

Development and validation of web-based risk score predicting prognostic nomograms for elderly patients with primary colorectal lymphoma: A population-based study

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ABSTRACT

Background and Objectives: Primary colorectal lymphoma (PCL) is an infrequently occurring form of cancer, with the elderly population exhibiting an increasing prevalence of the disease. Furthermore, advanced age is associated with a poorer prognosis. Accurate prognostication is essential for the treatment of individuals diagnosed with PCL. However, no reliable predictive survival model exists for elderly patients with PCL. Therefore, this study aimed to develop an individualized survival prediction model for elderly patients with PCL and stratify its risk to aid in the treatment and monitoring of patients. **Methods:** Patients aged 60 or older with PCL from 1975 to 2013 in the Surveillance, Epidemiology, and End Results database were selected and randomly divided into a training cohort ($n = 1305$) and a validation cohort ($n = 588$). The patients from 2014–2015 ($n = 207$) were used for external validation. The research team utilized both Cox regression and the least absolute shrinkage and selection operator (LASSO) regression to analyze potential predictors, in order to identify the most suitable model for constructing an OS-nomogram and an associated network version. The risk stratification is constructed on the basis of this model. The performance of the model was evaluated based on the consistency index (C-index), calibration curve, and decision curve analysis (DCA) to determine its resolving power and calibration capability. **Results:** Age, gender, marital status, Ann Arbor staging, primary site, surgery, histological type, and chemotherapy were independent predictors of Overall Survival (OS) and were therefore included in our nomogram. The Area Under the Curve (AUC) of the 1, 3, and 5-year OS in the training, validation, and external validation sets ranged from 0.732 to 0.829. The Receiver Operating Characteristic (ROC) curves showed that the nomogram model outperformed the Ann Arbor stage system when predicting elderly patients with PCL prognosis at 1, 3, and 5 years in the training set, validation dataset, and external validation cohort. The Concordance Index (C-index) also demonstrated that the nomogram had excellent predictive accuracy and robustness. The calibration curves demonstrated a strong agreement between observed and predicted values. In the external validation cohort, the C-index (0.769, 95%CI: 0.712–0.826) and calibration curves of 1000 bootstrap samples also indicated a high level of concordance between observed and predicted values. The nomogram-related DCA curves exhibited superior clinical utility when compared to Ann Arbor stage. Furthermore, an online prediction tool for overall survival has been developed: <https://medkuiwang.shinyapps.io/DynNomapp/>. **Conclusion:** This was the first study to construct and validate predictive survival nomograms for elderly patients with PCL, which is better than the Ann Arbor stage. It will help clinicians manage elderly patients with PCL more accurately.

Key words: elderly patients with primary colorectal lymphoma, external validation, online prediction tool, overall survival, nomograms

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BACKGROUND

Primary colorectal lymphoma is rare. It accounts for only 0.2% to 0.6% of all colon cancers and 15% to 20% of gastrointestinal lymphomas.^[1] There is a male predominance, with the highest incidence reported in the 50–70 age group.^[2] The most common variety of colonic lymphoma is non-Hodgkin's lymphoma (NHL). Diffuse large B-cell lymphoma is the most common histologic subtype.^[3,4] The clinical manifestations are usually nonspecific, leading to a delay in diagnosis. Primary extra-nodal NHL should be considered when pathologic changes of lymphoma are observed in one organ and there is no other clinical evidence of spread from distant lymph nodes or other primary organs.^[5] Histologic diagnosis is usually obtained after pathological examination of endoscopically or surgically removed tissue. Endoscopic findings are varied and include mucosal nodules, mucosal atrophy, mucosal ulcers, and masses with or without ulcers.^[6] Given the rarity of this disease, treatment recommendations are mostly based on case series data rather than large randomized clinical trials.^[7] As the traditional staging system for NHL, the Ann Arbor staging system uses the location of lymph node spread as the basis for staging.^[8,9] It does not include other factors that may affect long-term survival, such as age and treatment. In addition, the Ann Arbor staging system is not considered to be the best staging system for primary colorectal lymphoma.^[10,11] Nomograms are a dependable and easy-to-use prognostic tool that has been widely utilized in the field of oncology to forecast the overall probability of certain results by considering a number of prognostic elements.^[12–15] Elderly patients are more likely than younger patients to be intolerant of radical radiation therapy. Elderly patients typically possess a diminished physical state and a greater number of comorbidities, making them less tolerant of comprehensive treatment.^[16] The impact of various factors on the prognosis of elderly patients with PCL is significant, and thus, it is essential to consider these factors when predicting the survival of such patients.^[17]

Drawing from the SEER database, we have gathered data from a substantial number of patients to construct a survival prediction nomogram and a risk-stratifying system that can dynamically anticipate the long-term survival of elderly PCL.

METHODS

Patient and variables

All data in this study were obtained with SEER*Stat software version 8.4.0.1. In the SEER database, subjects with PCL were identified by histological code 9731/3 of the International Classification of Diseases of Oncology, Third

Revision (ICD-O-3). To enhance the representativeness of this study, elderly patients with PCL were extracted from three databases from SEER: those diagnosed between 2000 and 2015 were obtained through the SEER 18 registry data, patients diagnosed between 1992 and 1999 were extracted from the SEER 13 registry data, and those diagnosed between 1975 and 1991 were acquired through the SEER 9 registry data. Histological type is limited to lymphoma. Primary site codes (C18.0–C18.9, C19.9, and C20.9) to identify lymphomas primarily localized in the colon or rectum.^[18] The individualized data we extracted from the SEER database included Ann Arbor stage, survival time, age at diagnosis, sex, year of diagnosis, race, sex, and treatment (radiotherapy, chemotherapy, and surgery), vital status, and marital status, histological type, primary site. The criteria for exclusion were that individuals must not meet the following requirements: (1) Patients who were diagnosed by post-mortem or based on death certificates, or those for whom there was no active monitoring, were identified, (2) Patients with a survival time of 0 months or unknown survival time, (3) Patients with incomplete individualized data were not included in this study, (4) Age < 60 years old. The final day of follow-up was December 31, 2018. The endpoint of the study was OS and the follow-up period was defined as the period from diagnosis to death or the patient's last follow-up date or cut-off date. The patient screening process is illustrated in Figure 1. Detailed clinical information is provided in Table 1. Given that the SEER database is publicly available, and the data for all patients is anonymized, no institutional review board approval or informed consent was necessary for this study.

