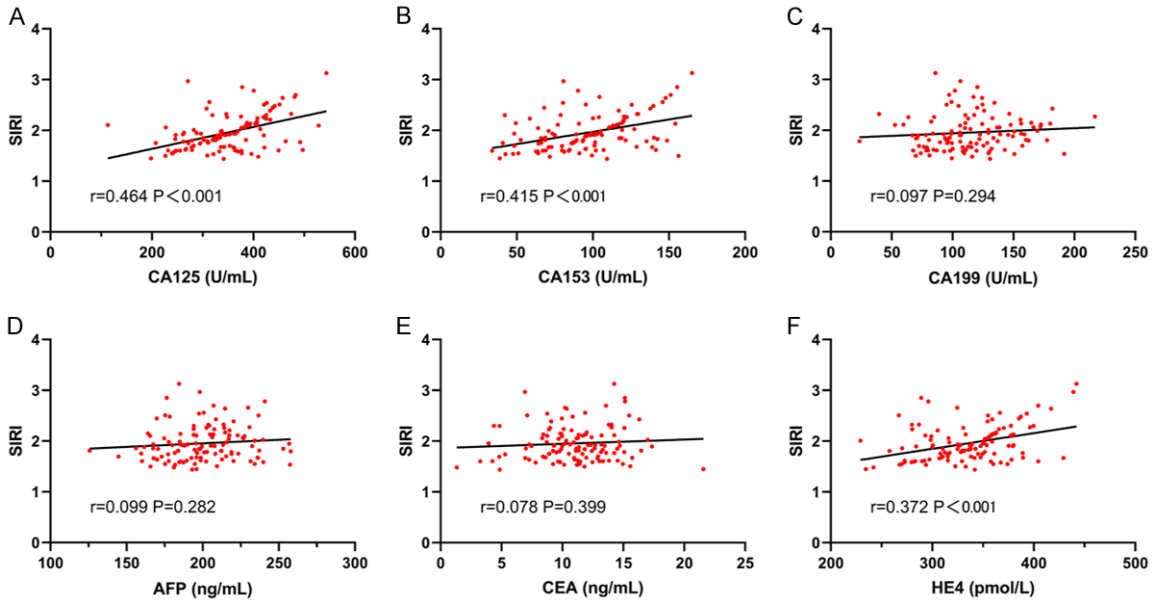


**Figure 3.** Scatter plot of SIRI and tumor markers. A. Association analysis of SIRI and CA125 in OC patients. B. Association analysis of SIRI and CA153 in OC patients. C. Association analysis of SIRI and CA199 in OC patients. D. Association analysis of SIRI and AFP in OC patients. E. Association analysis of SIRI and CEA in OC patients. F. Association analysis of SIRI and HE4 in OC patients. SIRI: Systemic immune-inflammatory response index; CA125: Carbohydrate antigen 125; AFP: alpha-fetoprotein; CEA: Carcinoembryonic antigen; HE4: Human epididymis protein 4.

**Table 4.** Cox regression analysis of factors affecting 5-year survival of OC patients

| Factor | Univariate Cox regression | | | Multivariate Cox regression | | |
|---|---|---|---|---|---|---|
| | *P*-value | HR-value | 95% CI | *P*-value | HR-value | 95% CI |
| Age | < 0.001 | 2.508 | 1.511-4.163 | 0.019 | 1.924 | 1.113-3.324 |
| FIGO staging | < 0.001 | 3.090 | 1.875-5.094 | 0.010 | 2.215 | 1.208-4.062 |
| Histological type | 0.187 | 1.381 | 0.855-2.231 | | | |
| Tumor size | 0.769 | 0.930 | 0.574-1.508 | | | |
| Lymph node metastasis | < 0.001 | 2.521 | 1.548-4.108 | 0.049 | 1.845 | 1.003-3.394 |
| Ascites | 0.939 | 0.980 | 0.581-1.654 | | | |
| NEUT | 0.056 | 1.877 | 0.983-3.585 | | | |
| LYM | 0.258 | 0.758 | 0.470-1.224 | | | |
| SIRI | 0.006 | 0.505 | 0.308-0.826 | < 0.001 | 0.272 | 0.159-0.466 |
| Therapeutic regimen | < 0.001 | 3.395 | 2.062-5.592 | 0.010 | 2.191 | 1.211-3.964 |

Notes: SIRI: systemic immune-inflammatory response indexes; FIGO: International Federation of Gynecology and Obstetrics.

