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ORIGINAL RESEARCH

A Nomogram for Predicting Overall Survival in Primary Central Nervous System Lymphoma: A Retrospective Study

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Purpose: Current prognostic scoring systems for newly diagnosed primary central nervous system lymphoma (PCNSL), such as IELSG prognostic score and MSKCC prognostic score, are widely used but have limitations in clinical practice. This study aimed to develop a novel prognostic model based on real clinical data and compare it with existing systems.

Patients and Methods: A total of 288 patients newly diagnosed with PCNSL were recruited. Patients were randomly allocated to the development and validation cohorts. The least absolute shrinkage and selection operator (LASSO) regression and multivariate Cox regression analysis were used to identify the risk factors for overall survival (OS) and construct a nomogram. Additionally, Kaplan-Meier survival curves were plotted to show the stratification ability of the risk groups.

Results: Eastern Cooperative Oncology Group performance status (ECOG-PS), albumin, and two inflammatory biomarkers D-Dimer, and neutrophil-to-lymphocyte ratio (NLR)—were independent predictors of inferior OS. The prognostic model demonstrated concordance Index (C-index) of 0.731 and 0.679 in the development and validation cohorts, respectively. In terms of the time dependent area under the curve (AUC) values for OS, the development cohort exhibited values of 0.765, 0.762, and 0.812 for 1-year, 3-year, and 5-year OS, respectively. The corresponding AUC values in the validation cohort were 0.711, 0.731, and 0.840, respectively. The calibration curves showed excellent concordance. The novel prognostic model also provided superior risk stratification for patients with PCNSL compared with existing scoring systems.

Conclusion: This study presents a novel prognostic model for predicting the OS of patients with newly diagnosed PCNSL. The model accurately and effectively stratifies the prognosis of patients with PCNSL and offers valuable clinical guidance for decision making.

Keywords: PCNSL, prognostic model, risk stratification, NLR, albumin, D-Dimer

Introduction

Primary central nervous system lymphoma (PCNSL) is a rare but highly aggressive extranodal non-Hodgkin lymphoma that is confined to the cerebral parenchyma, leptomeninges, spinal cord, and eyes, without involvement of the peripheral lymphatic system. PCNSL accounts for approximately 4% of central nervous system tumors and 4–6% of all extranodal lymphomas.[1] The incidence rate was 0.47 per 100,000 people, with the highest rates observed in patients aged 70–79.[2] Approximately 95% of PCNSL cases are diffuse large B-cell lymphoma (DLBCL).[3] Newly diagnosed PCNSL patients typically receive induction chemotherapy based on high-dose methotrexate (HD-MTX) combined with other agents. While this approach achieves remission in many cases, 10–15% exhibit resistance, and nearly half of responders relapse.[4] Treating refractory or relapsed PCNSL (R/R PCNSL) remains challenging, with no standard salvage therapy.[5] Existing salvage strategies include chemotherapy, targeted therapies, immunomodulators, and immune checkpoint inhibitors, but the prognosis remains poor despite treatment advancements. Without treatment, the median survival time is

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approximately 1.5 months, and even in elderly patients receiving treatment, the median survival is roughly 6 months.[2,6] Given the limited treatment options currently available for patients with PCNSL, risk stratification is critical for optimizing effective treatment planning and improving outcomes.

IELSG prognostic score and MSKCC prognostic score, are the most commonly used prognostic scoring systems for PCNSL. The IELSG prognostic score incorporates five prognostic factors: age, deep brain involvement, Eastern Cooperative Oncology Group performance status (ECOG-PS), lactate dehydrogenase (LDH) levels, and cerebrospinal fluid (CSF) protein levels.[7] The MSKCC score, developed by the Memorial Sloan Kettering Cancer Center, classifies patients based on age and Karnofsky Performance Status (KPS) into three groups: ≤50 years, >50 years with KPS ≥ 70, and >50 years with KPS < 70.[8] However, the IELSG score has limitations for predicting patient outcomes in clinical practice. For instance, the IELSG score cannot be applied to patients with contraindications for lumbar puncture.[9] The MSKCC score uses a limited number of variables and cannot sufficiently differentiate low- and medium-risk patients.[10] With recent advances in therapeutic options, including HD-MTX-based chemotherapy, immunomodulatory drugs, autologous hematopoietic stem cell transplantation, and CAR-T cell therapy, the prognosis for PCNSL has improved.[11,12] The accuracy of predicting prognosis using the existing prognostic evaluation systems should be re evaluated. Several prognostic models have been developed, based on small sample sizes.[13–16] This necessitates the development of more a reliable prognostic model suited to the current treatment landscape to predict outcomes in PCNSL patients. We established a new prognostic model based on a large sample size of clinical data from our center with the aim of accurately predicting the prognosis of patients with PCNSL and stratifying patients according to risk factors.

Materials and Methods

Patient Selection

This retrospective cohort study included 288 patients with newly diagnosed PCNSL between January 1, 2014, and March 1, 2024, at Huashan Hospital of Fudan University. Diagnosis was made according to the 2016 World Health Organization criteria.[17] Patients included in this study met the following criteria: (1) HIV seronegative status; (2) no history of immunosuppression or organ transplantation; (3) no other malignancies identified; and (4) availability of adequate clinical, laboratory, and follow-up data. The research plan was reviewed and approved by the Ethics Committee of the Huashan Hospital, Fudan University (Approval No. 2022–008). In accordance with the principles outlined in the Declaration of Helsinki, all participants were informed of the purpose of the study and provided signed informed consent before taking part in the study.