Statistical analysis

To construct and validate the nomogram and ensure the accuracy of the prediction model, we randomly allocated 70% ($n = 1305$) of patients from 1975 to 2013 to the training cohort, and 30% ($n = 588$) of patients from 1975 to 2013 to the validation cohort. For external validation, 207 patients in the SEER database from 2014–2015 were included in the external validation cohort. Cox regression models were evaluated to determine if the proportional hazards (PH) assumption was valid. Categorical variables were tabulated and the proportions reported, and the differences in the distribution of variables between the training and validation groups were assessed using chi-square tests. Under the assumption of normality and homogeneity of variance, continuous variables would be reported as mean and standard deviation and analyzed using *t*-tests, and if this condition was not met, median and interquartile range (IQR) would be reported and analyzed using Wilcoxon rank-sum tests. Prognostic correlations were screened based on univariate Cox regression and least absolute reduction and selection operator (LASSO).^[19,20] Variables corresponding to $P < 0.20$ in univariate analysis

Table 1. Clinical and Pathologic Characteristics of Elderly Patients with PCL

Characteristics	All patients (<i>n</i> = 1893)	Training (<i>n</i> = 1305)	Validation (<i>n</i> = 588)	<i>P</i>
Age (median [IQR])	74.000 [67.0, 80.0]	74.000 [67.0, 80.0]	74.000 [67.0 80.0]	0.8947
Year (%)				
1975-1999	458 (24.19)	312 (23.91)	146 (24.83)	0.6213
2000-2009	1013 (53.51)	694 (53.18)	319 (54.25)	
2010-2013	422 (22.29)	299 (22.91)	123 (20.92)	
Sex (%)				
Female	804 (42.47)	554 (42.45)	250 (42.52)	1
Male	1089 (57.53)	751 (57.55)	338 (57.48)	
Race (%)				
Black	80 (4.23)	54 (4.14)	26 (4.42)	0.946
Other ^a	210 (11.09)	146 (11.19)	64 (10.88)	
White	1603 (84.68)	1105 (84.67)	498 (84.69)	
Location (%)				
left	303 (16.01)	207 (15.86)	96 (16.33)	0.4404
Nos	245 (12.94)	180 (13.79)	65 (11.05)	
Rectum	290 (15.32)	198 (15.17)	92 (15.65)	
right	1055 (55.73)	720 (55.17)	335 (56.97)	
Ann Arbor Stage (%)				
I	874 (46.17)	607 (46.51)	267 (45.41)	0.4713
II	460 (24.30)	304 (23.30)	156 (26.53)	
III	91 (4.81)	65 (4.98)	26 (4.42)	
IV	468 (24.72)	329 (25.21)	139 (23.64)	
Radiation (%)				
None/Unknown	1735 (91.65)	1189 (91.11)	546 (92.86)	0.2375
Radiation	158 (8.35)	116 (8.89)	42 (7.14)	
Chemotherapy (%)				
No/Unknown	926 (48.92)	655 (50.19)	271 (46.09)	0.109
Yes	967 (51.08)	650 (49.81)	317 (53.91)	
Surgery (%)				
No	726 (38.35)	495 (37.93)	231 (39.29)	0.6102
Surgery	1167 (61.65)	810 (62.07)	357 (60.71)	
Histology (%)				
BL	58 (3.06)	43 (3.30)	15 (2.55)	0.6852
DCBCL	882 (46.59)	611 (46.82)	271 (46.09)	
FL	175 (9.24)	122 (9.35)	53 (9.01)	
MCL	192 (10.14)	132 (10.11)	60 (10.20)	
MZL	308 (16.27)	201 (15.40)	107 (18.20)	
Others ^b	278 (14.69)	196 (15.02)	82 (13.95)	
Marriage (%)				
Married	1221 (64.50)	838 (64.21)	383 (65.14)	0.737
No	672 (35.50)	467 (35.79)	205 (34.86)	

IQR, interquartile range; NOS, not otherwise specified; DCBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma, MZL, extranodal marginal zone lymphoma of mucosal-associated lymphoid tissue; Nos, not otherwise specified in colon. ^aOther includes: American Indian/Alaskan Native or Asian/Pacific Islander. ^bOther includes: Malignant lymphoma, NOS; Non-Hodgkin lymphoma, NOS; Malignant lymphoma, small B lymphocytic, NOS; Peripheral T-cell lymphoma, NOS; Non-Hodgkin lymphoma, NOS; Lymphoplasmacytic lymphoma; Anaplastic large cell lymphoma, ALK-positive; Malignant lymphoma, NOS.

