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Factors associated with five year overall survival in a retrospective cohort of 98 patients with diffuse large B cell lymphoma

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Abstract

Objective

To investigate the clinical characteristics, immunophenotypes, serum laboratory markers and prognostic factors associated with 5-year overall survival (OS) in patients with diffuse large B-cell lymphoma (DLBCL).

Methods

A total of 98 patients with pathologically confirmed DLBCL admitted across 13 clinical departments were retrospectively enrolled. Baseline clinical data, serum biomarkers and follow-up survival information were collected. Receiver operating characteristic (ROC) curves were used to determine the optimal cut-off values of laboratory parameters. The Log-rank test was used for univariate survival analysis.

Results

The cohort included 98 Patients. Cervical lymph nodes were the most common primary lesion site. The median interval from symptom onset to hospitalization was 6.02 months. Lung, lymph node, kidney, bone marrow or central nervous system (CNS) involvement was associated with poorer outcomes. Male sex, high International Prognostic Index (IPI) risk, activated B-cell-like (ABC) subtype, and elevated LDH (> 198 U/L), ALP (> 75.5 U/L), β_2-MG (> 3.125 mg/L), MUM1 expression were adverse prognostic factors. whereas CD10 expression predicted favorable survival. LDH showed the strongest prognostic value.

Conclusions

DLBCL presents with diverse clinical manifestations and easily leading to diagnostic delay. Combined evaluation of clinical manifestations, serum indicators and immunophenotyping may improve risk stratification and individualized management.

1 Introduction

Diffuse large B-cell lymphoma (DLBCL) represent the most prevalent subtype of non-Hodgkin lymphoma (NHL), accounting for approximately 30%-40% of all NHL cases worldwide[1]. DLBCL is characterized by prominent biological heterogeneity, an aggressive clinical course, divergent cellular origins, and unfavorable long-term survival outcomes. Significant inter-patient heterogeneity exists in clinical manifestations, immunophenotypes, and molecular genetic profiles across different patient populations.

The International Prognostic Index (IPI), established over three decades ago, remains the clinical standard for DLBCL risk assessment [2], which provides a framework for categorizing patients into distinct risk groups. However, its discriminative capacity has diminished in the rituximab era, particularly for identifying patients with exceptionally poor prognosis who may benefit from treatment intensification or novel therapeutic approaches[3]. This limitation has catalyzed investigation into complementary biomarkers capable of capturing the underlying biological heterogeneity that drives clinical outcomes. Despite substantial advancements in therapeutic strategies-including standard combined immunochemotherapy regimens (e.g., R-CHOP), targeted agent against CD20, Bcl-2, or PI3K signaling pathways, as well as innovative immunotherapies including chimeric antigen receptor T (CAR-T) cell therapy-a substantial proportion of patients develop primary treatment resistance or suffer disease relapse[4–7]. Notably, DLBCL-related mortality has gradually increased the past decade, particularly among elderly individuals and patients presenting with high-risk clinical features. This clinical reality highlights an urgent requirement for refined prognostic risk stratification and personalized therapeutic strategies.

In recent years, diagnostic techniques and therapeutic modalities for DLBCL have undergone continuous optimization, with immunochemotherapy remaining the mainstay of frontline disease management. Nevertheless, approximately 40%-50% of patients fail to achieve long-term remission after receiving first-line rituximab-based-CHOP consisting with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. Therefore, highly specific and sensitive prognostic biomarkers are urgently required to identify novel therapeutic targets, facilitate personalized treatment and enable post-therapeutic surveillance, and ultimately improve long-term survival outcome in DLBCL patients. Given the intrinsic heterogeneity and high relapse rate of DLBCL reliable early prognostic biomarkers are also indispensable for rational treatment allocation and accurate prognostic evaluation.

2 Materials and method

2.1 Patients

This single-center retrospective cohort study was approved by the Ethics Committee of Jinling Hospital, Nanjing University (Approval No.: 2026DZKY-137-01). Patients with a pathologically diagnosis of DLBCL were retrospectively enrolled from electronic medical database of Jinling, Nanjing University, between January 2012 to April 2026.

Two clinicians independently extracted and cross-checked all data to guarantee data accuracy. Collected clinicopathological parameters included age, gender, primary tumor site, initial visiting department, and disease duration. Laboratory biomarkers, such as the total immunoglobulin E antibody (IgEAb), interleukin-6 (IL-6), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), ferritin, β_2-microglobulin (β_2-MG), carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) were assessed for their prognostic significance in DLBCL.

Furthermore, the International Prognostic Index (IPI) was applied to stratify the prognostic risk of patients with DLBCL. Five clinical variables were included for scoring, with 1 point assigned for each adverse factor: age > 60 years, Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2, Ann Arbor stage III/IV, elevated serum lactate dehydrogenase (LDH) above the upper limit of normal, and involvement of ≥ 2 extranodal sites. The total IPI score ranged from 0 to 5, and patients were categorized into three risk subgroups: low risk (0–1 points), intermediate risk (2–3 points), and high risk (4–5 points). All clinical, laboratory, and prognostic index data were collected at the time of initial diagnosis.