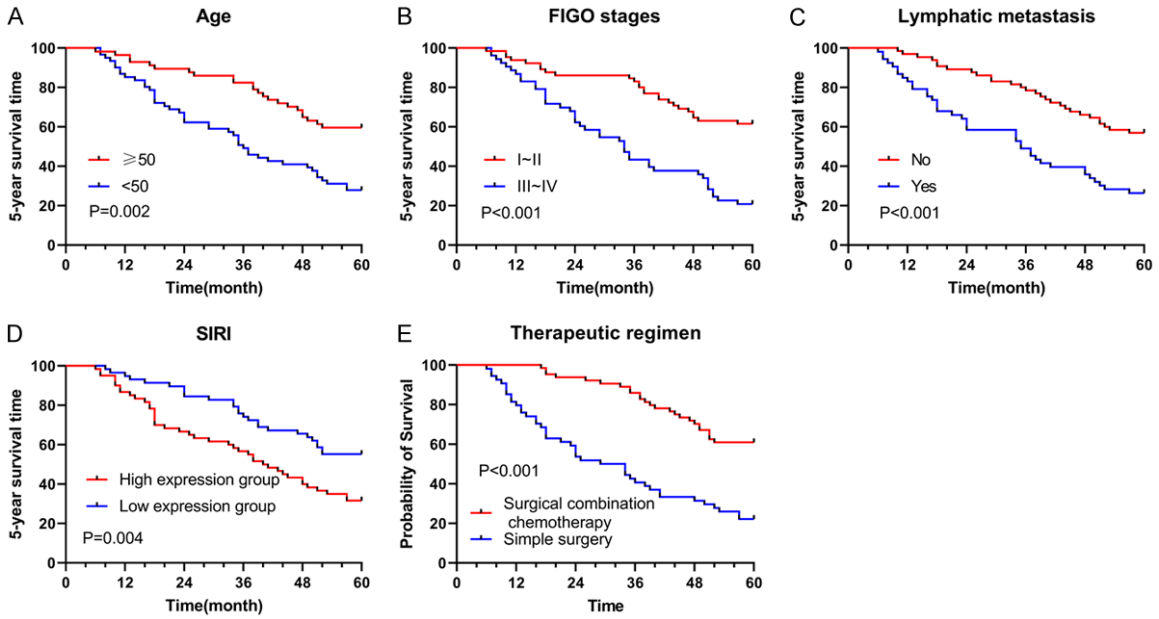


**Figure 4.** Prognostic factors and 5-year survival curves of patients. A. K-M curve of age and 5-year survival of patients. B. K-M curve of FIGO stage and 5-year survival of patients. C. K-M curve of lymph node metastasis and 5-year survival of patients. D. K-M curve of SIRI and 5-year survival of patients. E. K-M curve of therapeutic regimen and 5-year survival of patients. Note: K-M: Kaplan-Meier; SIRI: Systemic immune-inflammatory response index; FIGO: International Federation of Gynecology and Obstetrics.

role in the development and progression of tumors [17]. The blood routine test is the most basic part of clinical blood examination. When cells, tissues, organs, and systems have abnormal reactions, the indexes of blood routine examination will also change greatly or slightly, so it can predict the occurrence, progression, and outcome of diseases. This is of great significance for the clinical diagnosis of diseases [18, 19]. Peripheral blood cells include pro-inflammatory cells such as neutrophils, monocytes, and platelets, and also include anti-tumor immune cells such as lymphocytes, which can indirectly reflect the tumor microenvironment [20].

