BMC Gastroenterology

RESEARCH

Open Access

Inflammatory biomarker correlations and prognosis in high-risk gastrointestinal stromal tumor patients: a multicenter retrospective analysis

Tao Wang[1†], Lihua Qi[1†], Yang Zhao[1*], Xiaolan Ma[1] and Tao Li[1*]

Abstract

Background The accurate prognosis of gastrointestinal stromal tumors (GISTs) has garnered substantial attention, yet a gap persists in understanding the influence of inflammatory markers on the prognosis of high-risk GIST patients. This study investigated the relationship between various factors and the prognosis of high-risk GIST patients, with a specific focus on first recurrence-free survival (RFS) and overall survival (OS) as crucial prognostic indicators.

Methods A comprehensive collection of clinical data was conducted on 145 high-risk GIST patients meeting specific inclusion and exclusion criteria at 17 medical centers in Ningxia Hui Autonomous Region, China, covering the period from January 2013 to December 2019. Single-factor analysis and survival curves were used to analyze the variables, while the Cox regression model evaluated independent prognostic factors.

Results Within the cohort, a balanced male-to-female ratio of 1:1.1 was observed. Univariate analysis revealed compelling associations between RFS and age, preoperative neutrophil-to-lymphocyte ratio (NLR), preoperative platelet-to-lymphocyte ratio (PLR), preoperative systemic immune-inflammatory index (SII), preoperative prognostic nutritional index (PNI), mitotic index, and whether or not imatinib (IM) was taken regularly in high-risk GIST patients ($P < 0.05$). Except age, these other variables were also significantly correlated with OS ($P < 0.05$). Cox regression analysis showed that age, preoperative PNI, mitotic index and postoperative IM adjuvant therapy independently affected RFS ($P < 0.05$). In addition, preoperative PNI and postoperative IM adjuvant therapy were also independent factors of OS, with statistical significance ($P < 0.05$). Age was negatively correlated with RFS, and early routine IM treatment after operation significantly reduced the risk of recurrence and death. Higher mitotic index is closely related to poor RFS, and higher preoperative PNI indicates a better prognosis.

Conclusion A close correlation between young age, low preoperative PNI, high mitotic index, and lack of IM treatment had an unfavorable prognosis in high-risk GIST patients. Notably, the PNI was identified as a potential

†Tao Wang and Lihua Qi contributed equally to this work.

*Correspondence:
Yang Zhao
zhaoyang2775@gmail.com
Tao Li
litao2151@yeah.net

Full list of author information is available at the end of the article

additional prognostic factor, enhancing the accuracy of predicting treatment efficacy and patient outcomes in high-risk patients with GISTs. Therefore, we advocate for the serious consideration of the PNI as a valuable addition to standard clinical practice for managing high-risk GIST patients.

Keywords Gastrointestinal stromal tumors (GIST), High recurrence risk, NLR, SII, PLR, PNI, Imatinib

Introduction

Gastrointestinal stromal tumors (GISTs) are a distinct category of neoplasms arising in the interstitial space of the gastrointestinal wall or other abdominal soft tissues [1, 2]. These tumors primarily arise due to mutations in tyrosine kinase receptor (c-kit) or platelet-derived growth factor receptor-α (PDGFRA) genes [3]. Although relatively rare, GISTs present a complex challenge, affecting middle-aged and elderly individuals without sex predilection. While they can emerge anywhere within the digestive tract, the stomach (50–60%) and small intestine (30–35%) are the most common sites, whereas occurrences in the colon (5%) and esophagus (< 1%) are less frequent [4].

As for solid neoplasms, the cornerstone of GISTs treatment continues to be comprehensive surgical intervention (R0, complete tumor resection with no macroscopic residual disease). Notably, patient classification into extremely low, low, intermediate, and high-risk groups, primarily determined by tumor size, location, rupture status, and mitotic count, guides therapeutic decisions [5, 6]. High-risk GIST patients often receive postoperative adjuvant therapy, such as imatinib, in accordance with guidelines established by the National Comprehensive Cancer Network (NCCN) and the Chinese Society of Clinical Oncology (CSCO) [7]. Such protocols have led to improved prognoses for many patients [8]. However, some patients continue to experience recurrence or metastasis following surgery, profoundly impacting their quality of life and, in some cases, their survival [9, 10]. Therefore, the urgent clinical need revolves around the identification of novel risk factors for recurrence in high-risk GIST patients.

In recent years, evidence has highlighted the link between inflammation and cancer. Tumor cells can exploit inflammatory stimuli to promote angiogenesis, evade apoptosis, and enhance proliferation and metastasis [11–13]. In this context, inflammatory markers have gained prominence in oncology. Studies have shown the prognostic value of markers such as the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) in various cancers, including colorectal, bladder, and lung cancers [14–16]. Research has indicated that the NLR could predict recurrence risk in patients with GISTs [17, 18], and an elevated PLR is linked to poorer outcomes in patients with GISTs and patients with breast cancer [19, 20]. However, most of these studies were limited to single centers, and lacked insights from multicenter research.

Our study aimed to fill this gap by conducting a comprehensive regional multicenter analysis of inflammatory markers in the Ningxia region and assessing the relationship of these markers with the prognosis of high-risk GIST patients. Our hypothesis was that inflammatory factors affect survival in patients with high-risk GISTs. Our goal was to identify high-risk GIST patients with poor prognosis in advance by screening inflammatory markers, enabling targeted early clinical interventions and improving patient outcomes.

Materials and methods

Study population

Inclusion criteria

Patients with a pathological diagnosis of GIST or genetic test confirming GIST. Patients underwent R0 resection (complete tumor resection with no macroscopic residual disease). Postoperative finding in pathological review indicate a high risk of recurrence [5]. Complete medical records and follow-up data were obtained. Absence of concomitant malignancies. No clinical symptoms were indicative of the lack of any associated infection.

Exclusion criterion

Patients with concurrent other malignant neoplasms. History of recurrent GISTs. Perioperative mortality. Dysfunction of other major organs (refers to documented clinical conditions or diseases in which major organs, apart from the gastrointestinal system, exhibit substantive and unmanageable impairments or failures that might limit postoperative survival).