2.2 Stratified analysis of 5-year survival based on optimal cut-off values of biomarkers

The optimal probability threshold for identifying high risk patients was determined using Youden's index (sensitivity+specificity − 1). Receiver operating characteristic (ROC) curve analysis was performed to establish optimal cut-off values of clinical and laboratoy variables for predicting 5-year overall survival (OS), with an optimal threshold selected via Youden's index for subgroup classification. Based on the derived optimal thresholds, patients were dichotomized into high-level and low-level subgroups for each indicator. Kaplan-Meier survival analysis with the Log-rank test was used to compare 5-year OS between the high- and low-level subgroups for each clinical and laboratory parameter. The predictive efficacy of each biomarker was assessed by calculating the area under the ROC curve (AUC) with corresponding 95% confidence intervals (95% CIs) (Fig. 1).

2.3 Statistical analysis

All continuous variables were presented as mean values with corresponding ranges. Kaplan-Meier survival curves were generated to estimate ourcomes based on follow-up data. Cox proportional hazards regression analysis was performed to determine independent prognostic factors for 5-year OS, with clinical prognosis defined as the dependent variable. Spearman's rank correlation analysis was used to assess correlation between continuous variables. All statistical analyses were conducted using SPSS version 23.0 (IBM Corp., Armonk, NY, USA), and all figures were generated with GraphPad Prism version 9.0 (GraphPad Software Inc., San Diego, CA, USA). A two-sided p-value less than 0.05 was considered statistically significant.

3 Results

3.1 General clinical characteristics and survival data of patients

A total of 98 patients with newly diagnosed DLBCL were enrolled in this study, and their detailed clinical characteristics were summarized in Table 1. The patients were initially diagnosed or treated across 13 different clinical departments, including hematology and multiple non-hematological departments, reflecting the diverse clinical presentation of DLBCL (Table 1 and Figure S1A).

The cohort consisted of 53 male and 45 female patients, with a male-to-female sex ratio of 1.18:1. Kaplan-Meier survival analysis revealed a significant difference in overall survival according to gender (Fig. 2A, p = 0.0042). The median age at symptom onset was 62.0 years (range, 30 ~ 92 years). The mean interval from initial symptom onset to hospitalization at our institution was 6.02 months (range, 3 days ~ 10 years). Regarding lifestyle factors, 16 patients had a smoking history and 10 patients had a history of alcohol consumption. Univariate survival analysis demonstrated that age older than 56.5 years only exhibited a trend toward inferior survival (Fig. 2B, p = 0.0685), whereas smoking history exerted no significant adverse effect on overall survival (Fig. 2C, p = 0.9100).

Among all 98 patients, cervical lymph nodes represented the most common lesion site, while extranodal involvement occurred frequently with diverse anatomical distribution (Table 1 and Figure S1B). Kaplan–Meier survival curves were generated to compare overall survival across subgroups defined by primary lesion site (Figure S2A, p = 0.0490). Patients with kidney/adrenal gland-origin DLBCL (median survival,12.5 months) or bone marrow-origin DLBCL (10.5 months) experienced an early survival decline and exhibited poor prognosis. Lung-origin DLBCL had the shortest median survival among all subgroups at only 8.5 months. In contrast, the oropharyngeal-ocular-nasal subgroup (84 months) maintained the most favorable long-term survival. Gastrointestinal lesions conferred moderate long-term survival (24 months). Lymph node (23 months) and central nervous system (CNS) involvement yielded intermediate survival outcomes. The subgroup comprising parotid/thyroid, tonsil, and submandibular gland lesions (34 months), as well as the extremity and spinal column subgroup (40 months), also demonstrated intermediate survival.

The 5-year overall survival (OS) rate was 23.47%, with a mean OS of the entire cohort was 37.93 ± 37.3 months (range, 2-168 months) (Table 1 and Figure S2B). According to the IPI scoring system, patients were stratified into three risk groups. Specifically, 25 patients (25.51%) were catergorized as low risk, 46 (46.94%) as intermediate risk, and 27 patients (27.55%) as high risk, respectively. Patients in the high-risk IPI group exhibited significantly poor OS compared with those in the low-risk and intermediate-risk groups (Fig. 2D, p = 0.0145).

Ann-Arbor staging data were available for 75 patients, whereas stage information was not documented for 23 patients, corresponding to a missing rate of 23.5%. Stage III was the most prevalent Ann-Arbor stage (25 cases, 33.33%), followed by Stage IV (22 cases, 29.32%), Stage II (18 cases, 24.00%), and Stage I (10 cases, 13.33%). Patients with advanced-stage disease (Stage III and Stage IV) accounted for 62.67% (47 cases) of patients with complete staging data, indicating that most patients with DLBCL in this cohort presented with disseminated advanced disease. Univariate survival analysis demonstrated that patients with advanced-stage disease exhibited a trend toward inferior survival (Fig. 2E, p = 0.0990).