SIRI is a blood-based biomarker. Reportedly, a higher SIRI level indicates a stronger systemic immune-inflammatory response [21]. For example, Hua et al. [22] have revealed that SIRI can serve as an indicator to independently predict the survival rate of postmenopausal patients

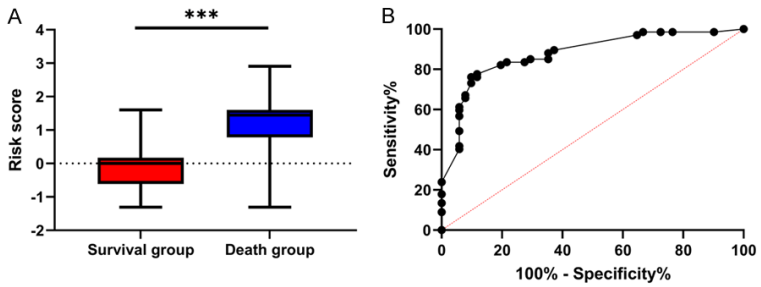


**Figure 5.** Risk score construction and predictive value analysis. A. Relationship between risk scores and patient survival. B. Efficacy of risk scores for predicting patient survival. Note: ***P < 0.001.

with breast cancer. According to one study by Pacheco-Barcia [23], SIRI is linked to survival rate of patients with metastatic pancreatic cancer and could help predict the prognosis of tumors treated with mFOLFIRINOX. All these studies demonstrate a close correlation between SIRI and tumor survival. In this study, the association of SIRI with OC patients' survival was evaluated. According to the results, compared to NEUT and LYM, SIRI had a higher level in patients who died from OC, and its area under the ROC curve was larger. The results suggest a close association of SIRI with the death of OC patients. Huang et al. [24] have revealed a correlation of SIRI with an ovarian malignant tumor and a role for SIRI in the differentiation between benign and malignant ovarian tumors and in the rough staging of ovarian malignant tumors. In this study, patients were grouped based on the cut-off value, and SIRI was found to be correlated with the clinical stage and LNM in OC patients, which was in agreement with the research finding of Huang et al. [24]. This further verifies the value of SIRI in OC.

Currently, the markers used for diagnosis of OC include CA125, CA153, CA199, AFP, CEA, and HE4. CA125 is a protein on the surface of some OC cells that can serve as a tumor marker in blood [25]. However, it is not unique to OC, and it may be increased by other factors, such as endometriosis, pelvic inflammatory disease, and liver and lung diseases [26]. CA153 is an antigen linnked to breast cancer and a tumor marker frequently used for clinical diagnosis of breast cancer [27]. With a correlation with cancer, it is sometimes combined with other diagnostic tests to monitor the progression of cancer or evaluate effectiveness of treatment [28]. CA199 is a lipid attached to the cell membrane, but is free in human serum in the form of mucin [29]. Although CA199 is not a specific or reliable tumor marker for OC, Li et al. [30] have revealed an association between an increased CA199 level and advanced OC and unfavorable prognosis. AFP and CEA are tumor markers usually associated with other types of cancer. AFP is usually used for liver cancer and germ cell tumors, while CEA is used for colorectal cancer, lung cancer, and breast cancer [31]. However, the two have been found to be elevated in OC patients [32]. HE4, a protein with overexpression in many types of OC, has been discovered to be a more specific tumor marker for OC than CA125 [33]. HE4 is particularly useful in detecting early OC, because the CA125 of OC cases may not increase [34]. In this study, the associations of SIRI with CA125, CA153, CA199, AFP, CEA, and HE4 were analyzed. According to the results, when CA125, CA153, and HE4 increased abnormally, SIRI also increased compared to traditional tumor markers, but SIRI had no correlation with CA199, AFP, or CEA.

