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Platelet-to-Lymphocyte Ratio as a Predictor of Metastasis in Testicular Germ Cell Tumors: Clinicopathological Features from a 10-Year Retrospective Cohort in Tibet

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Abstract

Objective

To investigate the predictive value of the platelet-to-lymphocyte ratio (PLR) for metastasis in patients with testicular germ cell tumors (TGCTs) in the Xizang region, and to characterize regional clinicopathological features and prognostic factors.

Methods

A total of 78 patients with TGCTs admitted to the People's Hospital of Tibet Autonomous Region between January 2015 and December 2024 were retrospectively included. Clinicopathological data, preoperative inflammatory markers, and follow-up information were collected. Receiver operating characteristic (ROC) curve analysis, univariate analysis, and multivariate logistic regression were performed to identify risk factors for metastasis. Survival analysis was conducted using the Kaplan-Meier method.

Results

Pediatric patients all had non-seminoma GCTs (NSGCTs), whereas adult patients were predominantly diagnosed with seminomatous GCTs. The incidence of metastasis was 45.91%. PLR demonstrated the best predictive performance for metastasis (AUC = 0.766). Multivariate analysis identified elevated PLR as an independent strong predictor of metastasis (OR = 10.89, P < 0.001), while higher body mass index (BMI) was a protective factor. Clinical stage and histological subtype significantly influenced Overall survival (OS), whereas adjuvant therapy did not significantly improve survival outcomes.

Conclusion

PLR is a simple and cost-effective inflammatory marker that may be useful for risk stratification of metastasis in patients with TGCTs in the Xizang region, providing a reference for individualized clinical diagnosis and treatment.

Introduction

Testicular Germ Cell Tumors (TGCTs), although relatively rare in the general population, represent the most common solid malignancy among men aged 15–44 years. Over the past several decades, the global incidence of TGCTs has increased steadily and significantly [1, 2]. A recent systematic review by Tateo et al. (2025) reported that this rising trend is no longer limited to Western countries but has also become evident in regions with historically low incidence rates, including parts of Asia such as Japan,

Thailand, and China [2–4]. Overall, an increasing trend in the estimated incidence of testicular cancer has been observed in most countries worldwide [5].

Current evidence suggests that the etiology of TGCTs is multifactorial. Genetic predisposition is estimated to account for approximately 44% of disease heritability, while established early-life risk factors include cryptorchidism, infertility, and increased adult height [4, 6, 7]. However, although these etiological factors have been extensively investigated in Caucasian populations [4, 8, 9], data regarding the Chinese population remain limited. China provides a unique epidemiological context because of its large geographic area and substantial ethnic diversity. Tibet, in particular, differs markedly from the eastern coastal provinces in terms of demographic composition and socioeconomic conditions. To date, detailed epidemiological data describing the burden of TGCTs in this region remain scarce, resulting in a significant knowledge gap that may hinder the development and optimization of regional healthcare strategies.

In addition to cancer incidence, the early identification of patients at high risk of metastasis remains a major challenge in urologic oncology. Although international guidelines provide criteria for risk stratification, clinical outcomes and survival rates may vary considerably according to regional healthcare accessibility and population characteristics. Therefore, validating predictive factors for metastasis, beyond established indicators such as cryptorchidism, is important for supporting decisions regarding adjuvant therapy and active surveillance in local clinical practice.

To address these gaps, we conducted a single-center retrospective study at a major tertiary hospital in Tibet, China. The objectives of this study were to: (1) describe the changing epidemiology of testicular cancer in this region within the context of global trends; (2) identify independent risk factors associated with tumor metastasis; and (3) evaluate long-term survival outcomes in this cohort. This study aims to provide updated regional evidence to complement national cancer registry data and improve prognostic assessment for patients with TGCTs in Tibet.

Materials and methods

Study Design and Patient Population

This retrospective observational study was conducted in the Department of Urology at the People's Hospital of Tibet Autonomous Region. We reviewed the medical records of all patients diagnosed with testicular tumors between January 2015 and December 2024. Patients were eligible for inclusion if they met the following criteria: (1) underwent radical orchiectomy at our institution; (2) had histopathological confirmed testicular malignancy; and (3) had complete clinical and follow-up data available. Both pediatric (≤ 18 years) and adult patients were included. Patients with incomplete medical records or secondary testicular involvement from extragonadal primary tumors were excluded. Based on these criteria, 71 patients were enrolled in the final analysis, comprising 10 pediatric patients and 61 adult patients.

Data Collection

Clinical and pathological data were retrospectively extracted from the electronic medical record system. The following variables were collected:

Demographic and clinical characteristics: Age at diagnosis, body mass index (BMI), and history of cryptorchidism.

Laboratory parameters: Preoperative serum tumor markers, including alpha-fetoprotein (AFP), β-human chorionic gonadotropin (β-hCG), and lactate dehydrogenase (LDH), were recorded. Complete blood count parameters, including absolute neutrophil count, lymphocyte count, and platelet count, were also collected to calculate systemic inflammatory indices, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII = platelet × neutrophil/lymphocyte).

Imaging findings: Preoperative imaging data obtained from scrotal ultrasonography, computed tomography (CT), and/or magnetic resonance imaging (MRI) were reviewed for staging purposes.

Pathological findings: Tumor size, laterality, histological subtype, and pathological T stage were recorded. Tumors were classified as seminomatous GCTs (SGCTs) or non-seminoma GCTs (NSGCTs) according to the World Health Organization (WHO) classification [10].

Staging and risk classification: Clinical staging was performed according to the 2016 Tumor, Node, Metastasis (TNM) classification of the International Union Against Cancer (UICC) [11]. For patients with metastatic disease, risk stratification was conducted using the International Germ Cell Cancer Collaborative Group (IGCCCG) classification system [12].

Follow-up data: Survival status, disease recurrence, and metastasis were assessed through outpatient follow-up visits and telephone interviews (Supplementary Material 1).

Statistical Analysis

Statistical analyses were performed using R software (version 4.0; R Foundation for Statistical Computing, Vienna, Austria). The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed variables were expressed as mean ± standard deviation (SD) and compared using Student's t-test or Welch's t-test when variances were unequal. Non-normally distributed variables were expressed as median and interquartile range (IQR) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages and compared using the chi-square ($\chi 2$) test or Fisher's exact test, as appropriate according to the expected cell counts. The discriminative abilities of inflammatory markers, including NLR, PLR, and SII, for predicting metastatic disease (clinical stage ≥ II) were evaluated using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) was calculated for each marker. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of metastatic disease. Variables

with P < 0.2 in the univariate analysis were included in the multivariate model. The results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). Overall survival (OS) was defined as the time from orchiectomy to death from any cause or the last follow-up visit. Survival curves were generated using the Kaplan-Meier method, and differences between groups were compared using the log-rank test. All statistical tests were two-sided, and P < 0.05 was considered statistically significant.