Patient selection

Based on the aforementioned inclusion and exclusion criteria, a total of 145 patients were selected from 17 public hospitals in Ningxia Hui Autonomous Region. The study encompassed the period from January 1, 2013, to December 31, 2019.

Ethical considerations

This study was conducted in compliance with the principles of the Declaration of Helsinki and received approval from the Medical Research Ethics Committee of General Hospital of Ningxia Medical University (Ethics-Number KYLL-2021-339). All study participants were provided with comprehensive information about the study, its

objectives, potential risks, and benefits, and voluntarily signed a notification of consent.

Data collection

Data sources

General clinical data of GIST patients who met the inclusion and exclusion criteria were collected from January 1, 2013, to December 31, 2019. These data were sourced from the medical records of 17 medical institutions (the data were collected from a consortium of 17 medical institutions, that were carefully chosen for their geographic distribution and diversity to ensure the broad representation of GIST patients from the Ningxia Hui Autonomous Region).

Data categories

The data were collected retrospectively and encompassed a range of clinical, pathological, and postoperative parameters, including but not limited to:

Clinical Data: sex, age, preoperative peripheral blood sample, neutrophil count, preoperative peripheral blood lymphocyte count, preoperative peripheral blood serum albumin value (g/L), and preoperative platelet count were collected. All laboratory blood test data were collected from tests performed on the patients' first admission prior to any treatment. all the procedures were carried out in strict accordance with the operating instructions, and all the experimental reagents matched the instruments.

Pathological data

Site of tumor occurrence, tumor diameter (measured in centimeters), The presence of bleeding or necrosis within the tumor, and mitotic index (number of mitoses per 50 HPFs; this parameter is utilized to assess the rate of cell division within the tumor).

Postoperative data

Imatinib was administered based on physician guidance and clinical indications (imatinib treatment was administered according to the guidance of the treating physician, primarily based on clinical evaluation and the presence of risk factors. According to the guidelines [2, 7], high-risk GIST patients should take targeted drugs to get intensive treatment after operation, however some patients gave up the treatment for personal reasons or economic reasons).

Data handling and security

To ensure data integrity and confidentiality, stringent data handling procedures were employed. The data were securely stored and managed to protect patient privacy and comply with ethical standards.

General data analysis

Calculation of indices

Several indices and ratios were derived from the collected data to facilitate the analysis of GIST patient profiles. The NLR was calculated as the preoperative neutrophil count divided by the preoperative lymphocyte count. PLR was calculated as the preoperative platelet count divided by the preoperative lymphocyte count. SII: Calculated as the product of the PLT and neutrophil count divided by the lymphocyte count. PNI was calculated as the sum of the serum ALB concentration (in g/L) and five times the total peripheral blood lymphocyte count (in ×10^9/L).

Threshold classification

The optimal critical points of the NLR, PLR, SII and PNI were determined by the ROC curve of the subjects, and they were divided into upper and lower groups according to the critical points. The specific values of these thresholds were determined to enable meaningful classification, with further details available in the statistical analysis section.

NIH classification criteria

Pathological data were classified according to the modified National Institutes of Health (NIH) classification criteria [5]. These criteria provide a framework for understanding and categorizing GISTs based on various pathological attributes, and further details on this classification are available in the relevant sections of this study.

Follow-up

Data collection methods

All study participants were subjected to follow-up assessments conducted through multiple means, including hospital outpatient medical records, telephone communication, and various other channels. This comprehensive approach was adopted to ensure the thorough tracking of patient progress.

Follow-Up parameters

The follow-up process included a range of critical parameters, including the following: Regular Adjuvant Therapy: Evaluation of whether patients consistently adhered to postoperative IM adjuvant therapy, as per physician recommendations. Recurrence and Metastasis: Detection of any instances of GIST recurrence or metastasis and detailed documentation of the timing of these events. Mortality: Patients were monitored for mortality, and when applicable, the exact time of death was recorded. Cause of death: Investigating whether the cause of death was attributed to GISTs or other factors.

