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Clinical features and prognostic nomogram development for cancer-specific death in patients with dual primary lung cancer: a population-based study from SEER database

Tenghao Rong[1†], Cheng Ai[1†], Tong Yang[2], Qingchen Wu[2*] and Min Zhang[2*]

Abstract

Objective This study aimed to develop a concise and valid clinical prediction model to assess the survival prognostic risk of cancer-specific death in patients with dual primary lung cancer (DPLC).

Data source Surveillance, epidemiology, and end results (SEER) database.

Design A retrospective population-based study.

Methods Data of DPLC patients from the database from 1992 to 2020 were collected. The number of DPLC patients was determined based on the first primary LC (FPLC) and second primary LC (SPLC), and patients were randomly assigned to a training set and a testing set in a 7:3 ratio. The primary endpoint was cancer-specific survival (CSS). Kaplan–Meier survival analysis was performed to construct survival curves. Cox analysis and bilateral stepwise regression were used to analyze prognostic factors for cancer-specific death in patients and establish the nomogram. The discriminative ability of the nomogram was assayed by C-index and calibration curves, decision-making ability was assessed by decision curve analysis (DCA), and nomogram performance was measured by receiver operating characteristic (ROC) curves.

Results This study included 997 DPLC patients, divided into a training set (n = 698) and a testing set (n = 299) in a 7:3 ratio. Age, gender, histological type, surgery, chemotherapy, T stage, N stage, and tumor size were identified as risk factors affecting CSS in DPLC patients ($P < 0.05$) and were utilized to establish a nomogram. The C-index of the nomogram in the training set was 0.671, and the AUC values of ROC curves for 1-year, 3-year, and 5-year survival rates were 0.84, 0.78, and 0.74, respectively. The C-index of the testing set was 0.644, and the AUC values were 0.72, 0.74, and 0.75, respectively. Calibration curves for both sets were close to the diagonal line, indicating good predictive ability of the nomogram. DCA curves demonstrated the good decision-making ability of the nomogram.

Conclusion This study revealed the clinical features of DPLC patients and developed an effective nomogram for predicting CSS, which can assist clinicians in making accurate and personalized clinical decisions regarding patient treatment.

Keywords Dual primary lung cancer, Lung cancer, Cancer-specific survival, Nomogram, SEER

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Introduction

Lung cancer (LC) is one of the most common malignant tumors in the world, and its high morbidity and mortality make it the leading cause of cancer deaths [1]. Among the LCs, multiple primary lung cancer (MPLC) is rarer and refers to the simultaneous occurrence of two or more primary malignant tumors of the lung in a single individual [2]. Dual primary LC (DPLC) is the predominant subtype [3], and it includes synchronous DPLC (simultaneous occurrence) and metachronous DPLC (occurrence at different times) as two subtypes [4]. Among patients with non-small cell LC (NSCLC) undergoing treatment, the incidence of DPLC takes up only 11% of LC cases [5]. It is worth noting that although DPLC is rare, it has lower survival rates and poorer prognoses compared to single primary LC, with five-year overall survival (OS) lower than 30% [6], while the five-year overall survival (OS) rate in NSCLC patients post-treatment is approximately 50% or higher [7].

Cancer-specific survival (CSS) is an insightful endpoint measure to study the influence of cancer on patients, representing the actual prognosis of survival [8, 9]. However, current studies on prognosis assessment for LC patients primarily focus on OS [10, 11], with limited in-depth research on CSS. The results of the few existing studies, if any, have mostly focused on single primary LC [12–14], whereas CSS studies for patients with DPLC have been insufficient to provide a reasonably accurate clinical assessment of survival prognosis for cancer-specific deaths (CSD) in patients with DPLC. To fill this gap, we believe that the development of a clinical prediction model specifically for DPLC patients is essential.