Data Collection

Basic demographic and clinical data were collected before treatment initiation. Demographic data included age and sex, while clinical data included peripheral blood neutrophil count (NEU), lymphocyte count (LYM), serum β2-microglobulin (β2-MG), albumin (ALB), lactate dehydrogenase (LDH), D-Dimer, total bilirubin, cerebrospinal fluid (CSF) protein, CSF tumor cells, KPS, ECOG-PS, lesion number and location, IELSG score, MSKCC score, induction and salvage therapy. Additionally, the neutrophil-to-lymphocyte ratio (NLR) and the prognostic nutritional index (PNI) were calculated.

Follow-up

Patients were followed up through phone calls or outpatient visits to confirm their survival status. The follow-up period will last until June, 2024. The main endpoint was overall survival (OS), measured as the time from initial diagnosis to death from any cause or the last follow-up. The secondary endpoint was progression-free survival (PFS). PFS was defined as the duration from the initial diagnosis of PCNSL to disease progression, death from any cause, or last follow-up date.

Determination of Cutoff Values

Continuous variables, such as LDH, β2-MG, albumin, and CSF protein levels, were converted into categorical variables based on the reference ranges. The cut-off value for the total bilirubin level was determined according to previously published studies.[18] The optimal cutoff values for NLR, PNI, and D-Dimer were determined using the maximally selected rank statistics method (MSRSM) implemented via the "maxstat" package (https://CRAN.R-project.org/package=maxstat) in R.[19–21]

Validation of the Novel Developed Model

The model was validated by using several metrics to assess and verify its predictive ability. Model discrimination was assessed using the concordance index (C-index) and the time-dependent receiver operating characteristic (ROC) curve. Calibration curves and decision curve analyses (DCA) were used to assess the performance and clinical applicability of the model. Kaplan-Meier (K-M) curves were used to estimate OS, and the Log rank test was used to assess the differences in OS.

Statistical Analysis

Categorical variables were described as frequencies and percentages. Chi-square or Fisher's exact tests were used to compare data between the two cohorts. The cutoff values for D-Dimer, PNI, and NLR were determined using the maximally selected rank statistics method (MSRSM), and patients were subsequently categorized into high and low groups. LASSO regression model was applied to prevent potential multicollinearity. All variables with complete data in the development cohort were included in the LASSO regression analysis using the "glmnet" package in R software. The model achieved optimal performance at Lambda.min, resulting in the identification of candidate variables. Multivariate Cox proportional hazards regression analysis was then further performed to identify independent prognostic factors associated with OS. These factors were subsequently integrated to construct a nomogram prognostic model by the "rms" package of R software. Survival curves were plotted using the Kaplan-Meier method, and comparisons between groups were made using the Log rank test. All statistical analyses were conducted using R software version 4.3.3 (The R Foundation for Statistical Computing, Vienna, Austria), with a P-value < 0.05, considered statistically significant.

Results

Baseline Characteristics

This study included 288 patients who were diagnosed with PCNSL between January 2014 and March 2024. The patients were randomly assigned to a development cohort (n = 144) or a validation cohort (n = 144). The baseline characteristics of the cohorts are presented in Table 1. In the development cohort, 85% of the patients had an ECOG-PS≥2, whereas 79% of the patients in the validation cohort had an ECOG-PS≥2. Regarding induction regimens, the majority of patients

Table 1 Baseline Characteristics of Development and Validation Cohorts

Characteristics	Development, n(%) (n = 144)	Validation, n(%) (n = 144)	P
Age			0.814
<60	70 (49)	73 (51)	
≥60	74 (51)	71 (49)	
Gender			0.806
Female	53 (37)	50 (35)	
Male	91 (63)	94 (65)	
KPS			0.749
<70	121 (84)	122 (85)	
≥70	23 (16)	22 (15)	

(*Continued*)

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Table 1 (Continued).

Characteristics	Development, n(%) (n = 144)	Validation, n(%) (n = 144)	P
ECOG-PS			0.217
<2	21 (15)	30 (21)	
≥2	123 (85)	114 (79)	
LDH			0.217
<250IU/L	114 (79)	123 (85)	
≥250U/L	30 (21)	21 (15)	
β2-MG			0.797
<2.5mg/L	137 (95)	135 (94)	
≥2.5mg/L	7 (5)	9 (6)	
D-Dimer			0.082
<2.41mg/L	113 (78)	99 (69)	
≥2.41mg/L	31 (22)	45 (31)	
ALB			0.321
<40g/L	99 (69)	90 (62)	
≥40g/L	45 (31)	54 (38)	
Total bilirubin			1.00
<12μmol / L	123 (85)	122 (85)	
≥12μmol / L	21 (15)	22 (15)	
Deep lesions			0.038
No	65 (45)	84 (58)	
Yes	79 (55)	60 (42)	
Multiple lesions			0.811
No	62 (43)	59 (41)	
Yes	82 (57)	85 (59)	
PNI			0.544
<45	52 (36)	58 (40)	
≥45	92 (64)	86 (60)	
NLR			1.00
<1.8	21 (15)	20 (14)	
≥1.8	123 (85)	124 (86)	
CSF protein			0.443
<0.6g/L	59 (41)	49 (34)	
≥0.6g/L	56 (39)	60 (42)	
Missing	29 (20)	35 (24)	
CSF tumor cells			0.565
No	81 (56)	81 (56)	
Yes	34 (24)	28 (19)	
Missing	29 (20)	35 (24)	
IELSG stratification			0.502
Low-risk	19 (13)	25 (17)	
Median-risk	85 (59)	76 (53)	
High-risk	11 (8)	8 (6)	
Missing	29 (20)	35 (24)	
MSKCC stratification			0.428
Low-risk	38 (26)	34 (24)	
Median-risk	6 (4)	11 (8)	
High-risk	100 (69)	99 (69)	