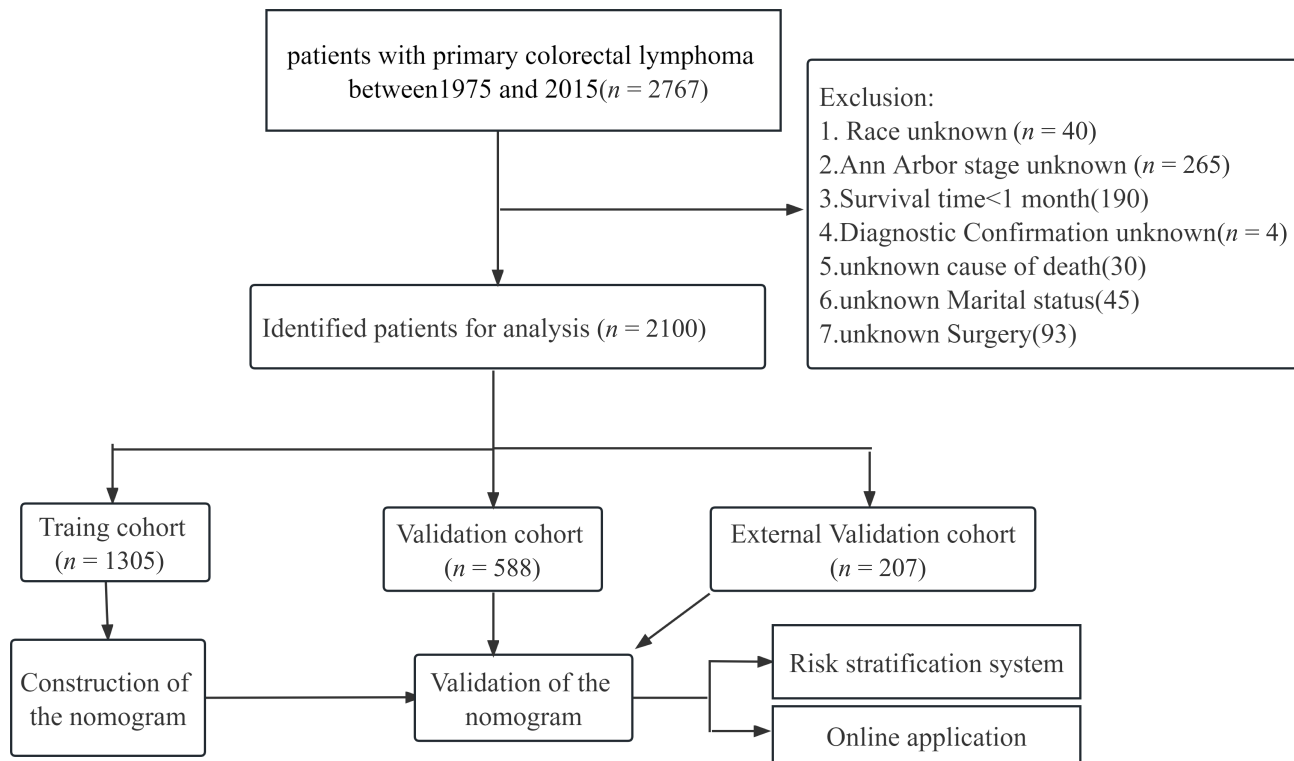


Figure 1: The flowchart of the inclusion and exclusion of patients.

or one standard error of the penalty coefficient (Lambda) of the least mean squared error (MSE) of the LASSO was incorporated into multivariate Cox regression with stepwise backward validation, respectively. Based on the results of multivariate Cox regression and stepwise backward analysis, a nomogram based on clinicopathological factors was created using the RMS package. The accuracy of the nomogram was evaluated using a receiver operating characteristic (ROC) curve and a concordance index (C-index) with 95% confidence intervals. Clinical predictive models can offer doctors and patients a numerical risk value based on current health status to anticipate future health status utilizing non-invasive, low-cost, and easily collected indicators, which has important health economics significance.^[21] The accuracy of the nomograms was evaluated using a C-index and ROC curve with 95% confidence intervals. Statistical analyses for this study were conducted using R language (version 4.2.2). A *P*-value of less than 0.05 was considered to indicate a statistically significant difference.

RESULTS

Patients characteristic

The study flowchart is depicted in Figure 1. In conclusion, a total of 1893 cases of elderly patients with PCL were identified in the SEER three database between January

1, 1975, and December 31, 2013, 1089 (57.53%) of whom were male and 1603 (84.68%) were White. The demographic and clinicopathological characteristics of patients are presented in Table 1. The median age of the patients at diagnosis is 74 years (IQR: 67 and 80 years). Among the different pathological types, the most common type was DLBCL (46.59%), followed by marginal zone B-cell lymphoma (16.27%), other/unclassified types (14.69%), mantle cell lymphoma (10.14%), follicular lymphoma (9.24%) and Burkitt's lymphoma (3.06%). The distribution of the Ann Arbor stage was 874 (46.17%) for stage I, 460 (24.30%) for stage II, 91 (4.81%) for stage III, and 468 (24.72%) for stage IV. A total of 1167 (61.65%) patients underwent Surgery, 967 (51.08%) received chemotherapy, and 158 (8.35%) underwent radiotherapy. No discernible statistical disparities were observed in the clinicopathological attributes between the training and validation cohorts. The external validation cohort's patient features can be found in the accompanying Supplementary Table S1.

Survival predictors screening

For each of the 1893 individuals within the training cohort, univariate Cox regression and LASSO regression analyses were systematically performed. A single-factor Cox regression analysis revealed statistically significant differences in age, Ann Arbor stage, histologic type,

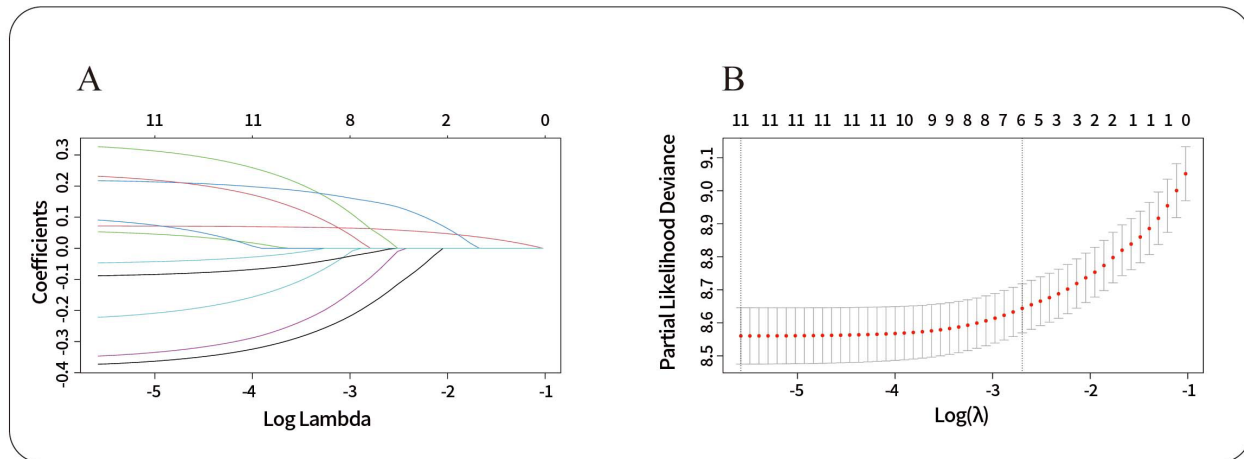


Figure 2: A LASSO regression coefficient distribution for OS. B Cross-validation plot for OS. Each colored curve presents the LASSO coefficient of a variable at a different lambda value.

gender, location, surgery, chemotherapy, marital status, and diagnosis year ($P < 0.20$). Lasso regression and cross-validation were conducted on 11 variables. Six factors for predicting elderly patients with PCL were identified through LASSO regression, including age, Ann Arbor stage, histology type, gender, chemotherapy, and marital status. (Figure 2) Combined with clinical experience, surgery was included for further screening multivariate Cox regression with stepwise backward validation. Ultimately, the prognostic factors for elderly patients diagnosed with PCL included age, Ann Arbor staging, histological subtype, sex, chemotherapy treatment, surgical intervention, and marital status. The corresponding multivariate Cox regression analysis, which yielded statistically significant results ($P < 0.05$), is presented in Table 2.