Ethical Considerations

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Tibet Autonomous Region People's Hospital (Approval No.:ME-TBHP-25-KJ-113). Owing to the retrospective design of the study, the requirement for written informed consent was waived by the ethics committee.

Results

Histological distribution

A total of 78 patients were identified in the study cohort. Pathological evaluation included 79 tumor specimens, as one case of bilateral synchronous testicular cancer was observed. This patient presented with histologically distinct neoplasms: a seminoma in the right testis and a mixed GCT in the left testis.

The study population was stratified by age into pediatric (n = 10) and adult (n = 69) groups. Table 1 summarizes the histological characteristics of the cohort. There was no statistically significant difference in the distribution of tumor types between children and adults (P = 0.58).

Table 1
Histological Classification of the Study Cohort

Pathological Classification	Total (n = 79)	Pediatric (n = 10)	Adult (n = 69)	*p*-value
GCT	72	10	62	0.58
SGCT	44	0	44 b	–
NSGCT	28	10 [a]	18	–
Mixed Germ Cell Tumor	15	0	15 b	–
Yolk Sac Tumor	7	6	1	–
Teratoma	5	4	1	–
Embryonal Carcinoma	1	0	1	–
NGCT	7	0	7	–
Primary Lymphoma	4	0	4	–
Mesenchymal Tumor [b]	3	0	3[c]	–

GCT, Germ Cell Tumors; NGCT, Non-Germ Cell Tumors; SGCT, Seminoma germ cell tumor; NSGCT, non-seminoma GCT. [a] Prepubertal-type Yolk Sac Tumor (n = 5), Postpubertal-type Yolk Sac Tumor (n = 1), Prepubertal-type Teratoma (n = 4); [b] One patient presented with bilateral tumors: a right-sided seminoma and a left-sided mixed germ cell tumor; [c] Mesenchymal tumors in the adult cohort included Leiomyosarcoma (n = 1), Rhabdomyosarcoma (n = 1), and Solitary Fibrous Tumor (n = 1).

In the pediatric group, all cases were NSGCT. Specifically, yolk sac tumor was the most common subtype, accounting for 60% of pediatric cases, followed by teratoma. In the adult group, GCT predominated (62/69, 89.86%), compared with non-germ cell tumor (NGCTs) (10.14%). The bilateral case was included in the GCT group, contributing two distinct tumor specimens to the analysis. The most frequent histological subtype among adults was seminoma, representing 70.97% of GCTs, while NSGCT accounted for 29.03%.

Clinical and laboratory characteristics of pediatric patients

Table 2 summarizes the demographic and clinicopathological characteristics of the pediatric subgroup (n = 10). The median age at diagnosis was 1 year (range, 0.58-14 years). The median duration of symptoms prior to clinical presentation was 3 months.

Table 2
Clinical and laboratory characteristics of pediatric patients with testicular germ cell tumors

Variable	Median (IQR)	Range (Min – Max)
Age (years),	1(1 ~ 2.75)	0.58 ~ 14
BMI(kg/m²)	17.81(16.48 ~ 18.45)	15.15 ~ 22.86
Laterality, n (%)		
Left Testis	6 (60.0%)	–
Right Testis	4(40.0%)	–
Cryptorchidism, n (%)		–
Yes	1 (10.0%)	–
No	9 (90.0%)	–
Symptom Duration (months)	3(1 ~ 10.75)	0.2 ~ 12
Max Diameter (cm)	4(3.2 ~ 5.5)	2.5 ~ 8
COG Stage, n (%)		
Stage I	10(100.0%)	–
Stage ≥ II	0 (0.0%)	–
Serum Tumor Markers		
AFP (ng/mL)	703(6.17 ~ 1984.43)	0.87 ~ 43942.18
β-HCG (mIU/mL)	0.85(0.85 ~ 1.11)	0.85 ~ 1.2
LDH(U/L)	333(293.50 ~ 380.50)	147 ~ 432
Hematology & Inflammation		
Hemoglobin (g/L)	111.5(96.5 ~ 134)	79 ~ 155
WBC(×10^9/L)	7.75(6.82 ~ 8.62)	2.5 ~ 13.7
Neutrophils (×10^9/L)	2.665(2.41 ~ 3.14)	0.39 ~ 9.09
Lymphocytes(×10^9/L)	4.03(3.2 ~ 4.62)	1.8 ~ 7.58
Platelet(×10^9/L)	466(457.25 ~ 494)	131 ~ 661
CRP (mg/L)	0.65(0.21 ~ 1.24)	0.02 ~ 6.44
Overall Survival (months)	20.5(13.75 ~ 45.5)	0 ~ 58

BMI, body mass index; COG, Children's Oncology Group; AFP, alpha-fetoprotein; β-hCG, beta-human chorionic gonadotropin; CRP, C-reactive protein; LDH, lactate dehydrogenase; WBC, white blood cell; IQR, interquartile range.

Tumor characteristics and markers

Radiologic and pathological assessment revealed a median maximum tumor diameter of 4 cm (range, 2.5-8 cm). Serum tumor marker analysis indicated wide variability, consistent with the heterogeneous nature of GCTs. The median AFP level was 703 ng/mL (IQR, 6.17-1984.43), while human chorionic gonadotropin (β-hCG) levels were 0.85 mIU/mL (IQR, 0.85–1.11). LDH levels had a median of 333 U/L (IQR, 293.50-380.50).

Survival outcomes

The median follow-up duration for the pediatric cohort was 20.5 months (IQR, 13.75–45.50). Three patients were lost to follow-up.

Histological characteristics of the adult cohort

The adult cohort included a diverse range of pathological subtypes. NGCTs were identified in seven cases. The most frequent NGCT was primary testicular lymphoma (n = 4), while rare mesenchymal neoplasms included leiomyosarcoma (n = 1), rhabdomyosarcoma (n = 1), and solitary fibrous tumor (n = 1).