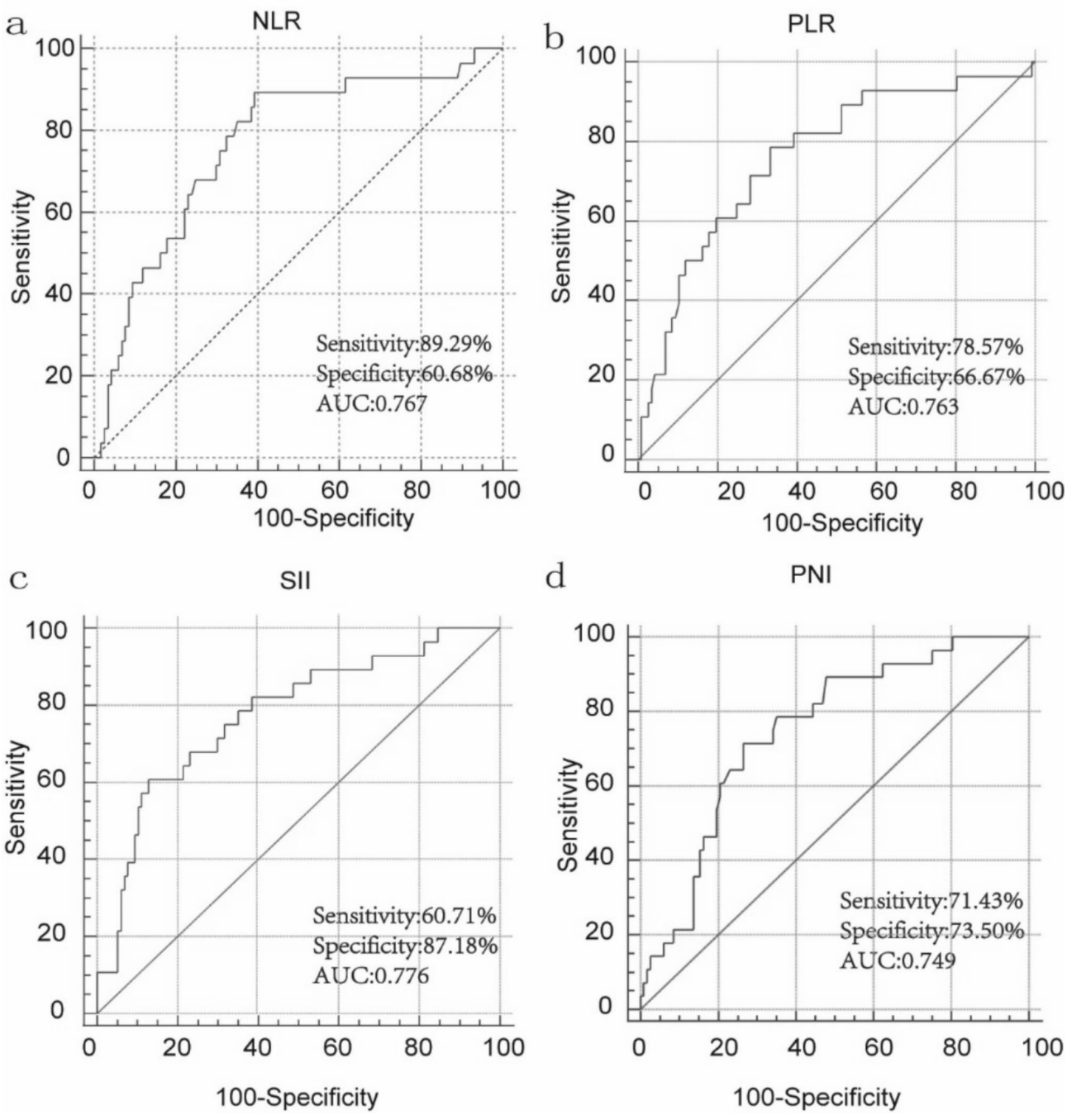

Fig. 1 Receiver operating characteristic curve of NLR (neutrophil-to-lymphocyte ratio), PLR (platelet-to-lymphocyte ratio), SII (systemic immune-inflammation index) and PNI (prognostic nutritional index) for High-risk Gastrointestinal Stromal Tumor Patients. **a**: NLR: AUC:0.767, associated criterion >2.34; **b**: PLR: AUC: 0.763, associated criterion >186.96; **c**: SII: AUC:0.776, associated criterion >482.13; **d**: PNI: AUC: 0.749, associated criterion ≤ 42.25

Data collection procedures

During follow-up, data were meticulously collected to ensure the accuracy and completeness of the patient records. This process included a combination of medical records, direct patient communication via telephone, and other suitable data collection methods. Specific forms and questionnaires were employed as required to facilitate systematic data capture.

Time intervals

Follow-up intervals were established to facilitate timely assessments and included an array of time frames for tracking specific events. The frequency and scheduling of these intervals were carefully considered to align with the objectives of this study.

Table 1 Univariate analysis of postoperative RFS and OS in high-risk gists based on clinical features

Clinical Feature	*n*(%)	RFS(month)	*P* value	OS(month)	*P* value
Sex			0.855		0.819
Male	69(47.6)	69.46		72.44	
Female	76(52.4)	70.25		74.66	
Age(years)			0.022*		0.286
<60	79(54.5)	64.18		72.55	
≥60	66(45.5)	76.71		74.70	
Preoperative NLR			0.001*		<0.001*
>2.34	71(49.0)	61.10		62.17	
≤2.34	74(51.0)	78.23		89.33	
Preoperative PLR			0.001*		<0.001*
>186.96	61(42.1)	59.78		59.75	
≤186.96	84(57.9)	76.68		86.38	
Preoperative SII			0.005*		0.001*
>482.13	87(60.0)	64.16		66.25	
≤482.13	58(40.0)	78.96		88.36	
Preoperative PNI			<0.001*		<0.001*
>42.25	94(64.8)	76.10		85.07	
≤42.25	51(35.2)	56.62		57.49	
Tumor location			0.123		0.308
Gastric	89(61.4)	73.81		75.12	
Non-gastric	56(38.6)	64.02		71.97	
Tumor size(cm)			0.905		0.722
<10	86(59.3)	71.01		74.08	
≥10	59(40.7)	68.18		74.30	
Mitotic index			0.001*		0.002*
≤5	46(31.7)	83.55		86.83	
>5	99(68.3)	62.07		65.51	
Hemorrhage/necrosis			0.759		0.913
Yes	93(64.1)	71.54		75.40	
No	52(35.9)	67.73		72.23	
Postoperative IM			0.029*		0.027*
Yes	93(64.1)	74.32		77.10	
No	52(35.9)	61.59		67.55	

Note: mitotic index: number/50HPF. HPF: high-power field, refers to the field of view on a pathological section visible through the eyepiece under an optical microscope with a 10x ocular lens and 40x objective lens. NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index, platelet count × neutrophil count/lymphocyte count; PNI: prognostic nutritional index, serum albumin level (g/L) + 5 × total peripheral lymphocyte count (×10~9/L). IM: Imatinib; * represents $P < 0.05$, indicating a statistically significant difference

Data integrity and confidentiality

Stringent measures were implemented to maintain data integrity and patient confidentiality throughout the follow-up period. These procedures were designed to protect the privacy and anonymity of the study participants while maintaining the highest ethical standards.

Data collection and statistical analysis

For data acquisition and management, Microsoft Office Professional Plus Excel 2021 software was used for meticulous data organization. IBM SPSS Statistics 26.0, a robust statistical analysis tool, was used to analyze the dataset. For univariate analysis, we applied the log rank model, and for the representation of survival curves, the method was used judiciously. In our pursuit of comprehensive insights, the multivariate analysis was performed with the Cox regression model to evaluate the associations among multiple covariates. A predetermined significance level, denoted by $\alpha = 0.05$, guided our statistical assessments. A p value (P) less than 0.05 indicated statistical significance.