OS and predictive determinants of clinical outcomes of the training set

In the training set, the median OS of elderly patients with PCL was 67 (1–380) months. the 1-, 3-, and 5-year overall survival rates were 76.6 % (95% CI: 0.743–0.789), 65.1 % (95% CI: 0.625–0.677), and 55% (95% CI: 0.524–0.578), respectively. The FL patients exhibited the highest five-year survival rate at 76.9% (95% CI: 69.8–84.8), whereas the BL patients had the lowest five-year survival rate at 44.2% (95% CI: 31.6–61.8). The median survival duration for patients diagnosed with MZL was observed to be the most extended, at 136 months, while patients with DCBCL experienced the briefest median survival period, recorded at 51 months. Surgery has been shown to improve overall survival in older PCL patients, but not in all populations. Kaplan-Meier curves demonstrate a significant difference between surgery and overall survival in Ann Arbor stage I patients ($P = 0.0032$), while no significant improvement

was found in Ann Arbor stage II, III, and IV patients ($P > 0.05$). The survival rates of patients diagnosed within the periods of 2010–2013 and 2000–2009 showed a significant increase compared to those diagnosed between 1975 and 1999 (with both $P < 0.05$). Chemotherapy patients may improve overall survival. The prognostic outcomes for patients in the initial stages of the Ann Arbor classification, as well as those who are married, demonstrated greater improvement compared to other distinct patient cohorts. (Figure 3)

Construction of nomogram for predicting 1-, 3-, and 5-year OS

Seven independent predictors were utilized to create the nomogram for OS. (Figure 4) By integrating the scores linked to each attribute and mapping the cumulative scores onto the lower axis, one can approximate the probability of OS at 1-year, 3-year, and 5-year intervals. Our predictive model can be used to predict individual patient outcomes based on their specific characteristics.

Prognostic nomogram model validation

The analysis of receiver operating characteristic curves revealed that the respective AUC for 1-year, 3-year, and 5-year overall survival rates were 0.745, 0.761, and 0.766 in the training dataset, while in the validation dataset, these values were 0.741, 0.727, and 0.732. The examination of the ROC demonstrated that the corresponding AUC values for overall survival rates at 1-year, 3-year, and 5-year intervals amounted to 0.817, 0.798, and 0.829 (Figure 5), respectively, within the external validation cohort. The ROC curves (Figure 5) demonstrated that the nomogram model was more accurate than the Ann Arbor stage system in predicting the prognosis of elderly patients with PCL

Table 2. The Univariate and Multivariate Cox Regression Analysis in the Training Cohort (*n* = 1305) of Elderly Patients with PCL for OS.

Characteristics	Univariate Cox regression		Munivariate cox regression	
	HR. 95% CI	P-value	HR. 95% CI	P-value
Age	1.08 (1.07–1.09)	<0.01	1.07 (1.06–1.08)	<0.01
Ann Arbor stage				
I	Reference		Reference	
II	1.57 (1.33-1.85)	<0.01	1.42 (1.20 - 1.69)	<0.01
III	1.63 (1.20 -2.22)	<0.01	1.75 (1.28 - 2.40)	<0.01
IV	1.89 (1.62-2.22)	<0.01	1.95 (1.65 - 2.31)	<0.01
Gender				
Female	Reference		Reference	
Male	1.15 (1.01-1.31)	0.043	1.44 (1.24 - 1.66)	<0.01
Histology				
BL	Reference		Reference	
DCBCL	0.85 (0.60-1.20)	0.347	0.62 (0.44 - 0.89)	0.011
FL	0.40 (0.26-0.61)	<0.01	0.36 (0.23 - 0.55)	<0.01
MCL	0.66 (0.45-0.98)	0.04	0.53 (0.36 - 0.80)	0.001
MZL	0.42 (0.29-0.62)	<0.01	0.38 (0.25 - 0.56)	<0.01
Others ^a	0.73(0.50-1.05)	0.092	0.54(0.36 - 0.79)	<0.01
Location				
Left	Reference		Reference	
Right	0.94 (0.76-1.09)	0.321	NA	NA
Nos	0.94 (0.74-1.19)	0.605	NA	NA
Rectum	0.79 (0.63-1.00)	0.053	NA	NA
Marital status				
Married	Reference		Reference	
No	1.46 (1.28-1.67)	<0.01	1.30 (1.12 - 1.51)	<0.01
Race				
Black	Reference		Reference	
White	1.11 (0.80-1.55)	0.534	NA	NA
Other ^b	0.86 (0.59-1.26)	0.443	NA	NA
Surgery				
No	Reference		Reference	
Surgery	0.91 (0.80-1.05)	0.192	0.78 (0.68 - 0.91)	<0.01
Radiation				
No/unknown	Reference		Reference	
Radiation	0.99 (0.79-1.24)	0.927	NA	NA
Chemotherapy				
No/unknown	Reference		Reference	
Chemotherapy	0.85 (0.75-0.97)	0.014	0.73 (0.63–0.84)	<0.01
Year				
1975-1999	Reference		Reference	
2000-2009	0.72 (0.62-0.83)	<0.01	0.72 (0.61–0.84)	<0.01
2010–2013	0.52 (0.41-0.64)	<0.01	0.53 (0.42–0.66)	<0.01

HR, hazard ratio; CI, confidence intervals; NA, not applicable. OS, overall survival. ^aOther includes: Malignant lymphoma, NOS; Non-Hodgkin lymphoma, NOS; Malignant lymphoma, small B lymphocytic, NOS; Peripheral T-cell lymphoma, NOS; Non-Hodgkin lymphoma, NOS; Lymphoplasmacytic lymphoma; Anaplastic large cell lymphoma, ALK-positive; Malignant lymphoma, NOS. ^bOther includes: American Indian/Alaskan Native or Asian/Pacific Islander. Supplementary tables: demonstrates the patients (*n* = 207) in the external validation group.