(*Continued*)

Table 1 (Continued).

Characteristics	Development, n(%) (n = 144)	Validation, n(%) (n = 144)	P
Induction therapy			0.365
HD-MTX+RTX	120(83.3)	123(85)	
HD-MTX+RTX+IDA	16(11.1)	17(12)	
MATRix	5(3.5)	4(3)	
WBRT	3(2.1)	-	
Salvage therapy			0.262
Ara-C	4 (2.8)	4 (2.8)	
Ara-C+TMZ	21 (14.6)	23 (16)	
Ara-C+ zanubrutinib	44 (30.6)	36 (25)	
PEM+Lenalidomide	2 (1.4)	-	
Re-treat with HD-MTX	5 (3.5)	16 (11.1)	
WBRT	9 (6.2)	10 (6.9)	
Untreated	9 (6.2)	9 (6.2)	

Abbreviations: ECOG-PS, Eastern Cooperative Oncology Group performance status; KPS, Karnofsky performance status; CSF, cerebrospinal fluid; LDH, lactate dehydrogenase; β2-MG, β2-microglobulin; ALB, albumin; Deep lesions, Tumor affecting in deep brain tissues included the basal ganglia, corpus callosum, brainstem, periventricular regions and cerebellum; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutritional index; IELSG, International Extranodal Lymphoma Study Group; MSKCC, Memorial Sloan Kettering Cancer Center; HD-MTX, high-dose methotrexate; RTX, rituximab; IDA, idarubicin; MATRix, methotrexate+ rituximab+ cytarabine+ thiotepa; WBRT, whole brain radiotherapy; Ara-C, Ara-C; TMZ, temozolomide, PEM, pemetrexed.

receive HD-MTX chemotherapy, while only 2.1% undergo whole-brain radiotherapy (WBRT). Salvage treatment strategies tailored to each patient on the basis of clinical and biological characteristics, as well as their socioeconomic status and access to healthcare resources. Salvage therapy was administered to 87.6% of patients following disease progression, including cytarabine (Ara-C), zanubrutinib, temozolomide (TMZ), re-treatment with HD-MTX, pemetrexed (PEM), lenalidomide and WBRT. The salvage treatment group demonstrated better OS compared to those who did not receive salvage treatment (Figure S1). The median PFS was 14.9 months in the development cohort and 11.8 months in the validation cohort, whereas the median OS was 63.2 months and 53.4 months, respectively (Figure S2A and B). The baseline characteristics of the two cohorts were comparable.

Construction the Novel Prognostic Model

Lasso regression was used to screen the parameters, and the coefficient of variation of these variables is displayed in Figure S3A. A 10-fold cross-validation was employed to optimize the regularization parameter λ in the LASSO regression model (Figure S3B). At the lambda.min value, ECOG-PS, LDH, D-Dimer, ALB, total bilirubin, multiple lesions, PNI, and NLR were identified as significant and selected to construct the optimal LASSO regression model. Among these, four variables were determined as independent risk factors using multivariate Cox regression analysis (ECOG-PS, D-Dimer, ALB, NLR $P < 0.05$, Table 2) and incorporated into the prognostic model, represented as a nomogram in Figure 1. The goodness-of-fit of the novel model and the significance of its parameters were assessed using the likelihood ratio, Wald, and Score tests. All *P*-values were less than 0.001 (Table 3), indicating that the model was well fitted. The results of univariable Cox hazards regression analysis for all variables included in the study are presented in Table S1.

Evaluation of the Novel Prognostic Model

In the development cohort, calibration curves were constructed by performing 1000 bootstrap resamples with 40 samples per group to assess the calibration of the novel inflammation-based model. The calibration curves indicated that the predicted probabilities strongly aligned with the observed outcomes (Figure 2A–C). The C-indices for the novel model and IELSG and MSKCC prognostic scoring systems were 0.731, 0.577, and 0.549, respectively. Additionally, the predictive performance of the novel model was compared to that of the classical IELSG and MSKCC prognostic scoring

Table 2 Multivariate Cox Regression Analysis in the Development Cohort

Characteristics	HR	95% CI	P
ECOG-PS≥2	5.995	1.769–20.320	0.004
LDH≥250U/L	1.882	0.947–3.738	0.071
D-Dimer≥2.41mg/L	2.763	1.441–5.300	0.002
ALB≥40g/L	0.398	0.192–0.826	0.023
Total bilirubin≥12μmol / L	0.481	0.184–1.253	0.134
Multiple lesions	1.377	0.769–2.467	0.282
PNI≥45	0.997	0.506–1.964	0.994
NLR≥1.8	4.953	1.632–15.031	0.005