Results

In this study, we investigated a cohort of 145 high-risk GIST patients, comprising an equal distribution of males and females. The optimal critical points of NLR, PLR, SII and PNI were determined by receiver ROC curve to be 2.34, 186.96, 482.13 and 42.25, respectively. According to the critical point, they are divided into upper groups and lower groups (Fig. 1). Our analysis employed the Kaplan-Meier method to assess the impact of various factors on first recurrence-free survival (RFS) and overall survival (OS) among high-risk GIST patients. The following variables were examined: sex; age; the NLR, PLR, SII and PNI; hemorrhage/necrosis; Tumor location; Tumor size; Postoperative IM and mitotic index. Our findings, as detailed in Table 1, reveal statistically significant associations between these variables and RFS and OS in high-risk GIST patients. Among them, for high-risk GISTs, age, the NLR, PLR, SII and PNI, mitotic index and whether IM adjuvant therapy is performed after operation have significant statistical differences for RFS and the NLR, PLR, SII and PNI, mitotic index and whether IM adjuvant therapy is performed after operation have significant statistical differences for OS (p values < 0.05). These results provide valuable insights into the prognosis and management of high-risk GIST patients.

We conducted a Cox multivariate regression analysis to examine the factors associated with the prognosis of RFS in high-risk GIST patients, building on the findings from previous univariate analyses. Our results revealed age, preoperative PNI, mitotic index, and postoperative IM as the independent factors significantly influencing RFS in high-risk GIST patients (p values < 0.05) (Table 2). The survival curve illustrating these findings can be found in Fig. 2.

We performed a Cox multivariate regression analysis to assess factors that exhibited correlations with the prognosis of OS in high-risk GIST patients via single-factor analyses. Our findings revealed two independent factors that significantly affect the OS of high-risk GIST

Table 2 Cox multivariate regression analysis (RFS)

Variable	Regression Coefficient	Wald Value	HR Value	95%CI	*P* Value
Age	-1.117	6.430	0.327	0.138–0.776	0.011*
Preoperative NLR	-0.426	0.489	0.653	0.198–2.157	0.484
Preoperative PLR	-0.046	0.009	0.995	0.368–2.477	0.925
Preoperative SII	-0.705	1.031	0.494	0.127–1.927	0.310
Preoperative PNI	1.011	5.821	2.749	1.209–6.250	0.016*
Mitotic index	1.532	5.572	4.630	1.297–16.527	0.018*
Postoperative IM	1.021	7.058	2.775	1.307–5.891	0.008*

Note: mitotic index: number/50HPF. HPF: high-power field, refers to the field of view on a pathological section visible through the eyepiece under an optical microscope with a 10x ocular lens and 40x objective lens. NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index, platelet count × neutrophil count/lymphocyte count; PNI: prognostic nutritional index, serum albumin level (g/L) + 5 × total peripheral lymphocyte count (×10 ~ 9/L). IM: Imatinib; * represents $P < 0.05$, indicating a statistically significant difference

patients: the preoperative PNI and postoperative IM (p values < 0.05) (Table 3). The survival curve illustrating these findings can be found in Fig. 3.

Discussion

The increasing incidence of GISTs, a form of soft tissue sarcoma, is becoming a major concern in the medical field, likely due to enhanced health awareness and advancements in diagnostic methods [21]. The evolution of therapeutic strategies for GISTs, transitioning from conventional surgical resection to a combination of