Among the 98 patients with DLBCL, 28 cases (28.57%) were categorized as germinal center B-cell (GCB) subtype, and 70 cases (71.43%) as the activated B-cell (ABC) subtype(Table 1). The 5-year mortality rate reached 82.86% in the ABC subgroupe versus 60.71% in the GCB subgroup, with a statistically significant

difference between the two groups ($p < 0.01$).Kaplan-Meier survival analysis revealed a significant difference in overall survival between the two subtypes (Fig. 2F, p = 0.0328).

Table 1
The summary of 98 patients diagnosed as DLBCL

Characterize	**Total (N = 98)**	**Chi square** **Log-rank (Mantel-Cox) test or** **Gehan-Breslow-Wilcoxon test**	***p* value**
Gender			
Male	53(54.08%)	χ^2=8.184	0.0042**
Female	45(45.92%)		
Age(y)(range,mix-max)	61.44 ± 11.6 (30–92)	χ^2=3.319	0.0685
Duration(y)	6.02 ± 15		
Initial visiting department			
Oncology	24 (24.48%)		
Hematology	18 (18.36%)		
Stomatology	13 (13.26%)		
Orthopedics	9 (9.18%)		
General Surgery	7 (7.14%)		
Otolaryngology	6 (6.12%)		
Urology	6 (6.12%)		
Respiratory Medicine	5 (5.10%)		
Neurosurgery	3 (3.06%)		
Integrated Traditional Chinese and western medicine	3 (3.06%)		
Interventional Therapy	2 (2.04%)		
Plastic Surgery	1 (1.02%)		
Dermatology	1 (1.02%)		

Note: M Male, F Female, y year, m month, Germinal center B-cell GCB, activated B-cell ABC, CHOP cyclophosphamide, doxorubicin, vincristine, prednisone, CHOPE CHOP plus etoposide, mini-CHOP dose-reduced CHOP for frail or elderly patients, A-CHOP CHOP combined with asparaginase, COP cyclophosphamide, vincristine, prednisone (without anthracycline), CVP cyclophosphamide, vincristine, prednisolone, a low-intensity palliative regimen.

Characterize	Total (N = 98)	Chi square Log-rank (Mantel-Cox) test or Gehan-Breslow-Wilcoxon test	*p* value
Fever	12		
Smoking	16	χ^2=0.01277	0.9100
Alcohol	10		
Primary Site			
Lymph nodes (Cervical, Submandibular, Inguinal region, Axillary, Supraclavicular)	36 (22.45%)	χ^2=15.57	0.0490**
Gastrointestinal and spleen	17 (8.16%)		
Upper and lower Extremities, Spinal column	8 (8.16%)		
Oropharynx, Ocular and Nose	6 (6.12%)		
Lung and Thorax	6 (5.10%).		
Kidney, Adrenal gland and Genitals	8(6.12%)		
Brain	3 (3.06%)		
Bone marrow	2 (2.04%)		
Tonsil, Thyroid gland, Parotid gland	13 (3.06%)		
Overall Survival(m)	37.93 ± 37.3 (2–168)		
Pathological subtype			
ABC	70 (71.43%)	χ^2=4.558	0.0328**
GCB	28 (28.57%)		
Bcl-2			
Positive	48 (43.98%)	χ^2=0.8203	0.3651
Negative	10 (10.20%)		
Not classified	36 (36.73%)		

Note: M Male, F Female, y year, m month, Germinal center B-cell GCB, activated B-cell ABC, CHOP cyclophosphamide, doxorubicin, vincristine, prednisone, CHOPE CHOP plus etoposide, mini-CHOP dose-reduced CHOP for frail or elderly patients, A-CHOP CHOP combined with asparaginase, COP cyclophosphamide, vincristine, prednisone (without anthracycline), CVP cyclophosphamide, vincristine, prednisolone, a low-intensity palliative regimen.

Characterize	Total (N = 98)	Chi square Log-rank (Mantel-Cox) test or Gehan-Breslow-Wilcoxon test	*p* value
Bcl-6			
Positive	52 (53.06%)	χ^2=0.03431	0.8531
Negative	15 (15.31%)		
Not classified	31 (31.63%)		
MUM-1			
Positive	68 (69.39%)	χ^2=6.513	0.0107**
Negative	12(12.24%)		
Not classified	18 (18.37%)		
c-Myc			
Positive	33 (33.67%)	χ^2=1.213	0.2708
Negative	5 (5.10%)		
Not classified	60 (61.22%)		
CD10			
Positive	25 (25.51%)	χ^2=4.442	0.0351**
Negative	57 (58.16%)		
Not classified	16 (16.33%)		
Ann Arbor Stage			
I	10 (13.3%)	χ^2=2.721	0.0990
II	18 (24.0%)		
III	25 (33.3%)		
IV	22 (29.3%)		
Treatment			

Note: M Male, F Female, y year, m month, Germinal center B-cell GCB, activated B-cell ABC, CHOP cyclophosphamide, doxorubicin, vincristine, prednisone, CHOPE CHOP plus etoposide, mini-CHOP dose-reduced CHOP for frail or elderly patients, A-CHOP CHOP combined with asparaginase, COP cyclophosphamide, vincristine, prednisone (without anthracycline), CVP cyclophosphamide, vincristine, prednisolone, a low-intensity palliative regimen.