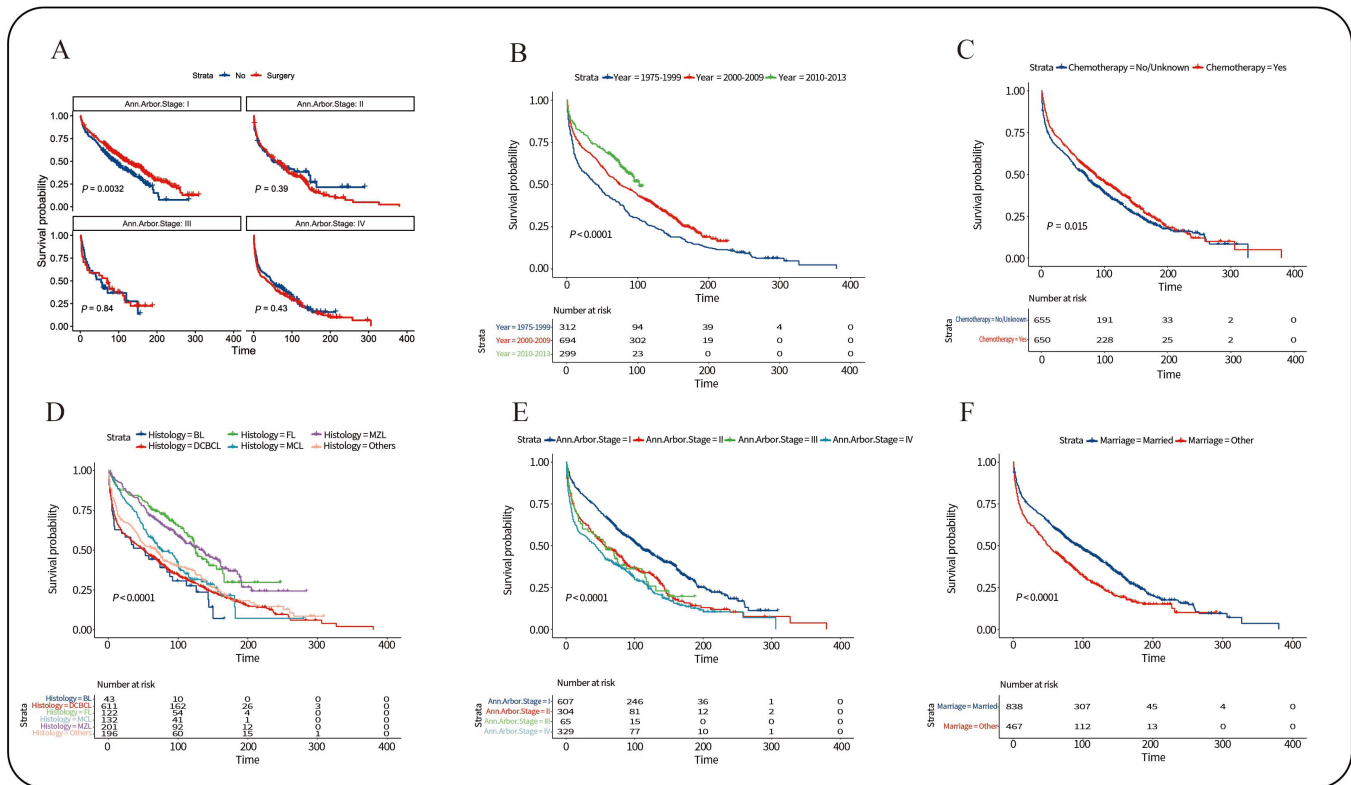


Figure 3: Kaplan-Meier survival analysis for elderly patients with PCL. (A) Surgery, (B) Year of diagnosis, (C) Chemotherapy, (D) Histology, (E) Ann Arbor stage, (F) Marital status.

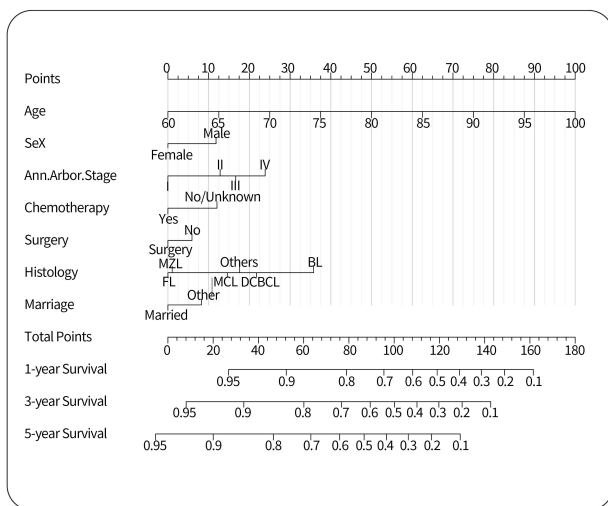


Figure 4: Nomogram for Predicting Overall Survival (OS) at 1, 3, and 5 Years in Elderly Patients with PCL.

at 1, 3, and 5 years in the training set, validation dataset, and external validation cohort. (Figure 6) Decision Curve Analyses (DCAs) revealed that the clinical utility of the nomograms was superior to that of the Ann Arbor stage system in the training cohort, validation cohort, and external validation. The C-index of the training cohort was

0.705 (95% CI: 0.687–0.723), indicating that the model had good discriminatory power. The C-index of the validation cohort was 0.744 (95% CI: 0.726–0.762), and the C-index of the external validation cohort was 0.769 (95% CI: 0.712–0.826), demonstrating the model's strong predictive ability. (Figure 7) The calibration curves of 1000 bootstrap samples pertaining to both the training and validation cohorts, employed to prognosticate OS, exhibit a robust association between the empirical observations and the predictions generated by the model.

Stratification of risk founded upon the prognostic nomogram

The comprehensive evaluation of patients' scores was conducted based on the principles delineated by the nomogram. The best cut-off point of the total score was determined by the cut-point value of the “survminer” package, according to prognostic status. Patients were stratified into two groups based on a cut-off value of 69.09 (Figure 8A). with those scoring higher being classified as high-risk and those scoring lower being classified as low-risk. In both the training and validation datasets, Kaplan-Meier curves demonstrated that the survival rate of patients in the high-risk group was significantly lower than that of the low-risk group. (Figure 8 B–C). The survival rates at one, three, and five years for the high-risk cohort were