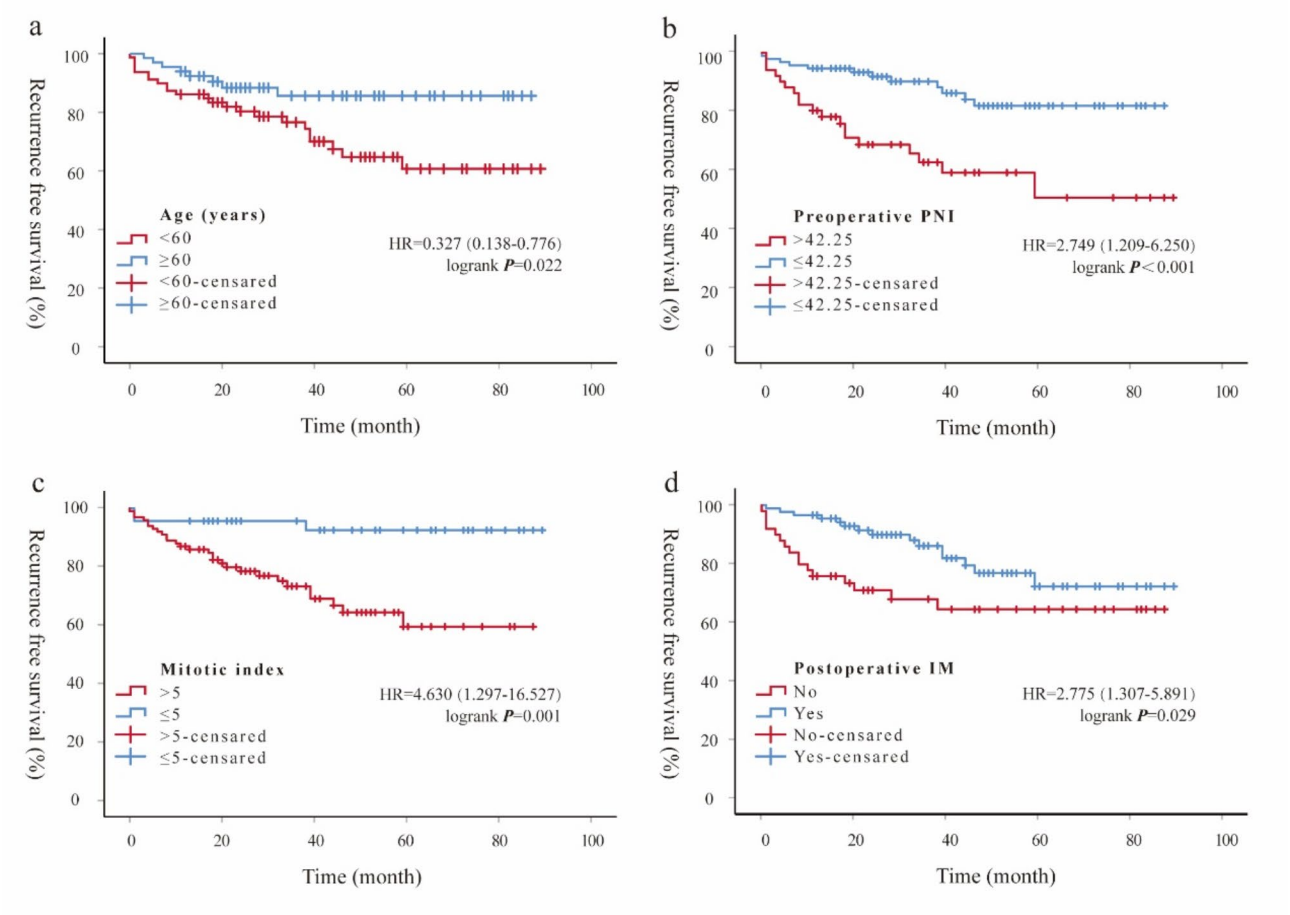

Fig. 2 Independent factors affecting postoperative RFS in high-risk GIST patients. **A**: Age; **B**: Preoperative PNI; **C**: Mitotic index; **D**: Postoperative IM adjuvant therapy. According to the age characteristics of China population, people over 60 years old are considered as the elderly group. The optimal critical points of the PNI were determined by the ROC curve of the subjects. Mitotic index was classified according to the modified National Institutes of Health (NIH) classification criteria

Table 3 COX multivariate regression analysis (OS)

Variable	Regression Coefficient	Wald Value	HR Value	95%CI	*P* Value
Preoperative NLR	-1.623	2.527	0.197	0.027–1.460	0.112
Preoperative PLR	-0.671	1.259	0.511	0.158–1.651	0.262
Preoperative SII	-0.410	0.147	0.663	0.081–5.411	0.702
Preoperative PNI	0.988	4.590	2.686	1.088–6.632	0.032*
Mitotic index	1.245	3.404	3.473	0.925–13.037	0.065
Postoperative IM	0.904	5.266	2.469	1.141–5.343	0.022*

Note: mitotic index: number/50HPF. HPF: high-power field, refers to the field of view on a pathological section visible through the eyepiece under an optical microscope with a 10x ocular lens and 40x objective lens. NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index, platelet count × neutrophil count/lymphocyte count; PNI: prognostic nutritional index, serum albumin level (g/L) + 5 × total peripheral lymphocyte count (×10 ~ 9/L). IM: Imatinib; * represents $P < 0.05$, indicating a statistically significant difference

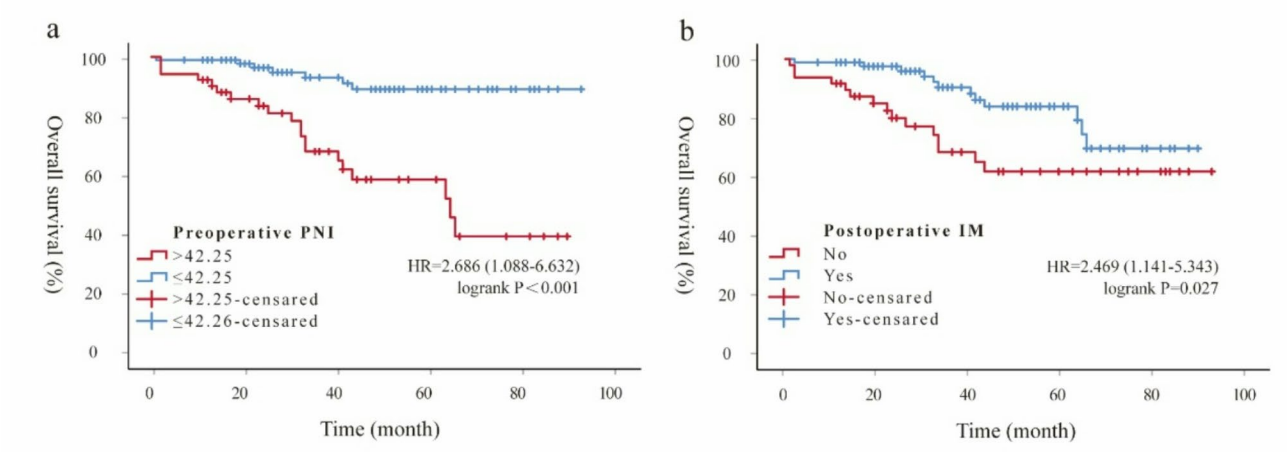

Fig. 3 Independent influencing factors on postoperative OS of high-risk GIST patients, **A**: Preoperative PNI; **B**: Mitotic index. The optimal critical points of the PNI were determined by the ROC curve of the subjects. Mitotic index was classified according to the modified National Institutes of Health (NIH) classification criteria

surgery and targeted therapies such as imatinib, represents a substantial advancement in this domain [22–24]. Despite these developments, the risk of recurrence or metastasis in high-risk GIST patients remains a critical issue, adversely affecting their quality of life and survival [25].

In managing high-risk GISTs, refining risk factors within the modified NIH risk stratification is essential, but it is equally important to incorporate additional factors, such as inflammatory markers, to guide treatment and prognostic assessments [26]. Recent studies have highlighted the role of the tumor microenvironment, particularly inflammatory reactions, in tumor cell migration and metastasis [18, 27, 28]. This is exemplified by research in early gastric cancer, where patients with adenocarcinoma had higher NLRs and PLRs than did those with adenoma, and those with undifferentiated adenocarcinoma had higher NLRs than did those with differentiated forms [29]. This growing body of evidence underscores the need for a more holistic approach in GIST patient management, integrating traditional risk assessments with factors such as inflammation to refine treatment strategies and improve outcomes [30, 31].

These findings underscore the pressing need for a more holistic approach to patient management that integrates these factors with traditional risk assessments. Such integration holds the promise of not only refining treatment strategies but also enhancing patient outcomes. To achieve seamless transition, it is paramount to connect the general trends in GIST incidence with the specific challenges faced by high-risk patients. Considering the evolving therapeutic landscape, refining risk factors is imperative. Exploring the importance of prognostic factors in predicting disease recurrence can provide better guidance for clinical decision-making and individualized monitoring schemes for patient treatment. Currently, in all GIST risk assessments, the modified National Institutes of Health risk prediction criteria have been widely applied in clinical practice, offering a standardized approach to predict the risk level of GIST patients after surgery [32]. Tumor location, tumor size, and mitotic index have been proven to be good predictors of the risk level of GIST patients [33]. However, exploring the prognostic influencing factors of high-risk GIST patients predicted by the modified NIH risk prediction criteria can further assist high-risk patients in obtaining a more

accurate risk assessment. In summary, as we navigate the complexities of GIST management, the integration of inflammatory factors with established risk assessments emerges as a pivotal avenue. By fostering a comprehensive understanding of the disease, we not only refined treatment strategies but also paved the way for improved patient outcomes.