Clinically, the NGCT subgroup exhibited a distinct profile compared with GCTs. The median age of patients with NGCT was 61 years (range, 30–76), which was notably higher than that of the GCT cohort (61 vs. 39 years). As expected, serum tumor markers (AFP and β-hCG) were negative in all seven cases, although LDH levels were elevated in patients with lymphoma (median 280 U/L). Due to their distinct pathogenesis and clinical behavior, these seven NGCT cases were excluded from the subsequent comparative analysis of GCTs.

Comparative analysis of adult GCTs

A total of 61 adult patients with confirmed testicular GCT were included in the final comparative analysis. The cohort was stratified based on histological classification into (SGCT, n = 43) and (NSGCT, n = 18).

Consistent with clinical staging guidelines, the patient with bilateral testicular cancer was classified into the NSGCT group due to the presence of a non-seminomatous component, which is the primary determinant of prognosis and therapeutic strategy.

Clinical and laboratory comparisons

(Table 3 and Table 4 summarize the differences between the two groups.) Among adult patients, several baseline clinicopathological variables differed significantly between the SGCT and NSGCT groups. Patients with NSGCT were younger at diagnosis compared with those with SGCT ($P < 0.05$). With respect to tumor markers, NSGCT was associated with higher serum AFP levels but lower LDH levels compared

with SGCT ($P < 0.05$ for both). As expected, patients with NSGCT more frequently fell into intermediate/poor IGCCCG risk categories and had inferior OS ($P < 0.01$).

Table 3
Baseline demographics and clinical characteristics of adult patients with testicular germ cell tumors

Variable	Total (n = 61)	SGCT (n = 43)	NSGCT (n = 18)	p-value
Demographics				
Age (years)	38.26 ± 9.35	40.33 ± 9.14	33.33 ± 8.11	0.0067
BMI (kg/m²)	21.66 (19.93–25.78)	21.88 (19.88–25.71)	21.34 (20.07–26.83)	0.6446
Laterality a				0.3391
Left testis	20 (32.8%)	12 (27.9%)	8 (44.4%)	
Right testis	41 (67.2%)	31 (72.1%)	10 (55.6%)	
Cryptorchidism	11 (18.0%)	9 (20.9%)	2 (11.1%)	0.4811
Socioeconomic status				0.7441
High	9 (14.8%)	7 (16.3%)	2 (11.1%)	
Medium	7 (11.5%)	4 (9.3%)	3 (16.7%)	
Low	45 (73.8%)	32 (74.4%)	13 (72.2%)	
Clinical Presentation				
Symptom duration (months)	4.00 (1.00–12.00)	4.00 (1.00–12.00)	5.50 (1.70–12.00)	0.5202
Maximum diameter (cm) b	8.88 ± 3.59	9.22 ± 3.77	8.11 ± 3.12	0.3057
Tumor location				0.1049
Scrotal	50 (82.0%)	34 (79.1%)	16 (88.9%)	
Inguinal	1 (1.6%)	0 (0.0%)	1 (5.6%)	
Abdominal	10 (16.4%)	9 (20.9%)	1 (5.6%)	
UICC stage				0.0815
Stage I	28 (45.9%)	20 (46.5%)	8 (44.4%)	
Stage II	16 (26.2%)	14 (32.6%)	2 (11.1%)	

SGCT, Seminoma germ cell tumor; NSGCT, non-seminoma germ cell tumor. BMI, body mass index; IGCCCG, International Germ Cell Cancer Collaborative Group; UICC, Union for International Cancer Control. Data are presented as mean ± SD, median (IQR), or n (%) as appropriate. [a] One patient presented with bilateral tumors (right-sided seminoma and left-sided mixed germ cell tumor). [b] Data available for 53 patients (SGCT = 37, NSGCT = 16). [c] IGCCCG risk classification applies only to patients with metastatic disease (Stage II–III, n = 33).

Variable	Total (n = 61)	SGCT (n = 43)	NSGCT (n = 18)	p-value
Stage III	17 (27.9%)	9 (20.9%)	8 (44.4%)	
IGCCCG risk classification c				< 0.001
Good prognosis	15 (50.0%)	15 (75.0%)	0 (0.0%)	
Intermediate prognosis	11 (36.7%)	5 (25.0%)	6 (60.0%)	
Poor prognosis	4 (13.3%)	0 (0.0%)	4 (40.0%)	

SGCT, Seminoma germ cell tumor; NSGCT, non-seminoma germ cell tumor. BMI, body mass index; IGCCCG, International Germ Cell Cancer Collaborative Group; UICC, Union for International Cancer Control. Data are presented as mean ± SD, median (IQR), or n (%) as appropriate. [a] One patient presented with bilateral tumors (right-sided seminoma and left-sided mixed germ cell tumor). [b] Data available for 53 patients (SGCT = 37, NSGCT = 16). [c] IGCCCG risk classification applies only to patients with metastatic disease (Stage II–III, n = 33).

Table 4
Laboratory Findings, Treatment, and Outcomes of Adult Patients with Testicular Germ Cell Tumors

Variable	Total (n = 61)	SGCT (n = 43)	NSGCT (n = 18)	p-value
Hematology & Inflammatory Markers				
Hemoglobin (g/L)	161.74 ± 26.70	160.91 ± 27.70	163.72 ± 24.80	0.7106
White blood cell (×10⁹/L)	5.50 (4.30–7.30)	5.10 (4.10–7.00)	6.05 (5.05–8.23)	0.0321
Neutrophils (×10⁹/L)	3.46 (2.64–4.69)	3.04 (2.46–4.62)	4.00 (2.87–6.03)	0.0968
Lymphocytes (×10⁹/L)	1.40 ± 0.56	1.30 ± 0.55	1.64 ± 0.53	0.0307
Platelet (×10⁹/L)	249.08 ± 73.67	248.98 ± 78.53	249.33 ± 62.60	0.9864
CRP (mg/L) [a]	9.50 (2.80–38.36)	10.27 (3.06–37.01)	4.21 (1.87–35.74)	0.4061
Serum Tumor Markers				
AFP (ng/mL) [b]	2.16 (1.34–17.57)	1.73 (1.17–2.31)	96.33 (30.30–1896.21)	< 0.001
β-hCG (mIU/mL) [c]	11.10 (2.20–83.93)	8.81 (2.83–48.22)	107.00 (1.39–574.81)	0.2822
LDH (U/L) [d]	565.50 (256.75–806.50)	624.00 (388.00–1087.00)	223.00 (213.00–372.00)	0.0087
Treatment				
Pathological diagnosis method				0.5484
Orchiectomy	58 (95.1%)	40 (93.0%)	18 (100.0%)	
Biopsy	3 (4.9%)	3 (7.0%)	0 (0.0%)	
Adjuvant therapy				
Radiotherapy	5 (8.2%)	3 (7.0%)	2 (11.1%)	0.6266
Chemotherapy	28 (45.9%)	22 (51.2%)	6 (33.3%)	0.2025
RPLND	1 (1.6%)	0 (0.0%)	1 (5.6%)	0.2951