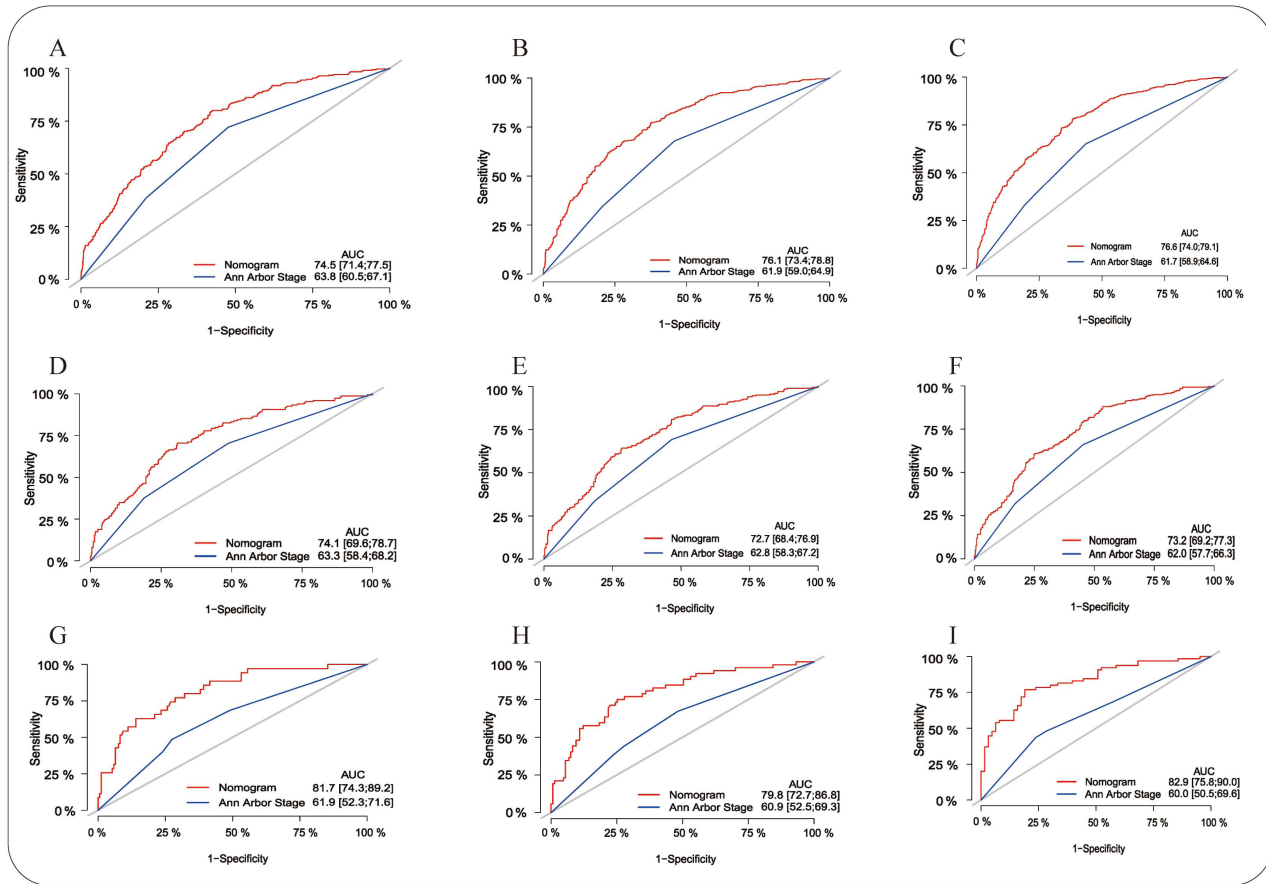


Figure 5: A-C ROC curves for 1, 3, and 5 years predicted by OS nomogram and Ann Arbor stage in training set. D-F ROC curves for 1, 3, and 5 years predicted by the OS nomogram and Ann Arbor stage in the Internal validation set. G-I ROC curves for 1, 3, and 5 years predicted by the OS nomogram and Ann Arbor stage in the External Verification set.

observed to be 67.1%, 51.4%, and 39.7%, correspondingly. Conversely, the low-risk cohort demonstrated survival rates of 91.1%, 86.0%, and 78.6% at the same one, three, and five-year intervals, respectively. This research established a risk prediction system that can accurately forecast the probability of elderly patients with PCL with OS, thus aiding clinicians in creating personalized treatment plans for patients. The proposed model has the potential to reduce the severity of illness in patients and optimize the utilization of medical resources, which is essential for tertiary prevention.

An online platform for predicting operating systems is proposed

The prognostic nomogram was made available via a free browser-based online calculator available at <https://medkuiwang.shinyapps.io/DynNomapp/>. The development of the web-based application was founded on the utilization of the R package “shiny” as its core framework. Upon inputting the characteristics of the patient, the calculated probability of survival can be

instantaneously obtained. In summary, this web-based prognostic instrument offers a user-friendly and efficient means for clinical utilization.

DISCUSSION

Given the infrequency of PCL occurrences, there is a scarcity of research conducted within a population-based context on this particular subject. To the best of our knowledge, no prognostic nomogram currently exists specifically for evaluating the outcomes of geriatric patients diagnosed with PCL. An accurate model was developed to calculate the OS rates of elderly PCL patients at 1-, 3-, and 5-years post-diagnosis based on the clinical data of elderly PCL patients from the SEER dataset. The Ann Arbor system is a commonly used approach in clinical practice for physicians and researchers to assess tumor prognosis and determine treatment plans.^[22,23] Nevertheless, it disregards significant risk factors such as age, race, and marital status. Furthermore, the International Prognostic Index (IPI) and related indices can also stratify the prognosis of lymphoma