OC is the most fatal disease among gynecologic tumors. Finally, this study analyzed the factors impacting the patients' 5-year survival rate according to Cox regression. According to the results, age, FIGO stage, LNM, SIRI, and therapeutic regimen were independent prognostic factors for their 5-year survival. Age, FIGO stage, LNM, and prognosis of OC patients have been reported in many studies [35, 36]. However, this study has verified for the first time that SIRI is linked to the prognosis in OC patients, which provides evidence for SIRI as a prognostic marker in OC. In addition, we concluded this study by constructing a risk model based on a Cox regression model and found that the risk model was highly expressed in patients in the mortality group and had an area under the curve greater than 0.8 for predicting 5-year survival. This suggests its value for clinical prediction.

This study has confirmed the value of SIRI in OC through analysis, but it still has some limita-

tions. First, only the 5-year survival data of patients had been collected, so whether SIRI is bound up the patients' overall survival requires further research support. Second, in such a single-center study, the samples collected are limited, so whether SIRI has the same prediction effect in other centers needs further verification. Finally, although SIRI demonstrates the prospect as a prognostic factor in OC, it is important to note that it has not been extensively used in clinical practice. Therefore, further research is needed to fully evaluate the clinical application of SIRI for OC and determine how it can be used with other prognostic markers to improve patients' prognosis.

In sum, patients with an increased SIRI level account for a large proportion of OC patients with a high FIGO stage and LNM, and the 5-year survival rate of patients with a high SIRI level is unfavorable. This suggests SIRI as an observation index for the prognosis of OC.

## Acknowledgements

This study was supported by a grant from the Gynecological Disease Treatment and Reproductive Medicine Centre (No. PPXK2018-06) and the Zhejiang Provincial Medical and Health Science and Technology Project (Observation of the efficacy of gene shearing down rondin with ovarian cancer ex vivo chemotherapy, No. 2021S158).

## Disclosure of conflict of interest

None.

**Address correspondence to:** Qiming Wang, Department of Obstetrics and Gynecology, Ningbo Women's and Children's Hospital, 339 Liuting Street, Haishu, Ningbo, Zhejiang, China. Tel: +86-13957885162; E-mail: wang19621026@hotmail.com

## References

[1] Stewart C, Ralyea C and Lockwood S. Ovarian cancer: an integrated review. Semin Oncol Nurs 2019; 35: 151-156.

[2] Armstrong DK, Alvarez RD, Bakkum-Gamez JN, Barroilhet L, Behbakht K, Berchuck A, Chen LM, Cristea M, DeRosa M, Eisenhauer EL, Gershenson DM, Gray HJ, Grisham R, Hakam A, Jain A, Karam A, Konecny GE, Leath CA, Liu J, Mahdi H, Martin L, Matei D, McHale M, McLean K, Miller DS, O'Malley DM, Percac-Lima S, Ratner E, Remmenga SW, Vargas R, Werner TL, Zsiros E, Burns JL and Engh AM. Ovarian cancer, version 2.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2021; 19: 191-226.

[3] Penny SM. Ovarian cancer: an overview. Radiol Technol 2020; 91: 561-575.

[4] Morand S, Devanaboyina M, Staats H, Stanbery L and Nemunaitis J. Ovarian cancer immunotherapy and personalized medicine. Int J Mol Sci 2021; 22: 6532.

[5] Matulonis UA. Ovarian cancer. Hematol Oncol Clin North Am 2018; 32: xiii-xiv.

[6] Kossai M, Leary A, Scoazec JY and Genestie C. Ovarian cancer: a heterogeneous disease. Pathobiology 2018; 85: 41-49.

[7] Eisenhauer EA. Real-world evidence in the treatment of ovarian cancer. Ann Oncol 2017; 28 Suppl 8: viii61-viii65.

[8] Rooth C. Ovarian cancer: risk factors, treatment and management. Br J Nurs 2013; 22: S23-30.

[9] Torre LA, Trabert B, DeSantis CE, Miller KD, Samimi G, Runowicz CD, Gaudet MM, Jemal A and Siegel RL. Ovarian cancer statistics, 2018. CA Cancer J Clin 2018; 68: 284-296.