Characterize	Total (N = 98)	Chi square Log-rank (Mantel-Cox) test or Gehan-Breslow-Wilcoxon test	*p* value
R-CHOP-based regimens (including R-CHOP, R-mini CHOP, Pola-R-CHP)	47 (47.96%)	χ^2=7.615	0.2677
Rituximab-free CHOP-type chemotherapy (including CHOP, CHOPE, mini-CHOP, A-CHOP, COP, CVP, and other related regimens.)	14 (14.29%)		
Second-line or subsequent salvage chemoradiotherapy	13 (13.27%)		
Combined chemoradiotherapy	7 (7.14%)		
Intensified immunochemotherapy	4 (4.08%)		
Posttoperative immunochemotherapy	2 (2.04%)		
No treatment	11 (11.22%)		

Note: M Male, F Female, y year, m month, Germinal center B-cell GCB, activated B-cell ABC, CHOP cyclophosphamide, doxorubicin, vincristine, prednisone, CHOPE CHOP plus etoposide, mini-CHOP dose-reduced CHOP for frail or elderly patients, A-CHOP CHOP combined with asparaginase, COP cyclophosphamide, vincristine, prednisone (without anthracycline), CVP cyclophosphamide, vincristine, prednisolone, a low-intensity palliative regimen.

3.2 Stratified analysis of 5-year survival based on optimal cut-off values of biomarkers

At the 5-year follow-up endpoint, 75 patients (76.53%) either death or loss to follow-up. Univariate survival analysis was performed for laboratory biomarkers (Table 1). According to the optimal cut-off values derived from receiver operating characteristic (ROC) curve analysis, patients were dischotomized into high- and low-level subgroups for each biomarker (Table 1 and Fig. 3). Log-rank analysis revealed that LDH > 198 U/L(p<0.0001), ALP > 75.5 U/L (p = 0.0091) and β_2-MG > 3.125 mg/L (p = 0.0089) were significantly associated with inferior 5-year OS. No statistically significant survival differences were observed for IL-6, ferritin, total IgEAb, CEA and AFP (all p > 0.05).

The areas under the curve (AUC) of each indicator for predicting 5-year OS were showed. (Table S1). Among evaluated biomarkers, LDH yielded the highest predictive performance for 5-year OS (AUC = 0.644), followed by β_2-MG and ALP, suggesting that serum LDH may serve as the most reliable serum biomarker for predicting poor 5-year survival in patients with DLBCL (Fig. 3A-H).

3.3 Expression of Bcl-6 and Bcl-2 and their Prognostic Significance

Among the included patients, 52 of 67 (77.61%) exhibited positive Bcl-6 expression, and 48 of 58 (78.57%) showed positive Bcl-2 expression. Bcl-6 positivity was significantly more frequent in the GCB subtype than in the ABC subtype (86.36% *vs.* 73.33%, $p < 0.001$). In contrast, Bcl-2 expression showed no obvious subtype preference between ABC and GCB subgroups (82.05% *vs.* 70.59%). Kaplan-Meier survival analysis was performed to assess the prognostic value of these immunohistochemical biomarkers in this DLBCL cohort (Figure S3).

MUM1 positivity was observed in 68 patients (85.0%) and was significantly correlated with inferior 5-year OS (Figure S3E, $p = 0.0107$). MUM1 positivity was significantly more frequent in the ABC subtype than in the GCB subtype (96.49% *vs.* 56.52%, $p < 0.001$)

CD10 positivity was observed in 25 patients (43.85%) and was predominantly present in the GCB subtype (74.07% *vs.* 9.09%, $p < 0.001$). Patients with CD10 positivity had a longer median survival time (34.0 months) compared with CD10-negative patients (19.0 months), indicating its favorable prognostic significance. (Figure S3F, $p = 0.0351$).

3.4 Patient treatment modalities

Table 1 summarized the therapeutic modalities of the 98 enrolled patients with DLBCL.R-CHOP-based regimens were the predominant treatment strategy (including R-CHOP, R-miniCHOP and Pola-R-CHP), while treatment modality was not associated with OS (Figure S2C, p = 0.2677).

4 Discussion

The present study enrolled 98 patients pathologically confirmed with DLBCL, whose initial diagnosis and treatment involved 13 clinical departments, highlighting the clinical heterogeneity of DLBCL. Diverse extranodal manifestations may lead to delayed diagnosis.In our cohort, the median interval from symptom onset to hospital admission reached 6.02 months, with a maximum delay as long as 10 years, emphasizing the need for early recognition and timely initiation of standardized therapy.

Epidemiologically, our cohort demonstrated male predominance with a male-to-female ratio of 1.18:1 and a median onset age of 62.0 years ranging from 30 to 92 years old, consistent with the demographic features of DLBCL reported in recent domestic and Western studies[8–10]. The cohort form Zhao *et al.* enrolled 86 males (57.3%) and 64 females (42.7%), with a mean age of 58.4 ± 12.7 years[8, 11]. Male sex was associated with inferior OS in our cohort, consistent with previous real-world studies, which may be partly attributable to differences in comorbidities, treatment tolerance, health-seeking behavior, or underlying biological differences between male and female patients. Age over 56.5 years only borderline prognostic value, while its trend toward unfavorable survival should be considered in clinical risk assessment, consistent with Ismayilov's report[10]. This borderline significance may be related to the

limited sample size and missing staging information in a portion of patients. Smoking history failed to predict long-term survival in the current cohort.