Abbreviations: HR, Hazard Ratio; CI, Confidence Interval; ECOG-PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; ALB, albumin; PNI, prognostic nutritional index; NLR, neutrophil-to-lymphocyte ratio.

systems using the time-dependent AUC (Figure 2D–F). In the development cohort, the AUC values for the 1-year, 3-year, and 5-year survival probabilities were 0.765 (95% CI 0.647–0.883), 0.762 (95% CI 0.669–0.855), and 0.812 (95% CI 0.711–0.913) respectively, which were better than the classical prognostic scoring systems. The IELSG and MSKCC scoring systems showed worse performance than the novel model, as indicated by both a lower C-index and less favorable time-dependent AUC. The net clinical benefit of the novel inflammation-based model was evaluated using DCA (Figure 2G). The results demonstrated that the novel model provided a better net clinical benefit than the existing IELSG and MSKCC scoring systems.

Risk Stratification by the Novel Prognostic Model

The score for each variable in the nomogram was shown in Table S2. The cumulative risk score for each patient derived from the nomogram was divided into high-, medium-, and low-risk group using the 33rd and 66th percentiles to achieve an effective risk stratification. Based on these cutoff values, the patients were divided into three groups: low-risk (≤177),

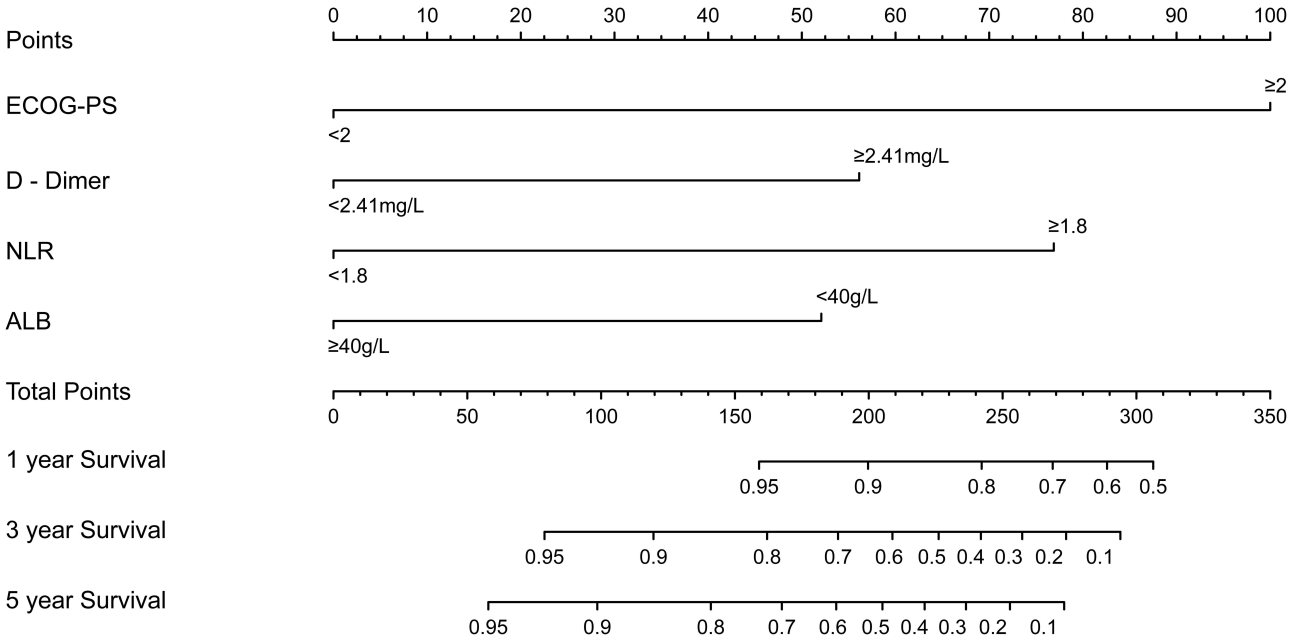

Figure 1 The nomogram based on the development cohort to predict OS of PCNSL patients. The scores of each independent risk factor could be obtained from the scale of the model, and the total score could be calculated by adding them, and the prediction probability corresponding to the total score was the probability of OS.

Table 3 Statistical Analysis of the Novel Prognostic Model

Indicator	P
Likelihood ratio test	<0.001
Wald test	<0.001
Score (log rank) test	<0.001

medium-risk (>177 to ≤229), and high-risk (>229). K-M survival curves for OS and PFS were plotted based on the risk stratification using a novel prognostic model (Figure 3A and B). In the development cohort, 21 patients (14.6%) were at high risk with a median OS of 14.5 months, 64 patients (44.4%) were at medium risk with a median OS of 36.8 months, and 59 patients (41.0%) were at low risk with the median OS not yet reached. The median PFS was 4.9, 14.5, and 20.9 months respectively. Subsequently, patients in the development cohort were stratified using IELSG scores for OS and PFS (Figure 3C and D), as well as MSKCC scores for OS and PFS (Figure 3E and F). The median OS and PFS of the three prognostic scoring models are shown in Table 4. In our study, the Kaplan-Meier curves for OS (IELSG: P=0.71; MSKCC: P=0.32, respectively) and PFS (IELSG: P=0.59; MSKCC: P=0.45, respectively) could not be discriminated clearly using the IELSG and MSKCC scores. The results demonstrated that the novel model effectively stratified patients by risk score, outperforming the classical MSKCC and IELSG scoring systems, as reflected by the significant separation of K-M curves for OS between risk groups ($P < 0.0001$). However, the novel model showed reduced discriminative ability for PFS ($P = 0.12$), indicating that the differences among the groups were not statistically significant. Nevertheless, a clear trend in risk stratification remained evident, suggesting the potential clinical relevance of the model in differentiating PFS across the groups.