We utilized patient information from Surveillance, Epidemiology, and End Results (SEER) to screen the clinicopathological characteristics relevant to DPLC patients. Independent prognostic factors affecting CSS in DPLC patients were identified by Cox proportional hazards modeling, and a prognostic nomogram was developed accordingly. This nomogram established a relatively systematic evaluation system that could accurately predict the 1-, 3- and 5-year survival rates of DPLC patients, and provided a reliable survival prediction model for DPLC patients for physicians' reference in clinical practice. Compared with existing studies, the model in this study was more targeted, which was developed specifically for DPLC patients, while most existing models were for single primary LC patients. In addition, this study ensured the predictive accuracy and clinical utility of the model through rigorous statistical methods and model validation. We believed that the development of this model could provide important support for the clinical management of DPLC patients and contribute to the improvement of patients' survival.

Methods

Data source

Our data was obtained from SEER. SEER was established in 1973 and supported by the national cancer institute (NCI) of the United States [15]. It is a significant population-based initiative that gathers data on cancer, including incidence, prevalence, and survival rates. Currently, it covers approximately 48% of the US population (https://seer.cancer.gov/about/overview.html). The SEER program, which is updated yearly, tracks patient variables such as age, race, marital status, histological disease type, diagnostic staging, tumor size, surgical procedures, as well as radiotherapy or chemotherapy received.

Patient selection

For this study, we employed patient data from SEER based on 12 centers (accessed on August 7, 2023). Selection of DPLC patients, specifically focusing on prognosis nomogram combining the clinical characteristics and CSD for patients with first primary LC (FPLC) and second primary LC (SPLC), was directly performed on SEER*Stat 8.4.2 software. The SEER data does not include any patient identifiers and is publicly available. Therefore, neither the patients' written informed permission nor institutional review board approval was necessary for our investigation.

The following criteria were used to identify eligible patients: (a) diagnosis years include 1992 to 2020; (b) Site recode ICD-O-3/WHO 2008 code: Lung and Bronchus (C34); (c) Behavior code ICD-O-3 indicating a malignant tumor; (d) patients with DPLC, defined as having an ID registered twice, with the first registration representing FPLC and the subsequent registration representing SPLC.

The following patients were excluded: (a) patients with only verbal or autopsy reports; (b) patients with 3 or more primary LCs; (c) patients with unknown grade; (d) patients with unknown T and N staging; (e) patients with M1 staging; (f) patients with unknown stage; (g) patients with unknown tumor size; (h) patients whose cause of death was missing or was unknown. The patient selection process for this study is shown in Fig. 1.

Variable collection

This study collected information on patient demographics, clinicopathology, treatment, and survival data. The demographic characteristics included age ($\leq 65, > 65$), sex (male, female), race (Black, White, Other), and marital status (married-married, married-unmarried, unmarried-married, unmarried-unmarried). Clinicopathology included laterality, primary site label, primary site, grade, stage, histological type, time interval (months since the first tumor to the second tumor of the DPLC), T stage,