Our study aimed to assess the factors influencing the overall survival risk during the initial postoperative progression survival period in 145 high-risk GIST patients. We evaluated basic clinical data, preoperative inflammatory markers levels (NLR, PLR, SII, and PNI), and postoperative pathological data. Our research results strongly suggest that inflammatory factors (NLR, PLR, SII) are not independent factors affecting patients' RFS and OS in high-risk GIST. Fortunately, our findings revealed that age, preoperative PNI, mitotic index, and postoperative IM were statistically significant factors for recurrence-free survival. Additionally, the preoperative PNI and postoperative IM were found to be independent risk factors for overall survival post-surgery. The correlation between age and GIST prognosis, where younger patients exhibit worse outcomes, is intriguing and may be attributed to delayed symptom recognition, genetic factors, and more aggressive tumor metabolism in younger individuals.

Our study shows that IM therapy is an independent prognostic factor for RFS and OS, and this result confirms the effectiveness of oral IM therapy after operation in reducing the recurrence risk and prolonging the survival time of high-risk GIST patients. Therefore, for high-risk GIST patients, adjuvant therapy with sufficient time and dose of imatinib after surgery is required, except for wild-type GIST [34–37].

It is estimated that 15–40% of cancer patients have malnutrition at diagnosis and 40–80% of cases will be malnourished during the treatment of the disease [38]. Malnutrition increases postoperative complications of patients and worsens RFS and OS of cancer patients [39, 40]. PNI is a simple and effective indictor for assessing nutrition status. Low PNI not only predicts poor survival in cancer patients, but also is associated with tumor stage [41, 42]. The role of the PNI in GIST prognosis, possibly through its influence on inflammatory reactions and immune suppression, warrants further investigation to elucidate its exact mechanism in tumor progression [43–45].

Limitations and future directions

Our study, while informative, has several limitations. Its retrospective nature may introduce biases in the data collection. Although univariate analysis revealed correlations between the preoperative NLR, PLR, and SII and postoperative outcomes, these correlations were not statistically significant according to multivariate analysis. Future studies with larger sample sizes are needed to explore these relationships further. Additionally, our study did not examine other clinicopathological factors, such as gene mutation status, which could be crucial in understanding GIST prognosis. A deeper exploration of the biological mechanisms linking inflammatory markers to GIST prognosis is also necessary.

Conclusion

In conclusion, our study identified key factors influencing the recurrence-free survival (RFS) of high-risk GIST patients. age, preoperative PNI, mitotic index, and postoperative IM are important predictors of postoperative outcomes. Notably, the PNI has emerged as a potential cost-effective biomarker for predicting treatment outcomes and patient prognosis as well as a possible focus of postoperative treatment in high-risk patients with GISTs, but unfortunately not the inflammatory markers that have proven to be important in other gastrointestinal malignancies. These findings have direct implications for the clinical management of high-risk GIST patients, suggesting the need for the integration of the PNI into routine clinical practice. Our study contributes to the evolving landscape of GIST management and underscores the need for further research to refine treatment strategies and improve patient outcomes in this challenging clinical context.

Abbreviations

GISTs	Gastrointestinal stromal tumors
RFS	Recurrence-free survival
OS	Overall survival
NLR	Neutrophil-to-lymphocyte ratio
PLR	Platelet-to-lymphocyte ratio
SII	Systemic immune-inflammatory index
PNI	Prognostic nutritional index
IM	Imatinib
PDGFRA	Platelet-derived growth factor receptor-α
NCCN	National Comprehensive Cancer Network
CSCO	Chinese Society of Clinical Oncology
NIH	National Institutes of Health

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-03710-8.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

The Ethics Committee of the General Hospital of Ningxia Medical University supported these studies.

Author contributions

Study design: Tao Li, Tao Wang, Lihua Qi, Yang Zhao. Data collection: Xiaolan Ma, Yang Zhao. Data analysis: Tao Wang, Lihua Qi, Yang Zhao. Manuscript draft: Tao Li, Tao Wang, Lihua Qi. Manuscript editing and review: all authors.

All authors approved the final published version. Tao Wang and Lihua Qi contributed equally to this work.

Funding
This project was supported by the Health Commission of Ningxia Hui Autonomous Region Science Foundation (Approval No. 2023-NWKYP-051) and the Ningxia Natural Science Foundation (Approval No. 2023AAC03625).

Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
This study complied with the Helsinki Declaration and was approved by the Medical Research Ethics Committee of Ningxia Medical University General Hospital (Ethics No. KYLL-2021-339). All study subjects were informed and signed an informed consent form.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Surgical Oncology II, General Hospital of Ningxia Medical University, Yinchuan, Ningxia 750004, China

Received: 24 January 2024 / Accepted: 18 February 2025
Published online: 26 February 2025