Validation of the Novel Prognostic Model

In the validation cohort, the predicted outcomes were consistent with the observed results, indicating that the predicted survival probabilities closely matched the actual outcomes (Figure 4A–C). The AUC values for 1-year, 3-year, and 5-year survival were 0.711 (0.615–0.806), 0.731 (0.629–0.834), and 0.840 (0.745–0.936), respectively (Figure 4D), with a C-index of 0.679. For the IELSG scores in the validation cohort, the corresponding AUC values were 0.593 (0.488–0.697), 0.513 (0.404–0.623), and 0.551 (0.422–0.680) (Figure 4E). For the MSKCC scores, the AUC values were 0.695 (0.648–0.742), 0.706 (0.616–0.796), and 0.683 (0.567–0.800), correspondingly (Figure 4F). Kaplan-Meier survival curves for OS and PFS demonstrated that the novel model exhibited robust discriminatory power in the validation cohort, as confirmed by the Log rank test (OS: $P = 0.00013$; PFS: $P = 0.00037$). Compared to the classical IELSG (OS: $P = 0.47$; PFS: $P = 0.18$) and MSKCC (OS: $P = 0.0039$; PFS: $P = 0.049$) prognostic scoring systems, the novel model achieved superior stratification for both OS and PFS (Figure 5A–F). While the MSKCC system also successfully stratified patients into distinct risk groups, the novel model demonstrated higher precision, particularly in differentiating between low- and medium-risk patients. This underscores its enhanced clinical utility for risk stratification.

Discussion

PCNSL is a rare and aggressive malignancy of the central nervous system with a rising incidence, particularly among the elderly population. The current standard treatment involves HD-MTX based chemotherapy, which has a high initial response rate. However, the treatment of R/R PCNSL remains challenging. There is still no consensus on the optimal treatment strategy for R/R PCNSL.[5] Therefore, developing a reliable prognostic model that can accurately stratify patients is important for improving therapeutic regimens and optimizing survival outcomes of patients with PCNSL.

We used Lasso regression and multivariate Cox regression analysis to evaluate a series of clinical parameters of patients with PCNSL in the development cohort and established a nomogram using four accessible parameters: ECOG-PS score, NLR, D-Dimer, and albumin, allowing for easy interpretation of a patient's predicted OS by summing the variable scores. The model consists of the physical condition, nutritional status, and inflammatory state of the patients