SGCT, Seminoma germ cell tumor; NSGCT, non-seminoma germ cell tumor. AFP, alpha-fetoprotein; β-hCG, beta-human chorionic gonadotropin; CRP, C-reactive protein; LDH, lactate dehydrogenase; RPLND, retroperitoneal lymph node dissection. Data are presented as mean ± SD, median (IQR), or n (%) as appropriate. [a] Data available for 45 patients (SGCT = 30, NSGCT = 15). [b] Data available for 48 patients (SGCT = 40, NSGCT = 18). [c] Data available for 55 patients (SGCT = 39, NSGCT = 16). [d] Data available for 30 patients (SGCT = 21, NSGCT = 9).

Variable	Total (n = 61)	SGCT (n = 43)	NSGCT (n = 18)	p-value
Outcomes				
Follow-up duration (months)	37.00 (15.00–58.00)	42.00 (23.00–68.50)	20.50 (7.25–45.50)	0.0309
Lost to follow-up	11 (18.0%)	6 (14.0%)	5 (27.8%)	0.2002
Death	8 (13.1%)	4 (9.3%)	4 (22.2%)	0.2196

SGCT, Seminoma germ cell tumor; NSGCT, non-seminoma germ cell tumor. AFP, alpha-fetoprotein; β-hCG, beta-human chorionic gonadotropin; CRP, C-reactive protein; LDH, lactate dehydrogenase; RPLND, retroperitoneal lymph node dissection. Data are presented as mean ± SD, median (IQR), or n (%) as appropriate. [a] Data available for 45 patients (SGCT = 30, NSGCT = 15). [b] Data available for 48 patients (SGCT = 40, NSGCT = 18). [c] Data available for 55 patients (SGCT = 39, NSGCT = 16). [d] Data available for 30 patients (SGCT = 21, NSGCT = 9).

Analysis of risk factors for metastatic disease

In our adult CGT study cohort, the proportion of patients presenting with metastatic disease (clinical stage II/III) was 54.10% (33/61). To identify potential predictors of metastatic disease, univariate logistic regression was performed (Table 5). Among continuous variables, higher BMI was significantly associated with reduced odds of metastasis (OR = 0.81, 95% CI: 0.69–0.95, P = 0.009). Hemoglobin level also demonstrated a modest protective association (OR = 0.98, 95% CI: 0.96-1.00, P = 0.042). Age (OR = 1.04, 95% CI: 0.98–1.10, P = 0.162) and maximum tumor diameter (OR = 1.14, 95% CI: 0.97–1.35, P = 0.108) showed trends toward significance but did not reach the conventional threshold of $P < 0.05$.

Table 5
Univariate and multivariate logistic regression analysis for predicting metastasis (clinical stage ≥ II)

variable	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Age (years)	1.04 (0.98–1.1)	0.162	1.06(0.99–1.15)	0.115
BMI (kg/m²)	0.81 (0.69–0.95)	0.009	0.76(0.61–0.92)	0.008
Symptom duration (months)	1.01 (0.98–1.03)	0.607	-	-
Max diameter (cm)	1.14 (0.97–1.35)	0.108	-	-
Histology (NSGCT vs SGCT)	1.09 (0.36–3.29)	0.883	-	-
PLR High (> 187.01)	0.12 (0.04–0.41)	< 0.001	10.89(2.82–54.78)	< 0.001
NLR High (> 2.84)	0.23 (0.08–0.68)	0.008	-	-
SII High (> 872.07)	0.18 (0.05–0.62)	0.007	-	-
Hemoglobin (g/L)	0.98 (0.96-1.0)	0.042	-	-

OR, odds ratio; CI, confidence interval. NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

Among inflammatory indices, elevated PLR (> 187.01), NLR (> 2.84), and SII (> 872.07) were all significantly associated with metastatic presentation in univariate analysis (all P < 0.01). Histological subtype (NSGCT vs. SGCT) was not a significant predictor of metastasis (OR = 1.09, 95% CI: 0.36–3.29, P = 0.883).

Variables with P < 0.2 in univariate analysis or established clinical relevance were considered for multivariate modeling. Given the collinearity among inflammatory indices (PLR, NLR, SII) and the constraint imposed by the events-per-variable rule (33 metastatic cases, approximately three predictors maximum), PLR was selected as the representative inflammatory marker based on its superior discriminative ability (AUC = 0.766) (Table 6, Fig. 1).

Table 6
Receiver operating characteristic curve analysis for predicting metastasis (clinical stage ≥ II)

Index	AUC (95% CI)	Cutoff	Sensitivity	Specificity	Youden	*p*-value
PLR	0.766 (0.646–0.886)	187.01	63.6	82.1	0.458	< 0.001
NLR	0.703 (0.572–0.835)	2.84	63.6	71.4	0.351	0.002
SII	0.710(0.579–0.841)	872.07	48.5	85.7	0.342	0.002

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index. AUC, area under curve.

The final multivariate logistic regression model included PLR group, age, and BMI. After adjustment, elevated PLR (> 187.01) remained the strongest independent predictor of metastasis, with patients in the high PLR group demonstrating approximately 11-fold increased odds of metastatic disease compared with those in the low PLR group (OR = 10.89, 95% CI: 2.82–54.78, P = 0.001). Higher BMI retained its protective association (OR = 0.76, 95% CI: 0.61–0.92, P = 0.008), while age was not statistically significant after adjustment (OR = 1.06, 95% CI: 0.99–1.15, P = 0.115).

OS in GCT Adult Patients

The median follow-up duration was 30 months (range, 0-122 months). Kaplan-Meier analysis demonstrated that both clinical stage (P = 0.038) and histological subtype (P = 0.028) were significantly associated with OS. The 5-year OS rates were 94.1% versus 64.5% for stage I versus stage II-III disease, and 83.7% versus 60.5% for SGCT versus NSGCT, respectively (Fig. 2 and Fig. 3). Treatment modality (surgery alone versus adjuvant therapy) did not significantly affect OS (79.1% vs. 77.0%, P = 0.668; Fig. 4).