[10] Mintz Y and Brodie R. Introduction to artificial intelligence in medicine. Minim Invasive Ther Allied Technol 2019; 28: 73-81.

[11] Jin Z, Wu Q, Chen S, Gao J, Li X, Zhang X, Zhou Y, He D, Cheng Z, Zhu Y and Wu S. The associations of two novel inflammation indexes, SII and SIRI with the risks for cardiovascular diseases and all-cause mortality: a ten-year follow-up study in 85,154 individuals. J Inflamm Res 2021; 14: 131-140.

[12] Zeidan A, Abdelgelil HT, Edwin E and Alqarni D. Apple Siri as communication conduit during COVID-19: between inside and outside the OR. BMJ Simul Technol Enhanc Learn 2020; 7: 274-275.

[13] Zhang Y, Xing Z, Zhou K and Jiang S. The predictive role of systemic inflammation response index (SIRI) in the prognosis of stroke patients. Clin Interv Aging 2021; 16: 1997-2007.

[14] Schietroma M, Romano L, Schiavi D, Pessia B, Mattei A, Fiasca F, Carlei F and Giuliani A. Systemic inflammation response index (SIRI) as a predictor of anastomotic leakage after total gastrectomy for gastric cancer. Surg Oncol 2022; 43: 101791.

[15] Javadi S, Ganeshan DM, Qayyum A, Iyer RB and Bhosale P. Ovarian cancer, the revised FIGO staging system, and the role of imaging. AJR Am J Roentgenol 2016; 206: 1351-1360.

[16] Orr B and Edwards RP. Diagnosis and treatment of ovarian cancer. Hematol Oncol Clin North Am 2018; 32: 943-964.