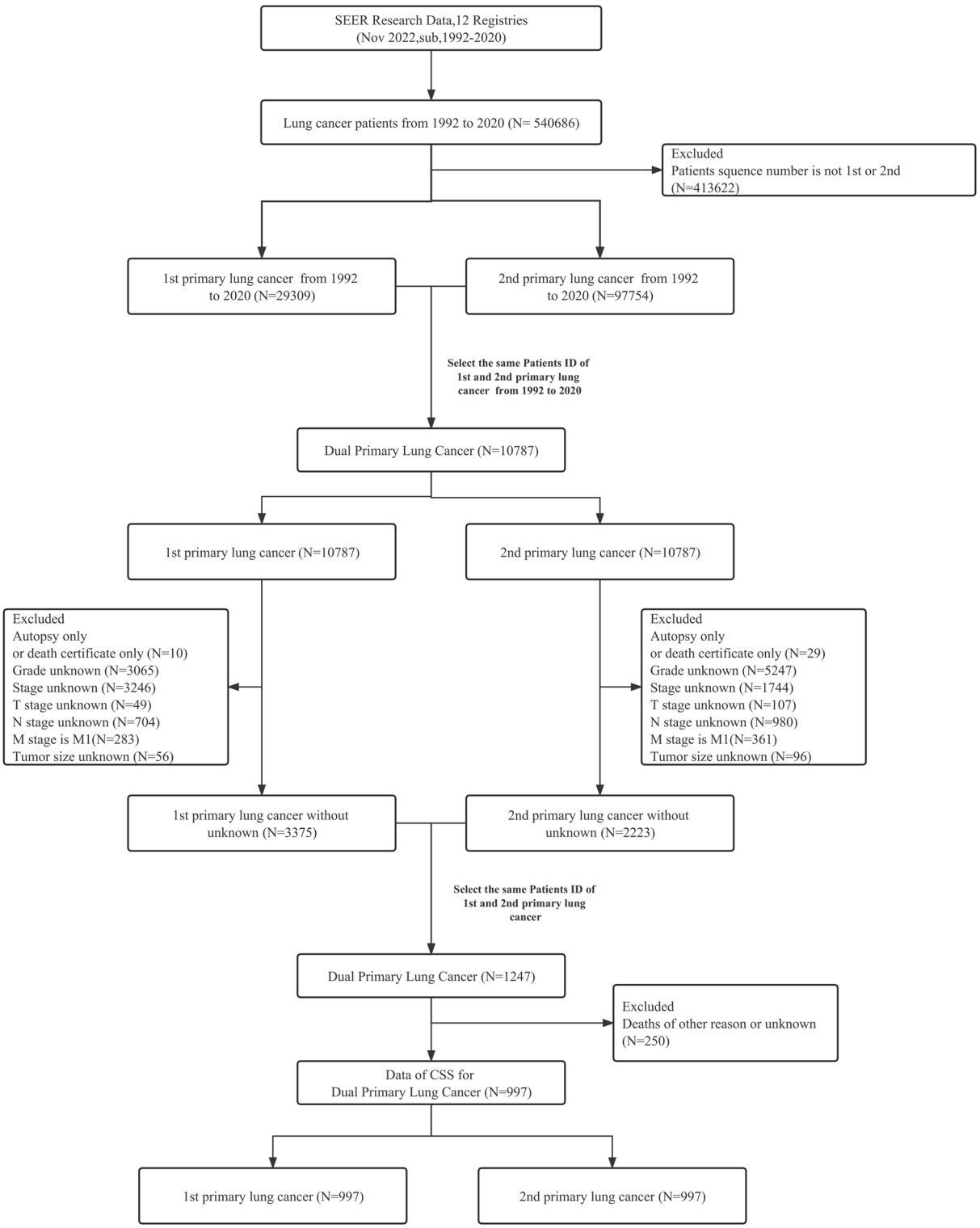

Fig. 1 Flowchart of the sample selection process

N stage, and tumor size. Treatment included whether surgery was performed, whether radiation therapy was administered and whether chemotherapy was given. Survival data consisted of survival time from diagnosis (DPLC) to death (measured in months), and survival status (alive, deceased). CSS was defined as the survival time from diagnosis to death due to LC. Based on the data collection information for the same patient's FPLC and SPLC, the age, grade, stage, and tumor size are derived from the SPLC data as the final data for this study on patients with DPLC. The remaining data are recorded using information collected from both the FPLC and SPLC at different times (e.g., Histology: Aden-squa).

Statistical analysis

Skewed distributed quantitative data were presented as median (interquartile range [IQR]), and group comparisons were performed using the Mann–Whitney U test. Categorical data were presented as percentages and compared using the chi-square test. Variables with $P<0.05$ (two-tailed) were deemed statistically significant. The patients were randomly assigned to a training set and a testing set in a 7:3 ratio to ensure the internal validation of the model. This design allowed the model to be constructed on the training set and its performance to be evaluated on the testing set, thereby preventing overfitting. Kaplan–Meier (KM) curves were utilized to plot survival curves for different factor groups.