References

1. Blay JY, Kang YK, Nishida T, von Mehren M. Gastrointestinal stromal tumors. Nat Rev Dis Primers. 2021;7(1):22. https://doi.org/10.1038/s41572-021-00254-5.
2. Casali PG, Blay JY, Abecassis N, Bajpai J, Bauer S, Biagini R, et al. Gastrointestinal stromal tumors: ESMO-EURACAN-GENTURIS clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(1):20–33. https://doi.org/10.1016/j.annonc.2021.09.005.
3. Wong NA, Garcia-Petit C, Dangoor A, Andrew N. A literature review and database of how the primary KIT/PDGFRA variant of a Gastrointestinal stromal tumor predicts for sensitivity to Imatinib. Cancer Genet. 2022. https://doi.org/10.1016/j.cancergen.2022.09.002.
4. Joensuu H, Vehtari A, Riihimaki J, Nishida T, Steigen SE, Brabec P, et al. Risk of recurrence of Gastrointestinal stromal tumor after surgery: an analysis of pooled population-based cohorts. Lancet Oncol. 2012;13(3):265–74. https://doi.org/10.1016/S1470-2045(11)70299-6.
5. Joensuu H. Risk stratification of patients diagnosed with Gastrointestinal stromal tumor. Hum Pathol. 2008;39(10):1411–9. https://doi.org/10.1016/j.humpath.2008.06.025.
6. Yang W, Shou C, Chen Z, Hong Y, Yu H, Wang X, et al. Reassessment of the recurrence risk of primary Gastrointestinal stromal tumor after complete resection. Scand J Gastroenterol. 2023;58(6):684–92. https://doi.org/10.1080/00365521.2022.2158752.
7. Serrano C, George S. Gastrointestinal stromal tumor: challenges and opportunities for a new decade. Clin Cancer Res. 2020;26(19):5078–85. https://doi.org/10.1158/1078-0432.CCR-20-1706.
8. Serrano C. New treatments in advanced Gastrointestinal stromal tumor. Curr Opin Oncol. 2021;33(4):323–8. https://doi.org/10.1097/CCO.0000000000000745.
9. von Mehren M, Kane JM, Riedel RF, Sicklick JK, Pollack SM, Agulnik M, et al. NCCN guidelines® insights: Gastrointestinal stromal tumors, version 2.2022: featured updates to the NCCN guidelines. J Natl Compr Canc Netw. 2022;20(11):1204–14. https://doi.org/10.6004/jnccn.2022.0058.
10. Li J, Ye Y, Wang J, Zhang B, Qin S, Shi Y, et al. Chinese consensus guidelines for diagnosis and management of Gastrointestinal stromal tumor. Chin J Cancer Res. 2017;29(4):281–93. https://doi.org/10.21147/j.issn.1000-9604.2017.04.01.
11. Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. Lancet Oncol. 2014;15(11):e493–503. https://doi.org/10.1016/S1470-2045(14)70263-3.
12. Wu L, Saxena S, Singh RK. Neutrophils in the tumor microenvironment. Adv Exp Med Biol. 2020;1224:1–20. https://doi.org/10.1007/978-3-030-35723-8_1.
13. Yuan C, Pan Y, Ning Y. Predictive value of IL-6 combined with NLR in inflammation and Cancer. Cancer Invest. 2021;39(6–7):489–504. https://doi.org/10.1080/07357907.2020.1858852.
14. Chen W, Xin S, Xu B. Value research of NLR, PLR, and RDW in prognostic assessment of patients with colorectal Cancer. J Healthc Eng. 2022;2022:7971415. https://doi.org/10.1155/2022/7971415.
15. Chen H, Wu X, Wen Z, Zhu Y, Liao L, Yang J. The clinicopathological and prognostic value of NLR, PLR and MLR in Non-Muscular invasive bladder Cancer. Arch Esp Urol. 2022;75(5):467–71. https://doi.org/10.56434/j.arch.esp.urol.202275505.68.
16. Wang J, Li H, Xu R, Lu T, Zhao J, Zhang P, et al. The MLR, NLR, PLR and D-dimer are associated with clinical outcome in lung cancer patients treated with surgery. BMC Pulm Med. 2022;22(1):104. https://doi.org/10.1186/s12890-022-01901-7.
17. Cananzi FCM, Minerva EM, Sama L, Ruspi L, Sicoli F, Conti L, et al. Preoperative monocyte-to-lymphocyte ratio predicts recurrence in Gastrointestinal stromal tumors. J Surg Oncol. 2019;119(1):12–20. https://doi.org/10.1002/jso.25290.
18. Goh BK, Chok AY, Allen JC Jr., Quek R, Teo MC, Chow PK, et al. Blood neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios are independent prognostic factors for surgically resected Gastrointestinal stromal tumors. Surgery. 2016;159(4):1146–56. https://doi.org/10.1016/j.surg.2015.10.021.
19. Chang WL, Yang WC, Zeng XY, Li CG, Xiong Z, Wang T, et al. Elevated preoperative platelet-to-lymphocyte ratio predicts poor prognosis of patients with primary Gastrointestinal stromal tumor. BMC Gastroenterol. 2020;20(1):124. https://doi.org/10.1186/s12876-020-01275-2.
20. Krenn-Pilko S, Langsenlehner U, Thurner EM, Stojakovic T, Pichler M, Gerger A, et al. The elevated preoperative platelet-to-lymphocyte ratio predicts poor prognosis in breast cancer patients. Br J Cancer. 2014;110(10):2524–30. https://doi.org/10.1038/bjc.2014.163.
21. Kokkali S, Georgaki E, Mandrakis G, Valverde C, Theocharis S. Genomic profiling and clinical outcomes of targeted therapies in adult patients with soft tissue sarcomas. Cells. 2023;12(22). https://doi.org/10.3390/cells12222632.
22. Yu M, Wang DC, Wei J, Lei YH, Fu ZJ, Yang YH. Meta-Analysis on the efficacy and safety of laparoscopic surgery for large gastric Gastrointestinal stromal tumors. Am Surg. 2021;87(3):450–7. https://doi.org/10.1177/0003134820951482.
23. Wang L, Ni Z, Xu W, Mei Y, Li C, Zhu Z, et al. Clinical characteristics and outcomes of Gastrointestinal stromal tumor patients receiving surgery with or without TKI therapy: a retrospective real-world study. World J Surg Oncol. 2023;21(1):21. https://doi.org/10.1186/s12957-023-02897-y.
24. Golcic M, Jones RL, Huang P, Napolitano A. Evaluation of systemic treatment options for Gastrointestinal stromal tumors. Cancers (Basel). 2023;15(16):4081. https://doi.org/10.3390/cancers15164081.
25. Dematteo RP, Ballman KV, Antonescu CR, Maki RG, Pisters PW, Demetri GD, et al. Adjuvant Imatinib mesylate after resection of localized, primary Gastrointestinal stromal tumor: a randomized, double-blind, placebo-controlled trial. Lancet. 2009;373(9669):1097–104. https://doi.org/10.1016/S0140-6736(09)60500-6.
26. Lartigue L, Neuville A, Lagarde P, Brulard C, Rutkowski P, Dei Tos P, et al. Genomic index predicts clinical outcome of intermediate-risk Gastrointestinal stromal tumors, providing a new inclusion criterion for Imatinib adjuvant therapy. Eur J Cancer. 2015;51(1):75–83. https://doi.org/10.1016/j.ejca.2014.10.014.
27. Saputra HM, Hidayatullah F, Kloping YP, Renaldo J, Chung E, Hakim L. Prognostic value of neutrophil-to-lymphocyte ratio (NLR) in penile cancer: A systematic review and meta-analysis. Ann Med Surg (Lond). 2022;81:104335. https://doi.org/10.1016/j.amsu.2022.104335.
28. Li B, Chen H, Yang S, Chen F, Xu L, Li Y, et al. Advances in immunology and immunotherapy for mesenchymal Gastrointestinal cancers. Mol Cancer. 2023;22(1):71. https://doi.org/10.1186/s12943-023-01770-6.
29. Yasui S, Takata T, Kamitani Y, Mae Y, Kurumi H, Ikebuchi Y, et al. Neutrophil-to-lymphocyte ratio is a useful marker for predicting histological types of early gastric cancer. J Clin Med. 2021;10(4):791. https://doi.org/10.3390/jcm10040791.