Discussion

In the present study, all pediatric patients (n = 10) were diagnosed with NSGCTs, with yolk sac tumor representing the predominant histological subtype (60%), followed by teratoma (40%). This distribution is consistent with the established understanding that yolk sac tumor is the most common testicular malignancy in the prepubertal population, whereas seminoma is exceedingly rare in this age group [13, 14]. Notably, our findings differ from those of several published studies in which teratoma was reported as the predominant histological subtype among pediatric testicular neoplasms [15–17]. Several factors may explain this discrepancy, including differences in patient selection criteria, referral patterns to tertiary care centers, geographic and ethnic variations in disease epidemiology, and the relatively small sample size of our single-center cohort. In addition, inter-institutional differences in histopathological classification standards may have contributed to the observed variations. Despite these inconsistencies, yolk sac tumor and teratoma remain the two most frequently reported histological subtypes of pediatric TGCTs in the literature.

From a clinical perspective, all pediatric patients in our cohort presented with a painless scrotal mass, which represents the cardinal manifestation of pediatric testicular neoplasms. This finding is consistent with previous studies reporting painless testicular enlargement as the most common initial presentation of pediatric testicular tumors [13, 18]. The insidious and asymptomatic nature of this presentation may contribute to delayed diagnosis, highlighting the importance of increased clinical vigilance and parental awareness of testicular abnormalities. Early recognition of this characteristic manifestation is essential for timely diagnosis, prompt therapeutic intervention, and improved long-term oncological outcomes.

Among the adult patients in our cohort, GCTs represented the predominant histological category, accounting for 89.6% (62/69) of cases. This finding is consistent with previous reports indicating that GCTs comprise approximately 90–95% of all primary testicular malignancies [19, 20]. Bilateral testicular involvement was identified in only 1.5% of cases, which is comparable to the 1–2% incidence reported in earlier studies of testicular tumors [21]. The low frequency of bilateral disease in our cohort further supports the observation that synchronous or metachronous bilateral testicular tumors remain uncommon, although clinically significant, entities that require individualized surveillance strategies.

Regarding the distribution of GCT subtypes, SGCTs were the predominant histological subtype, accounting for 70.5% (43/61) of adult cases, whereas NSGCTs comprised 29.5% (18/61). This distribution differs from that reported in several international studies, in which the proportion of NSGCTs ranged from 33.6% to 48%. Several factors may explain this discrepancy, including geographic and ethnic differences in tumor biology, region-specific environmental exposures, and variations in histopathological classification criteria among institutions. Furthermore, the unique high-altitude environment and distinct genetic background of the Tibetan population may contribute to the subtype distribution observed in this study, although this hypothesis requires further investigation. Referral patterns at our tertiary care center may also have influenced the observed distribution, as patients with seminoma may be more likely to be referred because of specialized treatment protocols or enrollment in clinical trials. Therefore, large-scale multicenter studies involving diverse geographic populations are needed to determine whether these findings reflect genuine regional differences in testicular tumor epidemiology or selection bias associated with single-center studies.

Given the distinct biological behavior, prognostic implications, and therapeutic strategies associated with SGCT and NSGCT, we performed a comparative analysis of clinicopathological characteristics, serum tumor markers, and systemic inflammatory parameters between these two histological subtypes. This subgroup analysis aimed to identify distinguishing features that may improve clinical decision-making and risk stratification in adult testicular GCTs.

Our analysis demonstrated that patients with NSGCT were significantly younger than those with SGCT ($P < 0.05$), which is consistent with established epidemiological evidence showing distinct age-incidence patterns between these tumor subtypes [1, 15, 20]. The biological basis for this age difference may be related to divergent differentiation pathways of germ cell neoplasms. Specifically, NSGCTs arise from pluripotent germ cells capable of differentiating into embryonal components (embryonal carcinoma and

teratoma) or extraembryonic components (yolk sac tumor and choriocarcinoma), processes that typically occur earlier in life. In contrast, seminomas originate from germ cells that retain a more primitive and undifferentiated phenotype and generally present during the fourth decade of life. This age-related difference has important clinical implications. In younger patients presenting with testicular masses, clinicians should maintain a higher level of suspicion for NSGCT and perform comprehensive evaluation, including assessment of serum tumor markers such as AFP and β-hCG, to guide subsequent management decisions.

As expected, serum AFP levels were significantly elevated in patients with NSGCT compared with those with SGCT. By definition, pure seminomas do not produce AFP; however, seminomas may exhibit mildly elevated β-hCG levels at diagnosis in up to 30% of cases. Therefore, a markedly elevated AFP level in a patient with apparent seminoma should prompt careful histopathological review for occult non-seminomatous components [22]. The significant difference in AFP observed in our cohort confirms the diagnostic utility of this marker in distinguishing NSGCT from SGCT and underscores the importance of routine serum tumor marker assessment in all adult patients with testicular tumors.

β-hCG can be elevated in both seminoma (usually mildly) and NSGCT (often markedly, particularly in choriocarcinoma) [23]. Our analysis revealed no significant difference in β-hCG levels between the SGCT and NSGCT groups. This overlapping pattern of β-hCG expression across tumor types likely explains the lack of a significant difference in our cohort and highlights that β-hCG alone cannot reliably distinguish SGCT from NSGCT.

Notably, our analysis demonstrated significantly lower LDH levels in NSGCT compared with SGCT patients. This finding appears counterintuitive given the generally more aggressive biological behavior attributed to NSGCT [24, 25]. Differences in stage distribution and delayed presentation may partly explain this result. These findings warrant further investigation in larger cohorts, as they may reflect unique biological characteristics of testicular tumors in our population or specific referral patterns to our institution.

The proportion of patients presenting with stage I disease in our cohort (45.90%, 28/61) was notably lower than that reported in Western series [26–29] but comparable to that observed in other developing countries [30–32]. This disparity is likely attributable to the socioeconomic profile of our population, with 85.25% (52/61) classified as low or middle socioeconomic status (SES). Limited health literacy, cultural barriers to seeking care for genital symptoms, and reduced access to healthcare services likely contribute collectively to delayed presentation. These findings highlight the need for public health initiatives promoting testicular self-examination and improving access to urological care in underserved regions.