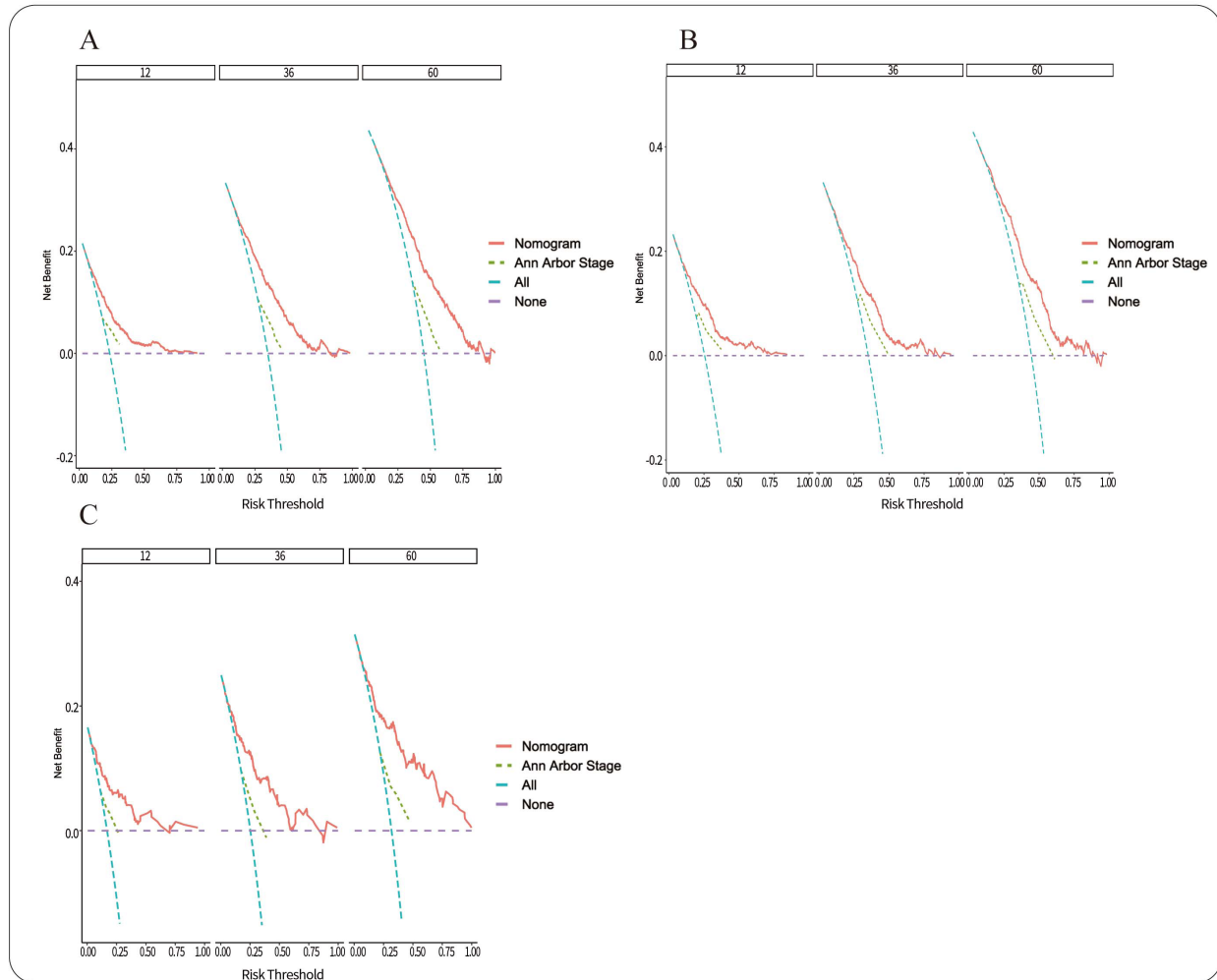


Figure 6: A DCA of the clinical benefit of the OS nomogram vs. Ann Arbor stage in the training set. B DCA of the clinical benefit of the OS nomogram vs. Ann Arbor stage in the Internal validation set. C DCA of the clinical benefit of the OS nomogram vs. Ann Arbor stage in the External Verification set. The y-axis represents the net benefit and the x-axis represents the threshold probability. The blue-magenta line indicates that no patients died, and the cyan line indicates that all patients died. When the threshold probability is between 20 and 60%, the net benefit of the model exceeds all deaths or no deaths.

into risk groups.^[24,25] The evaluation criteria comprised age, stage, ECOG score, extranodal lesions, and LDH level, yet do not incorporate cancer-related treatment information.

Hence, the development of a comprehensive model to predict the risk of PCL in the elderly population is imperative, as it facilitates the formulation of more tailored therapeutic approaches for each patient. In alignment with prior research, the majority of patients within this context are found to be male, of Caucasian descent, and married, having undergone surgical intervention.^[26] The prognosis of elderly patients is affected by a variety of factors. The biological differences of elderly patients, such as more aggressive histology and different distribution of disease, can have an impact on the prognosis.^[27,28] Elderly individuals tend to have a greater number of concurrent

medical conditions than their younger counterparts, which can negatively impact their prognosis.^[29] Being married is a significant predictor of outcomes for many types of cancer.^[12,30] This study found that marital status is a significant factor in OS. It is possible that married patients receive more emotional and financial support from their families, which may contribute to a better prognosis. Gender may influence patient outcomes due to differences in hormone levels. It has been widely documented that males are more likely to develop and have worse outcomes from most types of cancer.^[31] This study found that the prevalence of male patients with PCL was higher than that of female patients, and their prognosis was poorer. Chemotherapy has been shown to increase the likelihood of OS.^[32] In our study, 967 (51.08%) patients underwent chemotherapy, and the results indicated that chemotherapy

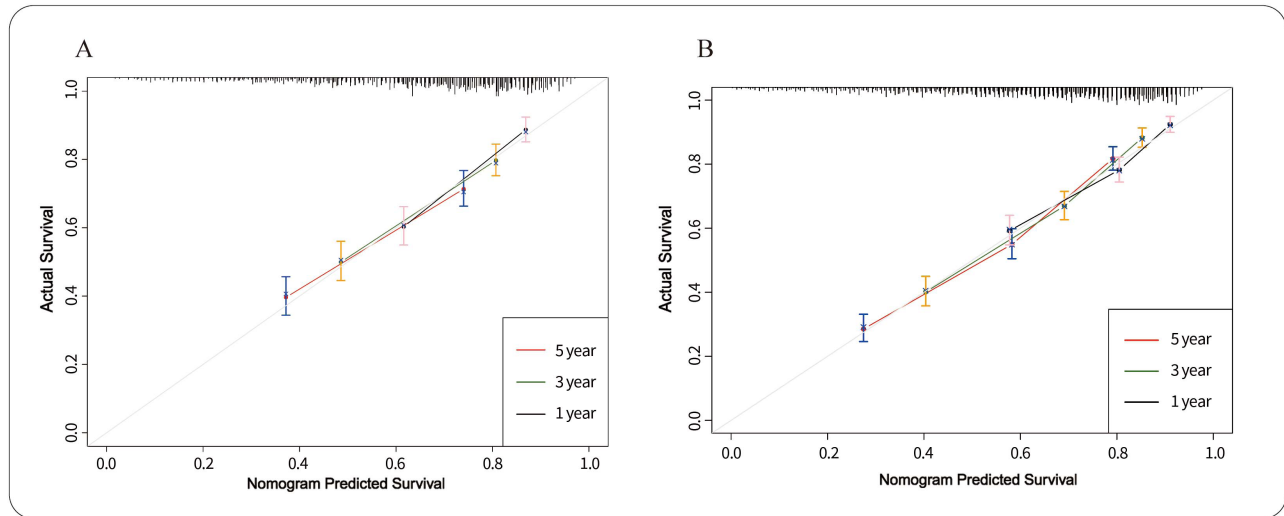


Figure 7: Calibration curves. The x-axis represents the predicted probability of survival. The y-axis represents the actual probability of survival. The diagonal lines (gray) indicate the “ideal” calibration curves (predicted probability equals true probability). **A** Calibration curves for 1, 3, and 5 years for the OS nomogram in the training set. **B** Calibration curves for 1, 3, and 5 years for the OS nomogram in the internal validation set.