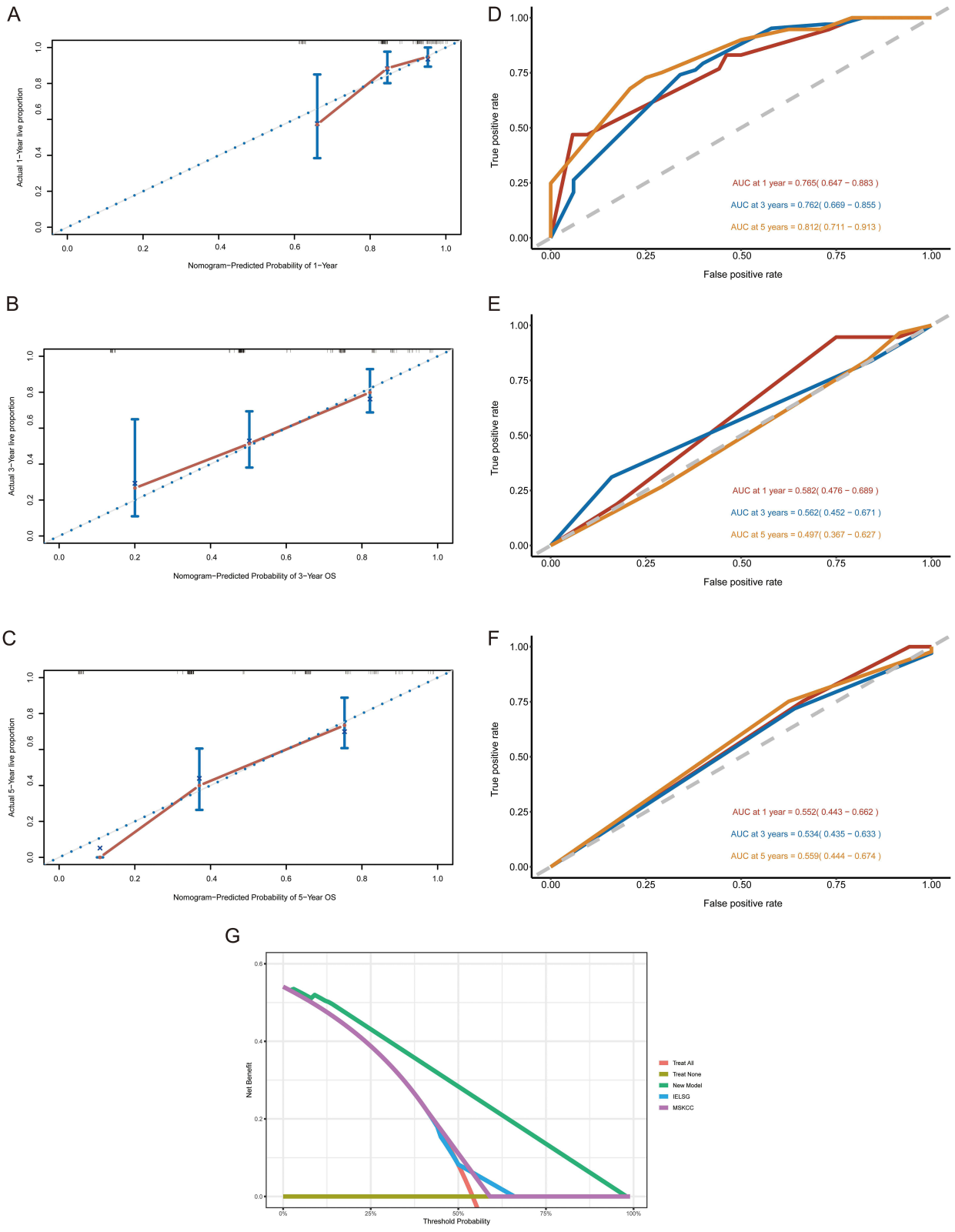

Figure 2 The calibration curve of the novel model for predicting 1, 3 and 5 year OS in the development cohort (**A-C**). The 1, 3 and 5-year ROC curves of the novel model, IELSG and MSKCC prognostic scoring system in the development cohort (**D-F**). (**G**) The DCA was used to estimate clinical usefulness of the three models for predicting OS.

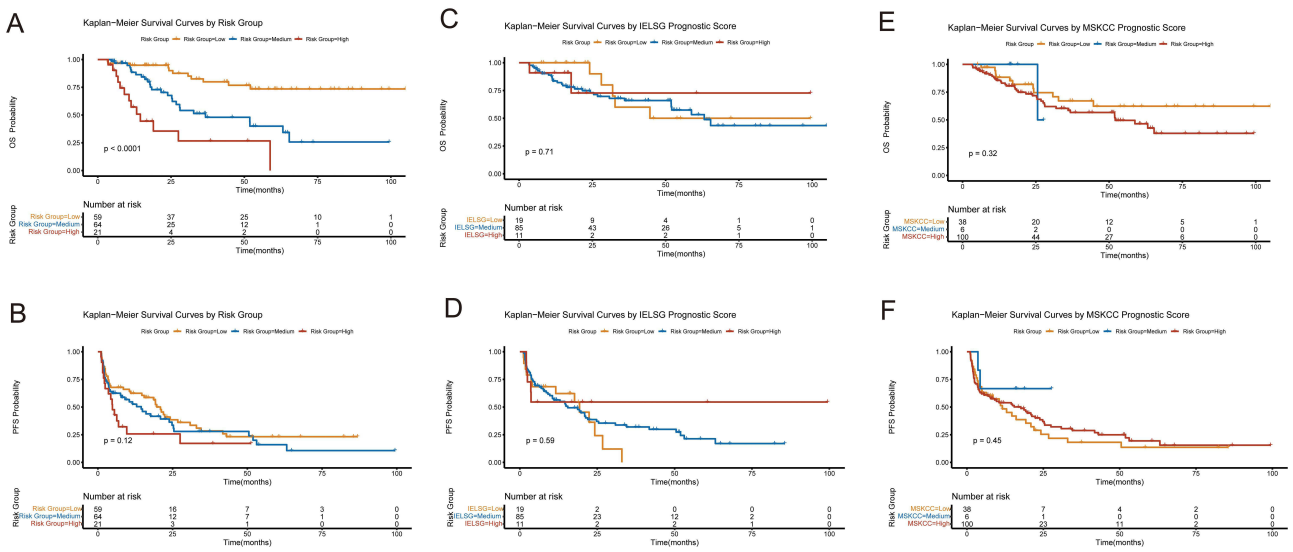

Figure 3 PCNSL patients were stratified into three groups using three models in the development cohort. Kaplan-Meier survival curves for OS and PFS in the development cohort were shown for the novel model (**A** and **B**), IELSG (**C** and **D**), and MSKCC prognostic scoring system (**E** and **F**).

with PCNSL. In the present study, the four factors were significantly correlated with OS: poorer OS was associated with higher ECOG-PS scores, NLR and D-Dimer levels, and worse serum albumin levels.