[17] Grabosch S, Bulatovic M, Zeng F, Ma T, Zhang L, Ross M, Brozick J, Fang Y, Tseng G, Kim E, Gambotto A, Elishaev E, P Edwards R and Vlad AM. Cisplatin-induced immune modulation in ovarian cancer mouse models with distinct inflammation profiles. Oncogene 2019; 38: 2380-2393.
[18] Gould MK, Huang BZ, Tammemagi MC, Kinar Y and Shiff R. Machine learning for early lung cancer identification using routine clinical and laboratory data. Am J Respir Crit Care Med 2021; 204: 445-453.
[19] Macuks R, Baidekalna I and Donina S. Diagnostic test for ovarian cancer composed of ovarian cancer symptom index, menopausal status and ovarian cancer antigen CA125. Eur J Gynaecol Oncol 2011; 32: 286-288.
[20] Bruand M, Barras D, Mina M, Ghisoni E, Morotti M, Lanitis E, Fahr N, Desbuisson M, Grimm A, Zhang H, Chong C, Dagher J, Chee S, Tsianou T, Dorier J, Stevenson BJ, Iseli C, Ronet C, Bobisse S, Genolet R, Walton J, Bassani-Sternberg M, Kandalaft LE, Ren B, McNeish I, Swisher E, Harari A, Delorenzi M, Ciriello G, Irving M, Rusakiewicz S, Foukas PG, Martinon F, Dangaj Laniti D and Coukos G. Cell-autonomous inflammation of BRCA1-deficient ovarian cancers drives both tumor-intrinsic immunoreactivity and immune resistance via STING. Cell Rep 2021; 36: 109412.
[21] Min L, Ziyu D, Xiaofei Z, Shunhe X and Bolin W. Analysis of levels and clinical value of CA19-9, NLR and SIRI in patients with pancreatic cancer with different clinical features. Cell Mol Biol (Noisy-le-grand) 2022; 67: 302-308.
[22] Hua X, Long ZQ, Huang X, Deng JP, Wen W, He ZY, Guo L, Zhang WW and Lin HX. The preoperative systemic inflammation response index (SIRI) independently predicts survival in postmenopausal women with breast cancer. Curr Probl Cancer 2020; 44: 100560.
[23] Pacheco-Barcia V, Mondejar Solis R, France T, Asselah J, Donnay O, Zogopoulos G, Bouganim N, Guo K, Rogado J, Martin E, Alcindor T and Colomer R. A systemic inflammation response index could be a predictive factor for mFOLFIRINOX in metastatic pancreatic cancer. Pancreas 2019; 48: e45-e47.
[24] Huang H, Wu K, Chen L and Lin X. Study on the application of systemic inflammation response index and platelet-lymphocyte ratio in ovarian malignant tumors. Int J Gen Med 2021; 14: 10015-10022.
[25] Dochez V, Caillon H, Vaucel E, Dimet J, Winer N and Ducarme G. Biomarkers and algorithms for diagnosis of ovarian cancer: CA125, HE4, RMI and ROMA, a review. J Ovarian Res 2019; 12: 28.
[26] Zhang M, Cheng S, Jin Y, Zhao Y and Wang Y. Roles of CA125 in diagnosis, prediction, and oncogenesis of ovarian cancer. Biochim Biophys Acta Rev Cancer 2021; 1875: 188503.
[27] Li M, Men X and Zhang X. Diagnostic value of carbohydrate antigen 72-4 combined with carbohydrate antigen 15.3 in ovarian cancer, cervical cancer and endometrial cancer. J BUON 2020; 25: 1918-1927.
[28] Li Y, Guo A, Tang J, Wang L, Wang J and Yu D. Role of preoperative sonography in the diagnosis and pathologic staging of pseudomyxoma peritonei. J Ultrasound Med 2013; 32: 1565-1570.
[29] Qing X, Liu L and Mao X. A clinical diagnostic value analysis of serum CA125, CA199, and HE4 in women with early ovarian cancer: systematic review and meta-analysis. Comput Math Methods Med 2022; 2022: 9339325.
[30] Lee JK, Song SH, Kim I, Lee KH, Kim BG, Kim JW, Kim YT, Park SY, Cha MS and Kang SB. Retrospective multicenter study of a clinicopathologic analysis of pseudomyxoma peritonei associated with ovarian tumors (KGOG 3005). Int J Gynecol Cancer 2008; 18: 916-920.
[31] Konishi I, Fujii S, Okamura H, Sakahara H, Endo K, Torizuka K, Suzuki A and Mori T. Analysis of serum CA125, CEA, AFP, LDH levels and LDH isoenzymes in patients with ovarian tumors--correlation between tumor markers and histological types of ovarian tumors. Nihon Sanka Fujinka Gakkai Zasshi 1986; 38: 827-836.
[32] Zhang F and Zhang ZL. The diagnostic value of transvaginal sonograph (TVS), color doppler, and serum tumor marker CA125, CEA, and AFP in ovarian cancer. Cell Biochem Biophys 2015; 72: 353-357.
[33] Scaletta G, Plotti F, Luvero D, Capriglione S, Montera R, Miranda A, Lopez S, Terranova C, De Cicco Nardone C and Angioli R. The role of novel biomarker HE4 in the diagnosis, prognosis and follow-up of ovarian cancer: a systematic review. Expert Rev Anticancer Ther 2017; 17: 827-839.
[34] Huang J, Chen J and Huang Q. Diagnostic value of HE4 in ovarian cancer: a meta-analysis. Eur J Obstet Gynecol Reprod Biol 2018; 231: 35-42.
[35] Hu Y, Zheng M, Wang S, Gao L, Gou R, Liu O, Dong H, Li X and Lin B. Identification of a five-gene signature of the RGS gene family with prognostic value in ovarian cancer. Genomics 2021; 113: 2134-2144.
[36] Yang Y, Qi S, Shi C, Han X, Yu J, Zhang L, Qin S and Gao Y. Identification of metastasis and prognosis-associated genes for serous ovarian cancer. Biosci Rep 2020; 40: BSR20194324.