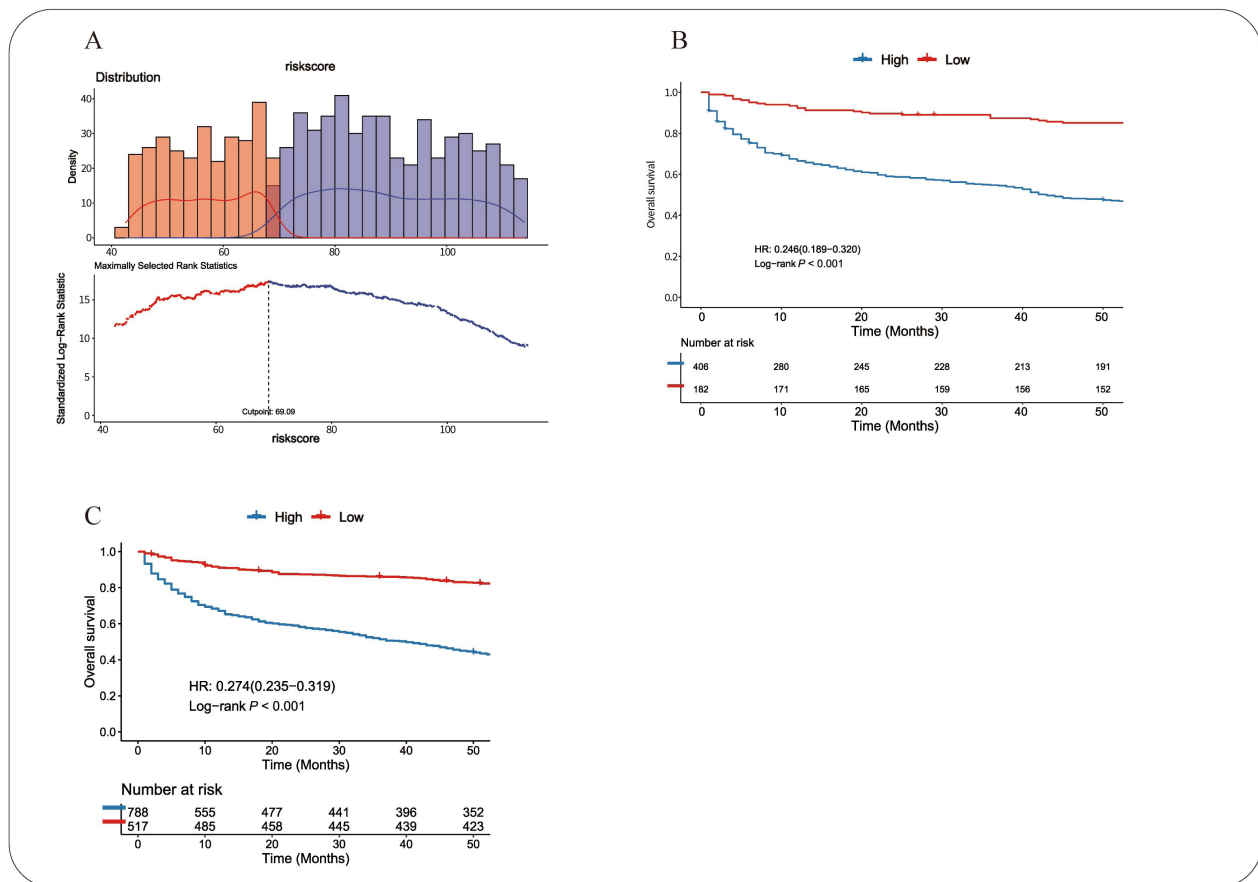


Figure 8: A Patients were stratified into two groups based on a cut-off value, Kaplan-Meier curves of OS for patients in the low- and high-risk groups in the training cohort (**B**), validation cohort (**C**).

is a prognostic factor. Additionally, a statistically significant improvement in overall survival was observed in Ann Arbor stage I patients who underwent surgery compared to those who did not ($P = 0.0032$). However, no significant difference in overall survival was found in Ann Arbor stage II, III, and IV patients ($P > 0.05$). The results of this study suggest that the Ann Arbor stage and histological subtypes of elderly PCL patients are significantly associated with their survival. Patients with early-stage lymphoma were found to have a better prognosis, which is in agreement with previous research.^[33] As the outlook for individuals with primary colorectal lymphoma has improved, attention has shifted to identifying and addressing potential risk factors in vulnerable populations, particularly the elderly.^[34] Elderly age at diagnosis is still one of the most significant factors associated with a poor prognosis. The prognosis of PCL patients has been improving over time, largely due to the advancement of diagnostic techniques such as imaging, blood testing, immunohistological evaluation, and the efficacy of targeted medications, particularly rituximab.^[35–40]

It is important to recognize the limitations of this study, such as its retrospective nature, which may have introduced selection bias. Given the rarity of elderly PCL patients, a large-scale prospective study appears to be unfeasible. Additionally, due to the lack of detailed treatment data (*e.g.* chemotherapy and radiotherapy regimens) in the SEER database, the impact of treatment on outcomes cannot be further assessed. It is not uncommon for studies utilizing SEER data to encounter certain limitations. However, despite such shortcomings, SEER is a valuable resource for investigating the rarity of tumors, provided that these restrictions are properly considered. The study at hand renders significant illumination for aged individuals with PCL, immensely informative with regards to prognostic elements and survival rates in this specific demographic.

CONCLUSIONS

A nomogram was created and validated to accurately assess the OS of aging patients with PCL conditions. The impressive accuracy of the nomogram was verified through various analytical methods, including ROC curves, calibration curves, and decision curve analysis.

Supplementary Information

Supplementary materials are only available at the official site of the journal (www.intern-med.com).

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None.

Author Contributions

Wang K designed the study. Zhao LY and Che TY searched the data from the database. Zhou CH and Qin XZ performed the analysis of the data. Hong Y, Che TY and Gao WT implementation of the computer code and supporting algorithms. Wang K, Che TY and Zhao LY wrote the original draft of the manuscript. Zhang L, Gu YB and Zou DW supervised this work revised the manuscript. All authors had read and approved the final manuscript.

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Ethical Approval

Not applicable.

Informed Consent

Not applicable.

Conflict of Interest

No potential conflicts of interest were disclosed.

Data Availability Statement

The SEER database allows for the retrieval of data. <http://seer.cancer.gov/>.

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