Among the systemic inflammatory markers evaluated, PLR demonstrated the highest diagnostic accuracy for predicting metastatic disease (AUC = 0.766), outperforming both NLR and SII. Multivariate analysis identified elevated PLR as the sole independent predictor of metastasis (OR = 8.92; P = 0.002), corresponding to nearly nine-fold higher odds of advanced-stage disease. Biologically, elevated PLR

reflects both enhanced pro-metastatic activity through platelet-mediated tumor cell protection and impaired antitumor immunity due to relative lymphocytopenia. Notably, platelet counts did not differ significantly between SGCT and NSGCT, whereas lymphocyte counts were significantly higher in NSGCT patients, suggesting that lymphocyte variation is the primary driver of PLR's prognostic value in testicular GCT.

Lower BMI was associated with metastasis in univariate analysis but lost statistical significance in multivariate modeling, suggesting that the inflammatory state captured by PLR may underlie both cancer-associated cachexia and metastatic progression. Similarly, histological subtype was not an independent predictor of metastasis (P = 0.419), implying that systemic inflammation may contribute to tumor dissemination regardless of histological origin.

These findings are consistent with emerging evidence supporting the prognostic value of PLR in urological malignancies [33–37]. The strong effect size observed (OR = 8.92) suggests that PLR may serve as a cost-effective risk stratification tool, particularly in resource-limited settings where it can be readily derived from routine blood counts.

Most patients with testicular cancer are cured, with a 5-year relative survival rate of approximately 95% [38]However, GCT survivors still experience an excess mortality of 36%-40% compared with the general population [39, 40]Survival analysis demonstrated that both histological subtype and clinical stage significantly influenced OS [41]. Patients with NSGCT exhibited inferior OS compared with those with SGCT (P = 0.028). Similarly, patients presenting with stage II-III disease had significantly worse OS than those with stage I disease (P = 0.038), reinforcing the importance of early detection. Notably, receipt of additional adjuvant therapy did not significantly impact OS (P = 0.67), a finding consistent with the broader TGCT literature [42]. Platinum-based chemotherapy or radiotherapy may increase the risk of secondary malignancies and other adverse effects, thereby contributing to excess non-testicular cancer mortality [43–45]. Collectively, these results support current risk-adapted management strategies [21, 42], which aim to minimize treatment-related toxicity without compromising survival outcomes.

Several limitations warrant consideration. The retrospective, single-center design may introduce selection bias, thereby limiting the generalizability of the findings. PLR values may be influenced by factors unrelated to malignancy, including infections and medications, which were not systematically controlled in this study. In addition, there is no universally accepted PLR cutoff value for TGCTs, and our relatively modest sample size necessitates validation in larger, independent cohorts. Future prospective, multi-center studies are therefore required to validate these findings and to establish optimal cutoff values for clinical application.

Conclusion

In conclusion, our study identifies the PLR as a readily accessible and cost-effective biomarker that independently predicts metastatic disease in TGCT patients. The strong predictive value of PLR, driven predominantly by the lymphocyte component, underscores the importance of host immune status in

determining metastatic potential and supports the incorporation of inflammatory markers into clinical risk stratification frameworks.

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Author Contribution

Y. H. and W.J. designed the research ,Y.H. andD.Z.andT.X.collected clinical data. S.J.andW.J.andZ.B.performed statistical analysis,P.P.andG.Y. disposal datas Z.L.andL.F. collect literature All authors read approved the final manuscript.

Data availability

The data that support the findings of this study are available from the corresponding author on reasonable request.

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Figures

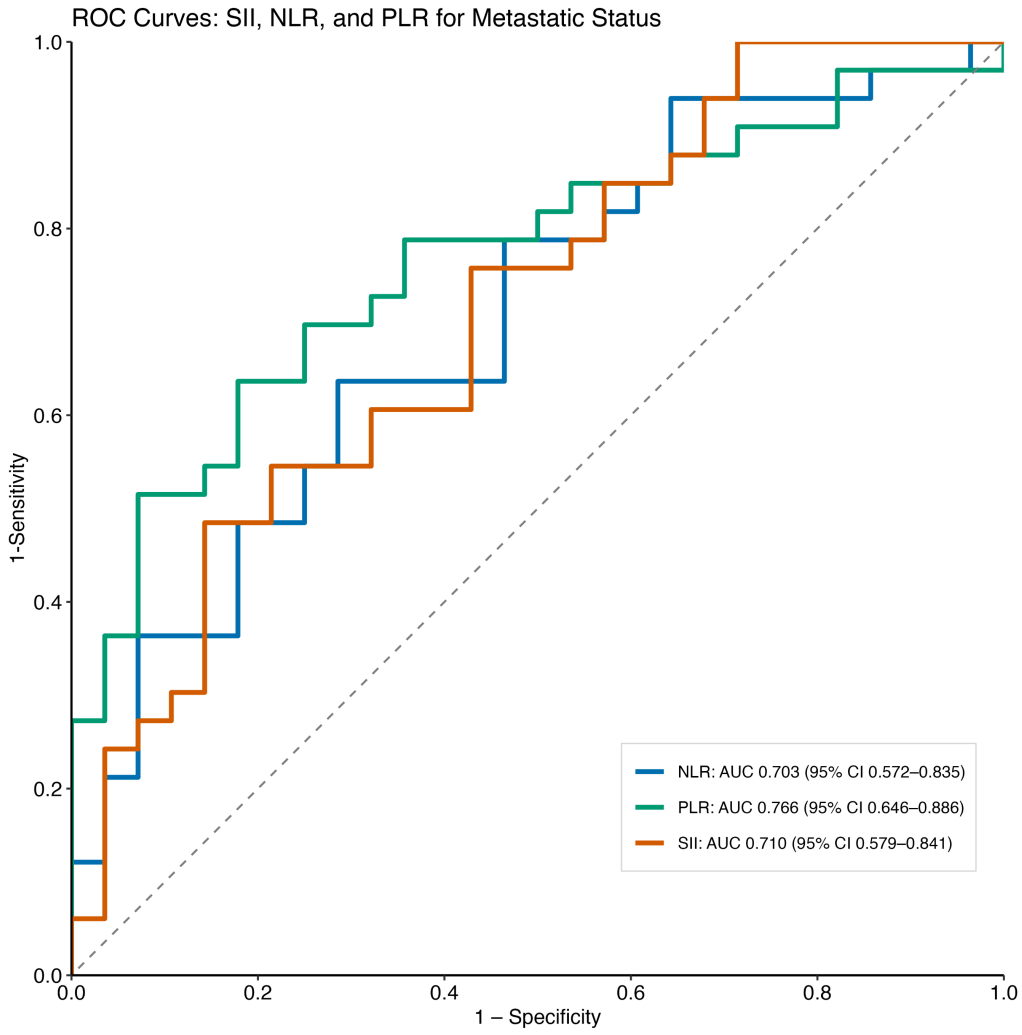


Figure 1

ROC curves of SII, NLR, and PLR for discriminating metastatic from non-metastatic testicular germ cell tumors. AUCs with 95% CIs (DeLong method) are shown in the legend.