The ECOG-PS is a standardized system used to assess physical function and daily living abilities of patients with cancer. The ECOG-PS scores range from 0 to 5, with higher scores indicating a poorer performance status. As one of the key factors in predicting prognosis in PCNSL, the ECOG-PS score has frequently been incorporated into various prognostic models to predict the survival of PCNSL patients.[16,22,23] Additionally, the ECOG-PS score was used in the PCNSL-related clinical studies to assess patient eligibility for enrollment.[24] Patients with lower ECOG-PS scores are generally considered to have better treatment toleranceand treated with more aggressive treatment approaches. In this study, the ECOG-PS played the most significant role in the overall model. However, to some extent, the ECOG-PS scores

Table 4 The Median OS and PFS of Three Models in the Development Cohort

Stratification	Median OS (months)	Median PFS (months)
Novel prognostic model		
Low-risk Medium -risk High-risk	NA 36.8 14.5	20.9 14.5 4.9
IELSG prognostic score		
Low-risk Medium -risk High-risk	44.6 63.2 NA	19.3 15.5 NA
MSKCC prognostic score		
Low-risk Medium -risk High-risk	NA 25.6 52.1	11.6 NA 17.7

Abbreviations: OS, overall survival; PFS, progression free survival; NA, not applicable; IELSG, International Extranodal Lymphoma Study Group; MSKCC, Memorial Sloan Kettering Cancer Center.

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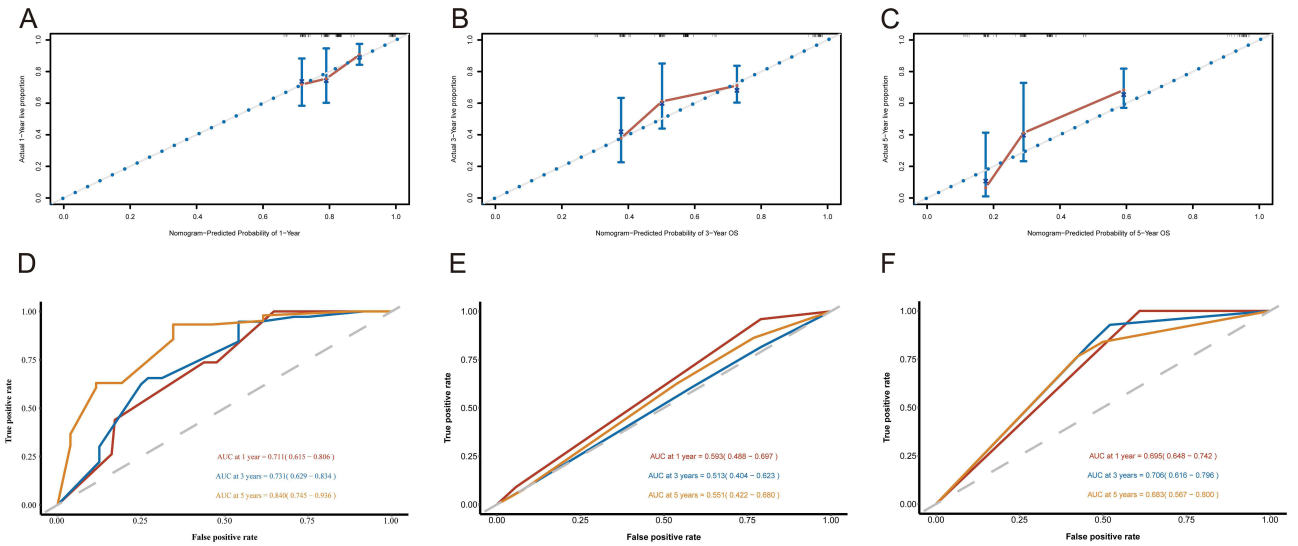

Figure 4 The calibration curve of the novel model for predicting 1, 3 and 5-year OS in the validation cohort (**A-C**). The 1, 3 and 5-year ROC curves of the novel model, IELSG and MSKCC prognostic scoring system in the validation cohort (**D-F**).

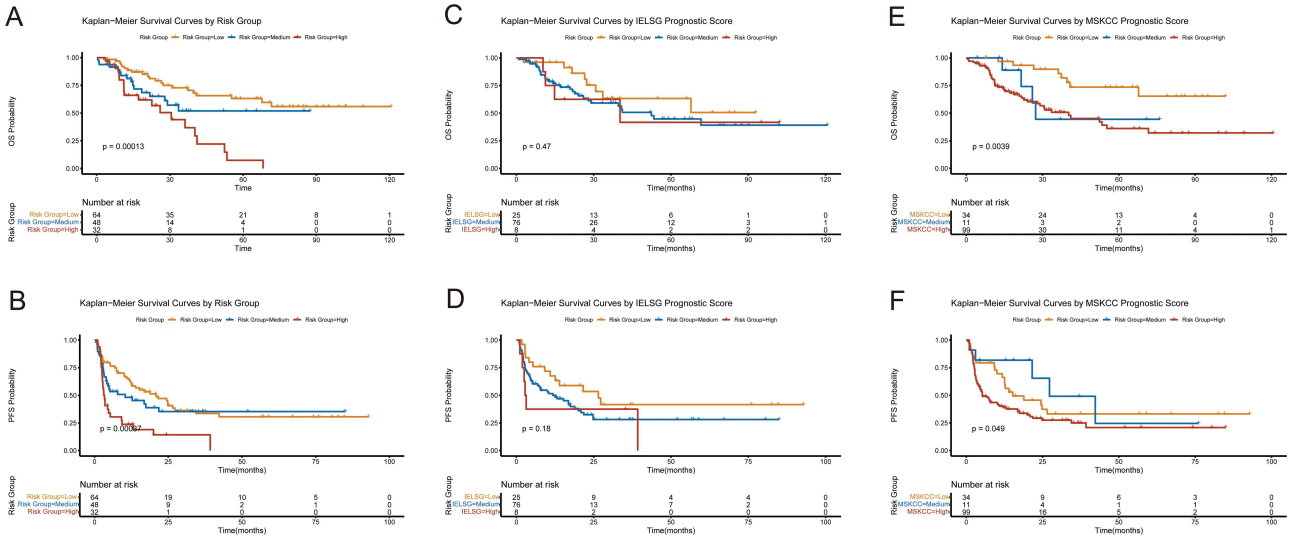

Figure 5 Kaplan-Meier survival curves for OS and PFS in validation cohort according to the novel model (**A** and **B**), IELSG (**C** and **D**) and MSKCC prognostic scoring system (**E** and **F**).

cannot be quantified in detail and are partly subjective. Thus, combining ECOG-PS with other biomarkers and clinical indicators, such as those in this model, yields a more comprehensive prognosis.