Primary lesion site was identified as a prognostic determinant in the present DLBCL cohort, with statistically significant survival differences observed across anatomical subgroups (P = 0.0490). Patients with lung and thoracic, kidney/adrenal/genital, and bone marrow-origin disease exhibited particularly poor long-term survival, whereas those with oropharyngeal-ocular-nasal lesions achieved the most favorable prognosis. Extranodal DLBCL displays substantial biological heterogeneity, and the prognostic impact of primary site has been repeatedly documented in real-world cohorts[2, 7, 11–13]. Tumors arising in thoracic, pulmonary, or hematopoietic sites often present with disseminated disease and intrinsic aggressive features, while head-and-neck mucosal lesions may be detected earlier and are relatively more amenable to local and systemic therapy. These findings highlight that anatomical origin should not be overlooked during risk stratification, especially for patients with high-risk extranodal presentations.

As expected, IPI risk stratification effectively discriminated survival outcomes in our patients; high-risk IPI patients exhibited substantially worse prognosis relative to intermediate- and low-risk subgroups. This finding reinforces the clinical utility of the IPI system for initial risk stratification, consistent with decades of validation in DLBCL populations worldwide[3, 10, 14].

In the present cohort, 21 patients (21.43%) were categorized as the GCB subtype, a proportion consistent with the findings reported by Shi *et al.*and Zheng *et al.*[9, 15]. Furthermore, we observed that ABC subtype patients had significantly inferior survival compared with GCB subtype patients. This aligns with the well-established biological behavior of ABC-DLBCL, which is characterized by constitutive NF-κB activation, anti-apoptotic signaling, and a generally more aggressive clinical course[16, 17].

The overall 5-year OS rate of the entire cohort was low, consistent with the relatively high proportion of advanced-stage and ABC-subtype patients in this retrospective series. This result was comparable to the findings reported by Kassaw *et al*[18]. and Gradel *et al*[14]. In Kassaw's study of HIV-associated DLBCL, the 5-year OS rate was 25%, with a median survival of 36 months[18], while Gradel *et al.* reported a median survival of 35.47 months[14]. Nevertheless, our survival outcome was relatively poor than those described by Chen *et al*. [11]and Ismayilov *et al.* [10]

ROC curve analysis identified elevated LDH (> 198 U/L), ALP (> 75.5 U/L) and β_2-MG (> 3.125 mg/L as significant predictors of poor 5-year overall survival, among which LDH yielded the highest AUC value. These results highlight serum LDH as the most reliable serological biomarker for clinical risk stratification in DLBCL. As a ubiquitous cytoplasmic enzyme, LDH released into peripheral blood during tumor proliferation, invasion, and metastasis, reflecting tissue damage and tumor burden accumulation.Consistent with previous reports [11, 12, 18–22], our study confirmed that elevated LDH correlates closely with inferior survival, further supporting its well-established prognostic role in DLBCL.

In accordance with prior studies, our cohort demonstrated that increased β_2-MG independently predicts reduced OS in DLBCL[21, 23]. Mechanically, β_2-MG elevation is closely linked to advanced Ann Arbor stage, higher IPI score, and altered CD8 + T cell immune responses, implying its active involvement in tumor progression and treatment resistance[21]. Additionally, elevated β2-MG, bone marrow infiltration, and anemia have been validated as robust and accessible prognostic marker for EBV-positive DLBCL, reinforcing the clinical applicability of β2-MG based risk evaluation prospective studies [13]. In contrast, several biomarkers including IL-6, ferritin, Ki-67, total IgEAb, CEA, and AFP did not exhibit independent prognostic significance in our univariate analysis.

Survival analysis demonstrated that traditional single biomarkers including Bcl-2, Bcl-6, c-Myc, and Ki-67 failed to predict 5-year OS in our DLBCL patients. Although Bcl-2, c-Myc, and high Ki-67 proliferation index are generally regarded as adverse prognostic indicators in DLBCL in many previous studies[24, 25], their independent prognostic value was not validated in the current population. This discrepancy may be partially explained by differences in baseline clinical characteristics, treatment regimens, sample size, and patient inclusion criteria across different centers, suggesting that the prognostic role of individual biomarkers may vary in real world retrospective cohorts.

Conversely, MUM1 and CD10 possessed reliable prognostic predictive efficacy in DLBCL. MUM1 positivity, which was detected in 85.0% of patients, was strongly associated with inferior long-term survival, consistent with the intrinsic aggressive behavior of MUM1 activated B cell phenotype. In contrast, CD10 expression was predominantly restricted to the GCB subtype and served as a favorable prognostic marker. Patients with CD10 positivity achieved a remarkably longer median survival (34.0 months *vs.* 19.0 months) and significantly better 5-year OS outcomes. These findings further verify that CD10-defined germinal center origin represents a beneficial prognostic feature, whereas MUM1 expression indicates an activated, high risk phenotype,which was consistent with Li's [26]study. Therefore, routine detection of CD10 and MUM1 expression contributes to refined risk stratification.