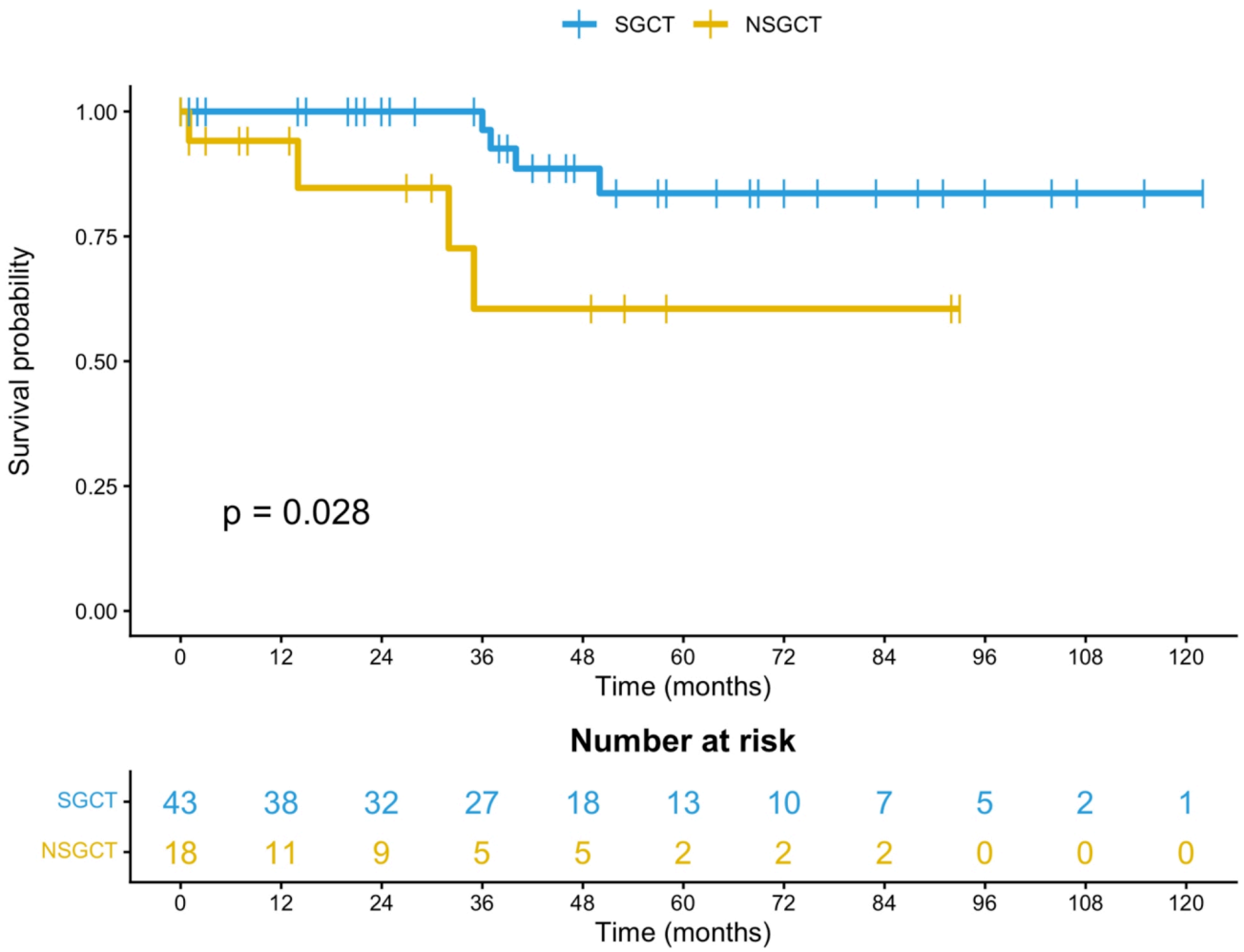


Figure 2

Kaplan–Meier overall survival by histology (SGCT vs NSGCT), Censored patients are marked with ticks; numbers at risk are shown below each panel. P values are two-sided log-rank tests.