The NLR represents a novel indicator for monitoring systemic inflammation and has been widely investigated as a potential biomarker for assessing tumor prognosis.[25–28] A retrospective analysis revealed that NLR was associated with PFS and OS in patients with multiple myeloma (MM) who received transplant therapy.[29] Additionally, elevated NLR at initial diagnosis was associated with poor prognosis in PCNSL patients,[30] whether or not with corticosteroid treatment used.[31] In this study, NLR remained as an independent predictor of poor prognosis in patients with PCNSL, as previously reported.

Elevated D-Dimer levels are correlated with worse tumor prognosis.[32–35] In cancer patients, elevated D-Dimer levels typically indicate high coagulation and fibrinolytic activity, which may reflect a more severe inflammatory state and higher tumor burden.[36] DLBCL patients with elevated D-Dimer levels have been reported to have poorer OS.[34]

Moreover, D-Dimer levels reflect the systemic inflammatory response and tissue damage.[37] Although D-Dimer level alone may be insufficient as a reliable prognostic marker owing to the influence of various confounding factors, this study is the first to highlight its potential value in predicting the prognosis of patients with PCNSL.

Serum albumin level is often considered as a clinical indicator for monitoring systemic inflammatory response.[38] Chronic inflammation is common in patients with tumors, and a decrease in serum albumin level can reflect the extent of inflammation. During a systemic inflammatory response, immune cells activate and release cytokines that inhibit hepatic albumin synthesis.[39] In cancer patients, albumin levels frequently decrease owing to increased metabolic demands caused by the disease and its treatment. Additionally, in patients with PCNSL, severe hypoalbuminemia can lead to fluid leakage into tissues, third-space fluid retention, and impaired methotrexate (MTX) clearance, negatively affecting the treatment response and tolerance. Studies have shown that low albumin level is an adverse prognostic factor for various cancers. Serum albumin levels are used as independent prognostic indicator.[40–42] For example, the modified Glasgow Prognostic Score (mGPS) combines albumin and C-reactive protein (CRP) levels to assess the prognosis of patients with cancer patients.[43] The health and nutritional status of a patient can be assessed based on the level of albumin, which provides an important guide for treatment. For patients with low albumin levels, improving nutrition and treating inflammation should be prioritized before further treatment. Albumin is a cost-effective prognostic indicator in patients with PCNSL.

The MSKCC and IELSG scoring systems are widely used and are therefore of great importance. However, their limitations have gradually become evident with the advent of intensified therapies.[44] For example, CSF protein levels, a key element in the IELSG system, may not always be available for some patients with PCNSL with contraindications for lumbar puncture. Gao et al reported that the MSKCC system could not accurately distinguish low- and medium-risk patients.[10] In our study, Kaplan-Meier survival curves also illustrated that there was no statistical difference in OS among all three risk groups according to the MSKCC prognostic model, and the survival curve of the high-risk group intersected with the other two curves during the follow-up period. In addition, no significant differences in OS were found when the IELSG system was used. Conversely, OS could be precisely discriminated in the development cohort using our model, and the high-risk group predicted poor prognosis. As we suspected, this model also showed excellent risk stratification ability in the validation cohort, which confirmed the robustness of our model. Moreover, time-dependent ROC curve analysis was implemented in both the development and validation cohorts, and when compared with the IELSG and MSKCC scoring systems, this model improved the predictive efficiency of 1-year, 3-years and 5-years OS in patients with PCNSL.

However, despite these advantages, this model has several limitations. First, this is a single-center study, and external validation is needed to confirm its predictive accuracy in a multicenter prospective cohort study. Furthermore, owing to the retrospective nature of the data, there may have been bias in the research. Fortunately, the data from single-center study have good uniformity and comparability. Nonetheless, PCNSL is a rare disease and the development of this prognostic model based on a large sample size with complete variables and validation makes it a promising tool for clinical use.

Conclusion

In summary, we developed a novel prognostic model for patients with PCNSL, which is presented in the form of a nomogram, providing a practical tool for stratifying patients into distinct risk groups based on readily available clinical data. Besides, this robust predictive model may provide guidance for clinicians to evaluate PCNSL risk stratification and optimize treatment strategies. The prognostic utility of the nomogram should be further validated through multicenter studies.

Data Sharing Statement

Data collected for this study, including individual patient data, cannot be made publicly available due to privacy/regulatory restrictions but can be requested by the corresponding author.

Ethics Approval and Informed Consent

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Huashan Hospital, Fudan University (Approval No. 2022-008). All participants provided signed consent before participating in the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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