The distribution of treatment modalities in our 98-patient cohort reflected real-world clinical patterns for DLBCL with R-CHOP-based chemoimmunotherapy (47.96%) representing the predominant therapeutic strategy.Various other treatment modalities, including CHOP-based chemotherapy, intensified immunochemotherapy, salvage therapy, and radiotherapy, were applied according to individual clinical conditions. However, no significant difference in overall survival was observed among different treatment groups, which may be attributed to treatment heterogeneity and limited sample size.

Several limitations of this study should be noted. First, this was a single-center retrospective analysis with a moderate sample size of 98 patients, which may introduce inherent selection bias. Second, only univariate survival analysis was performed in the current research; multivariate Cox proportional hazards regression is needed to screen independent prognostic factors and eliminate confounding variables in subsequent work. Third, dynamic longitudinal monitoring data of serum biomarkers during treatment and follow-up were unavailable, so we could not evaluate whether serial changes of these indicators reflect therapeutic response or disease relapse.

5 Conclusion

The cross-departmental presentation and broad extranodal distribution of DLBCL frequently result in diagnostic delay. Clinical features including male gender, advanced age and adverse lesion involvement sites, combined with serum biomarkers (LDH, ALP, β_2-MG), Hans cell-of-origin subtype, core immunohistochemical markers (MUM1 positive) and IPI risk stratification collectively determine the survival of DLBCL patients. ABC subtype, elevated LDH represent robust signals of poor prognosis, while CD10 expression correlate with superior survival. Integrated assessment combining clinical manifestations, serological indicators and pathological immunophenotyping can facilitate individualized risk evaluation, early diagnosis and optimized treatment strategies for DLBCL patients in multidisciplinary clinical settings.

Declarations

Ethics approval

This single-center retrospective cohort study was approved by the Ethics Committee of Jinling Hospital, Nanjing University (Approval No. 2026DZKY-137-01). The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate

The Ethics Committee of Jinling Hospital, Affiliated Hospital of Medical School, Nanjing University, waived the requirement for informed consent because this retrospective study involved only anonymized information obtained from pre-existing medical records and did not involve any additional interventions or direct contact with patients.

Consent for publication

Not applicable as this study does not include identifiable personal data or images.

Competing interests

The authors declare no competing interests.