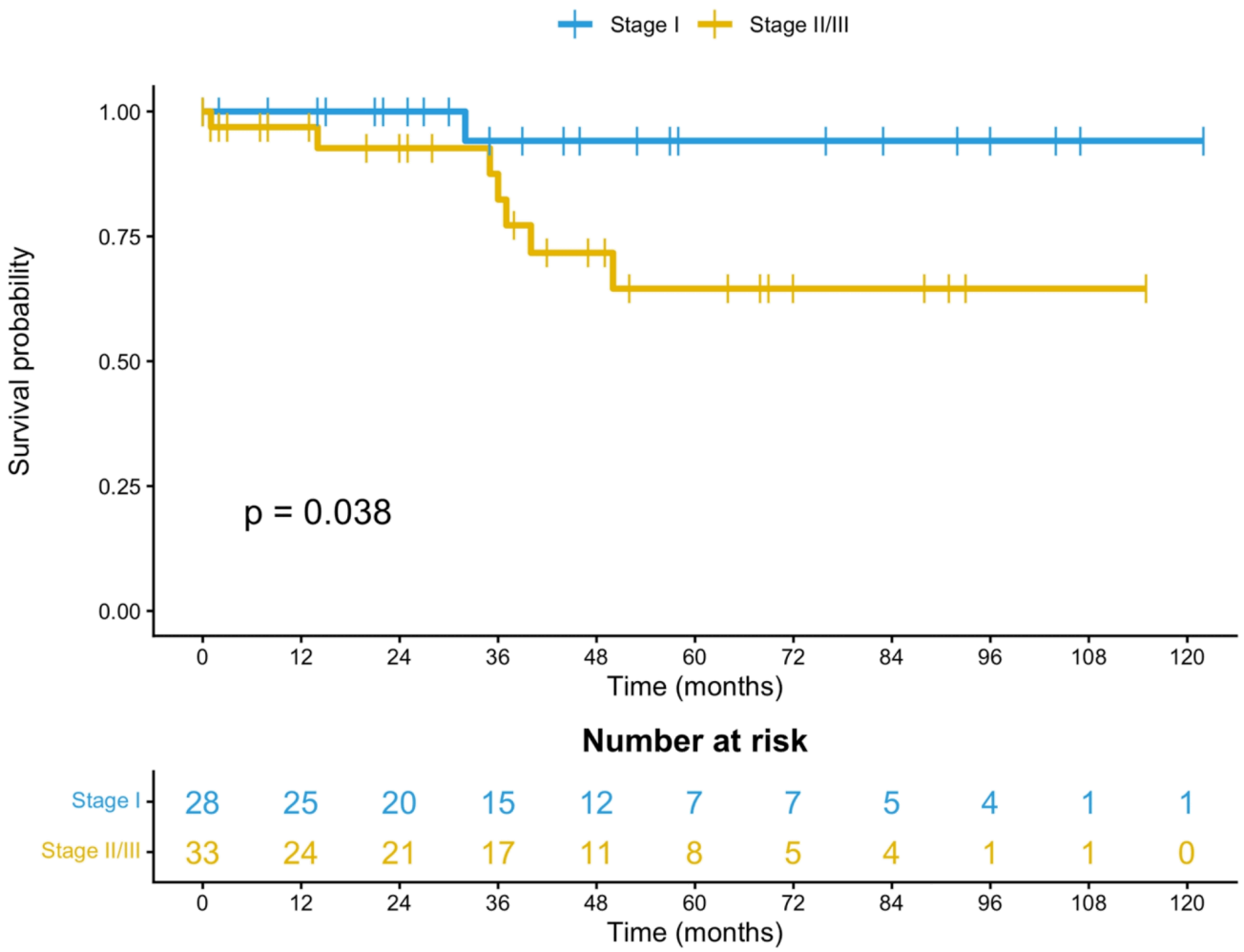


Figure 3

Kaplan–Meier overall survival by stage (I vs II/III). Censored patients are marked with ticks; numbers at risk are shown below each panel. P values are two-sided log-rank tests.

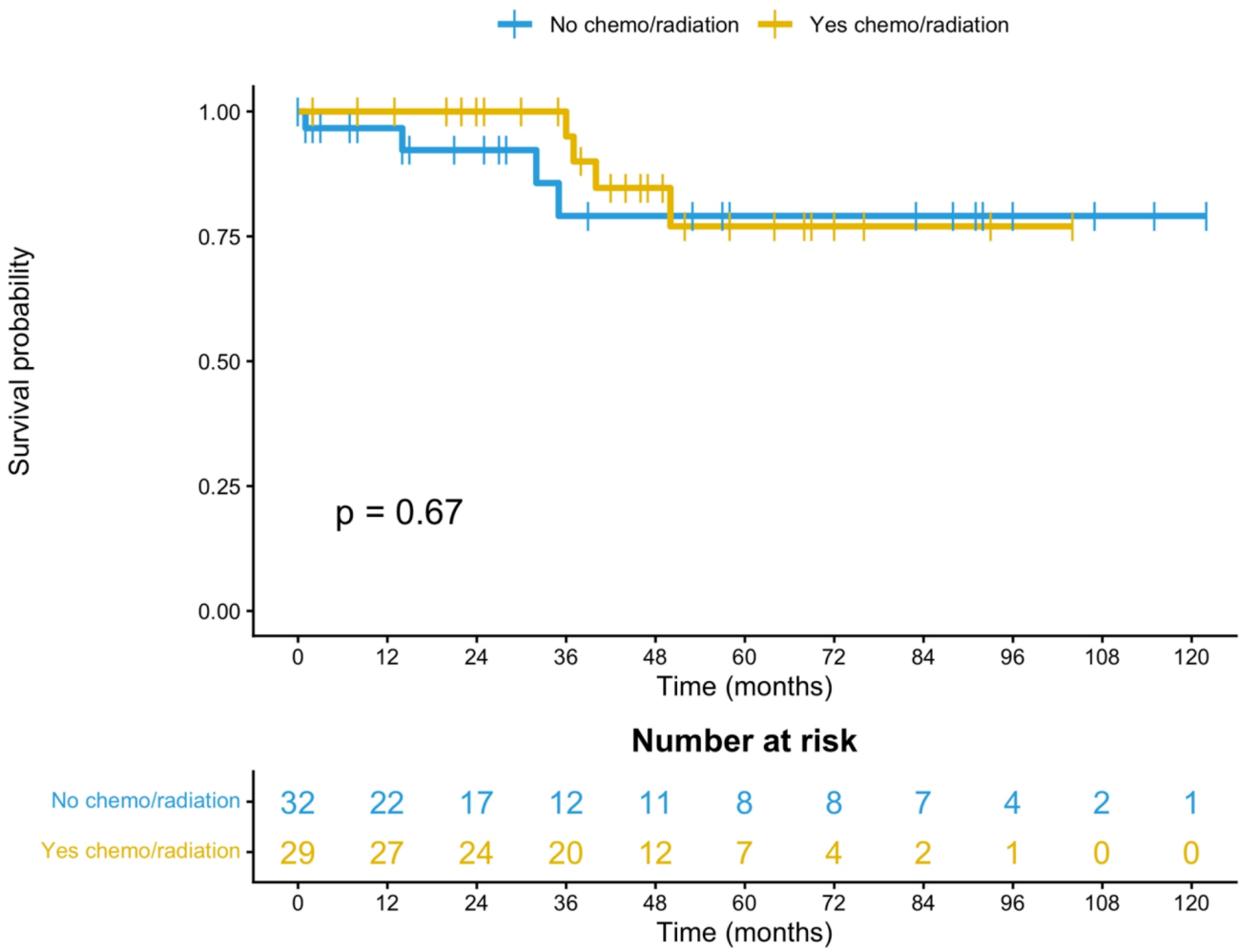


Figure 4

Kaplan–Meier overall survival by adjuvant therapy (surgery only vs chemo/radiotherapy). Censored patients are marked with ticks; numbers at risk are shown below each panel. P values are two-sided log-rank tests.