30. Yilmaz A, Mirili C, Bilici M, Tekin SB. A novel predictor in patients with Gastrointestinal stromal tumors: systemic immune-inflammation index (SII). J BUON. 2019;24(5):2127–35.
31. Feng F, Tian Y, Liu S, Zheng G, Liu Z, Xu G, et al. Combination of PLR, MLR, MWR, and tumor size could significantly increase the prognostic value for Gastrointestinal stromal tumors. Med (Baltim). 2016;95(14):e3248. https://doi.org/10.1097/MD.0000000000003248.
32. Khoo CY, Chai X, Quek R, Teo MCC, Goh BKP. Systematic review of current prognostication systems for primary Gastrointestinal stromal tumors. Eur J Surg Oncol. 2018;44(4):388–94. https://doi.org/10.1016/j.ejso.2017.12.006.
33. Serrano C, Martin-Broto J, Asencio-Pascual JM, Lopez-Guerrero JA, Rubio-Casadevall J, Bague S, et al. 2023 GEIS guidelines for Gastrointestinal stromal tumors. Ther Adv Med Oncol. 2023;15(Print):1758–8340. https://doi.org/10.1177/17588359231192388.
34. McMillan DC. Systemic inflammation, nutritional status and survival in patients with cancer. Curr Opin Clin Nutr Metab Care. 2009;12(3):223–6. https://doi.org/10.1097/MCO.0b013e32832a7902.
35. Sharaiha RZ, Halazun KJ, Mirza F, Port JL, Lee PC, Neugut AI, et al. Elevated preoperative neutrophil: lymphocyte ratio as a predictor of postoperative disease recurrence in esophageal cancer. Ann Surg Oncol. 2011;18:3362–9. https://doi.org/10.1245/s10434-011-1754-8.
36. Ceze N, Thibault G, Goujon G, Viguier J, Watier H, Dorval E, et al. Pretreatment lymphopenia as a prognostic biomarker in colorectal cancer patients receiving chemotherapy. Cancer Chemother Pharmacol. 2011;68(5):1305–13. https://doi.org/10.1007/s00280-011-1610-3.
37. Uzunoglu H, Tosun Y, Akinci O, Baris B. Gastrointestinal stromal tumors of the stomach: A 10-year experience of a single-center. Niger J Clin Pract. 2021;24(12):1785–92. https://doi.org/10.4103/njcp.njcp_558_20.
38. Ravasco P. Nutrition in cancer patients. Clin Med. 2019;8(8):1211. https://doi.org/10.3390/jcm8081211.
39. Matsui R, Rifu K, Watanabe J, Inaki N, Fukunaga T. Impact of malnutrition as defined by the GLIM criteria on treatment outcomes in patients with cancer: A systematic review and meta-analysis. Clin Nutr. 2023;42(5):615–24. https://doi.org/10.1016/j.clnu.2023.02.019.
40. Zheng HL, Lu J, Li P, Xie JW, Wang JB, Lin JX, et al. Effects of preoperative malnutrition on Short- and Long-Term outcomes of patients with gastric cancer: can we do better?? Ann Surg Oncol. 2017;24(11):3376–85. https://doi.org/10.1245/s10434-017-5998-9.
41. Dai M, Sun Q. Prognostic and clinicopathological significance of prognostic nutritional index (PNI) in patients with oral cancer: a meta-analysis. Aging. 2023;15(5):1615–27. https://doi.org/10.18632/aging.204576.
42. Sun K, Chen S, Xu J, Li G, He Y. The prognostic significance of the prognostic nutritional index in cancer: a systematic review and meta-analysis. J Cancer Res Clin Oncol. 2014;140(9):1537–49. https://doi.org/10.1007/s00432-014-1714-3.
43. Yin Z, Gao J, Liu W, Huang C, Shuai X, Wang G, et al. Clinicopathological and prognostic analysis of primary Gastrointestinal stromal tumor presenting with Gastrointestinal bleeding: a 10-Year retrospective study. J Gastrointest Surg. 2017;21(5):792–800. https://doi.org/10.1007/s11605-017-3385-2.
44. Ding P, Wu J, Wu H, Sun C, Guo H, Lowe S, et al. Inflammation and nutritional status indicators as prognostic indicators for patients with locally advanced Gastrointestinal stromal tumors treated with neoadjuvant Imatinib. BMC Gastroenterol. 2023;23(1):23. https://doi.org/10.1186/s12876-023-02658-x.
45. Duymus ME, Ugur M, Dal MB, Aslan ER, Donmez Y, Ozgur T, et al. Prognostic value of prognostic nutritional index (PNI) for 5-year recurrence-free survival in surgically resected Gastrointestinal stromal tumors. Ann Ital Chir. 2023;94:19–26.

Publisher's note