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Figures

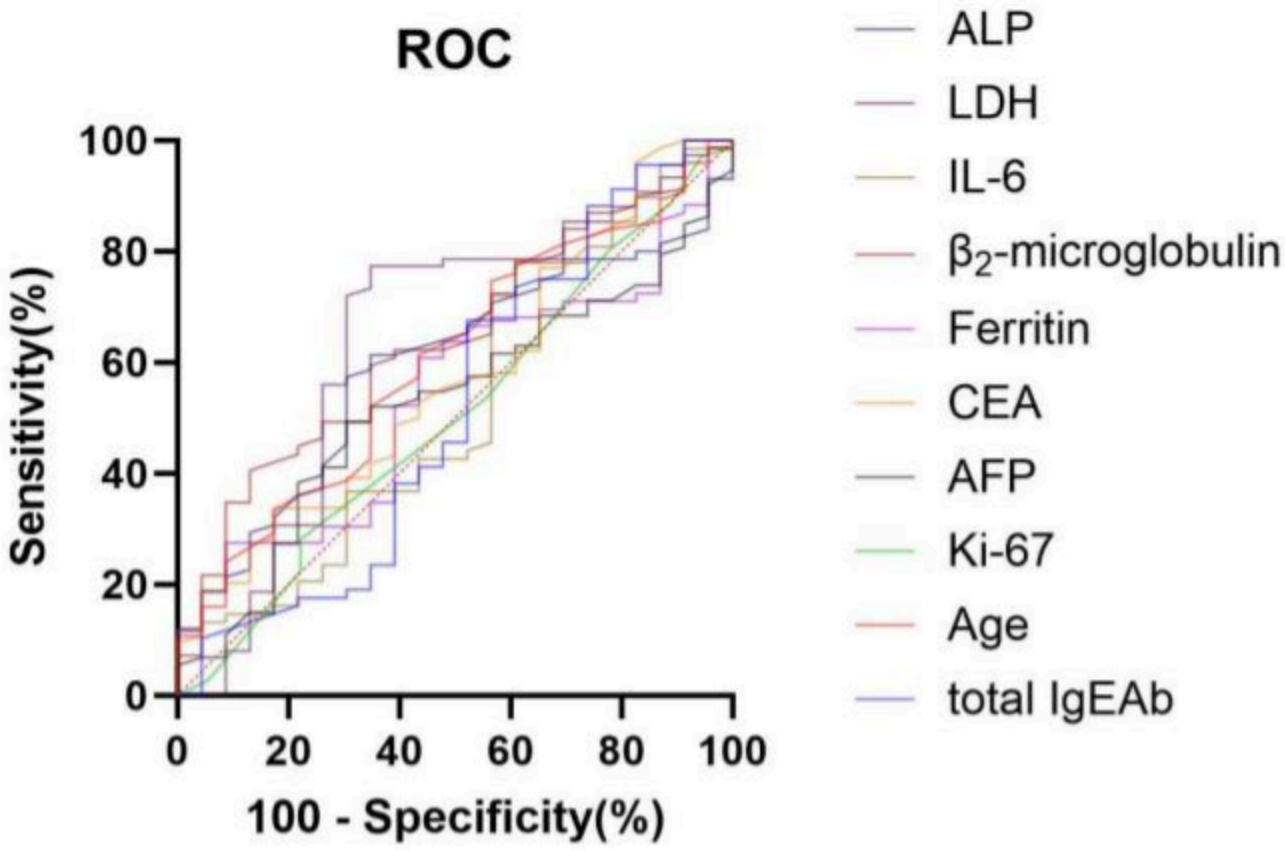


Figure 1

The receiver operating characteristic (ROC) curves of laboratory biomarkers and clinical parameters for predicting 5-year overall survival in patients with DLBCL. The analyzed indicators included ALP, LDH, IL-6, β_2-microglobulin(MG), ferritin, CEA, AFP, Ki-67, age, and total IgEAb.

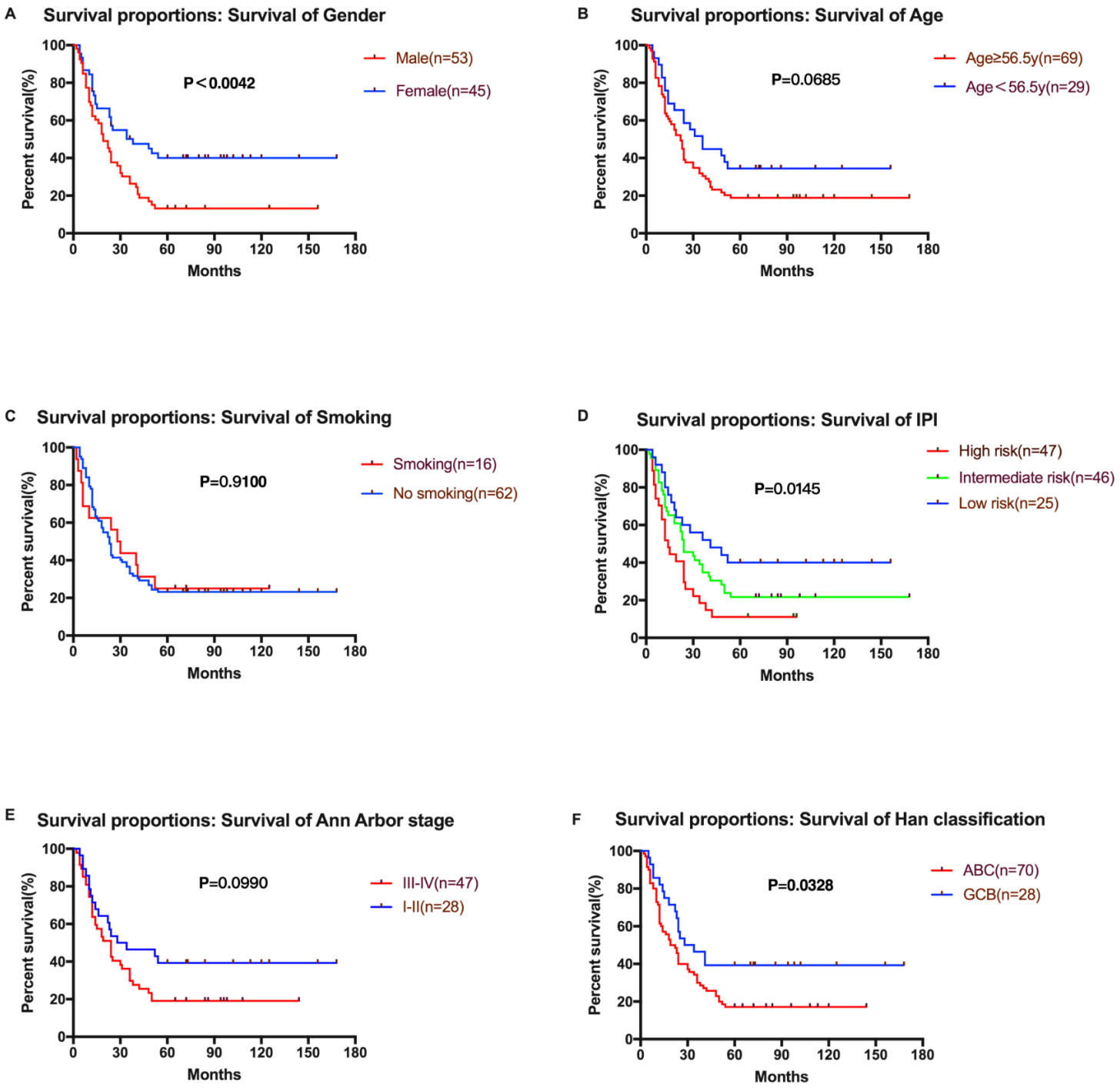


Figure 2

Univariate analysis of 5-year overall survival (OS) in patients with DLBCL. Kaplan-Meier survival curves showing OS stratified by key clinical parameters: (A) Gender, (B) Age, (C) Smoking, (D) International

Prognostic Index (IPI), (E) Ann Arbor stage, (F) Han classification, germinal center B-cell (GCB), activated B-cell (ABC). Log-rank P-values are indicated on each panel. Male, ABC, higher IPI score were all significantly associated with inferior 5-year OS (**p< 0.05).

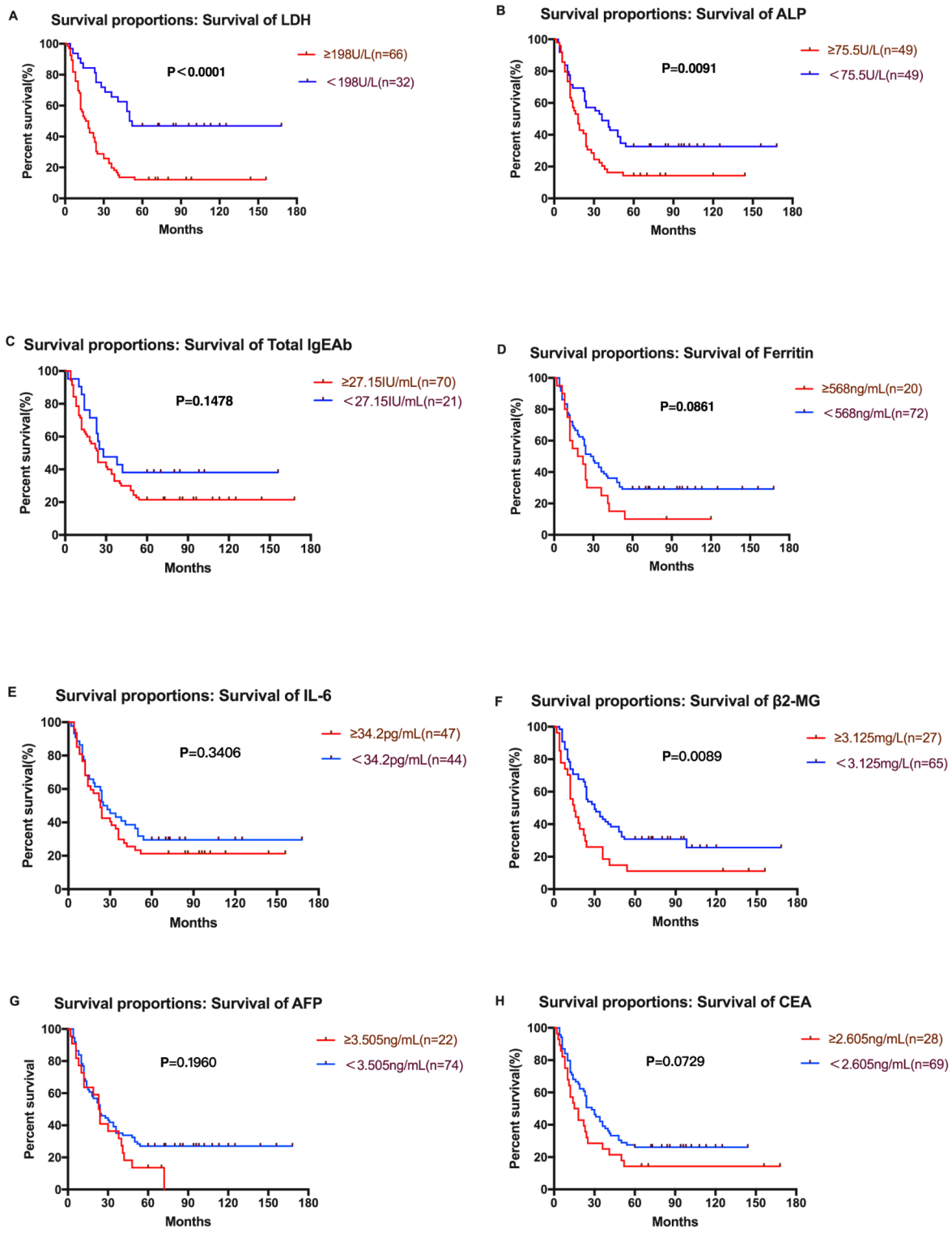


Figure 3

Univariate analysis of 5-year overall survival (OS) in patients with DLBCL. Kaplan-Meier survival curves showing OS stratified by key clinical parameters: (A) lactate dehydrogenase (LDH), (B) Alkaline phosphatase (ALP), (C) total immunoglobulin E antibody (IgEAb), (D) Ferritin, (E) interleukin-6, (IL-6), (F) β2-microglobulin (β2-MG), (G) alpha-fetoprotein (AFP), (H) carcinoembryonic antigen (CEA). Log-rank P-values are indicated on each panel. Increased LDH, elevated β2-MG, increased ALP were all significantly associated with inferior OS (**p< 0.05).

Supplementary Files

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- SupplementaryMaterial260908.docx