Univariate Cox regression models were employed to integrate variables with $P<0.05$ (statistically significant) into multivariate analysis. Bidirectional stepwise regression was used for model variable selection, and HRs with 95% CIs and *P*-values were used to estimate relative risks. Based on the results of the multivariate analysis using the Cox proportional hazards model, independent prognostic factors affecting CSS in patients with DPLC were identified. A nomogram was constructed to visually display the impact of these factors on patient survival prognosis. Additionally, the study comprehensively evaluated the discrimination, calibration, and decision-making ability of the nomogram using the C-index, receiver operating characteristic (ROC) curve, calibration curve, and decision curve analysis (DCA). The C-index was used to assess the consistency between the nomogram predictions and observed outcomes. The calibration curve visually compared the prognostic predictions of the nomogram with actual results. The ROC curve demonstrated the predictive accuracy of the nomogram, quantified by the area under the curve (AUC). The bootstrap method was employed to generate 300 repeated calibration plots, and DCA assessed the clinical utility and net benefits.

In this study, all statistical analyses were conducted using R (version 4.2.3), except for the optimal cutoff value analysis for tumor size (≤ 25 mm; >25 mm), which was performed using X-tile software and the Kaplan–Meier survival curve method. R packages included openxlsx, rms, MASS, car, rmda, survival, survminer, foreign, ggDCA, timeROC, and regplot.

Results

Baseline characteristics

This study included 997 patients with DPLC. Characteristics are presented in Table 1. The median age at FPLC diagnosis was 67 years (IQR: 61–73), while at SPLC diagnosis, it was 70 years (IQR: 63–75). The upper lobe was the most common primary site for both FPLC (64.5%) and SPLC (56.2%), followed by the lower lobe and middle lobe. Regarding clinical treatment, surgical treatment was administered to 888 cases (89.1%) of FPLC and 756 cases (75.8%) of SPLC. The number of patients who did not have radiotherapy was significantly higher than those who did, accounting for over 78% in both cohorts. Similarly, the number of patients who did not have chemotherapy was also significantly higher than those who did, with 696 cases (69.8%) and 763 cases (76.5%), respectively. Based on tumor grade and stage, Grade II accounted for a higher proportion in both FPLC (45%) and SPLC (43.5%) patients compared to other grades ($P<0.001$). Grade I accounted for a significant proportion of both FPLC and SPLC patients, with 69.8% and 76.2%, respectively. In terms of pathological staging, the most common stages were T1 (46.4%, 67.3%) and N0 (79%, 84.5%). The median tumor volumes for FPLC and SPLC were 25 mm (IQR: 17–39 mm) and 17 mm (IQR: 11–25 mm), respectively (Table 1). To ensure a balanced distribution of clinical characteristics between groups, there were no significant differences in any variables between the two groups after patients were randomly allocated to training and testing sets in a 7:3 ratio (All $P>0.05$) (Table S1).

Study on CSS risk factors in DPLC patients

KM survival analysis of different risk factors showed that age, sex, histological type, surgery, radiotherapy, chemotherapy, tumor size, and tumor grade were linked to CSS prognosis in DPLC patients (All $P<0.05$, Fig. 2). Patients aged ≤ 65 years had significantly better prognosis than those aged >65 years ($P<0.0001$, Fig. 2A). Male patients had a worse prognosis compared to female patients ($P<0.0001$, Fig. 2B). Patients with tumor volume ≤ 25 mm had a better prognosis ($P<0.0001$, Fig. 2G). Among the factors such as histological type, surgery, radiotherapy, and chemotherapy, patients with adenocarcinoma (Fig. 2C), who underwent two surgical treatments (Fig. 2D), did not receive radiotherapy (Fig. 2E) and received chemotherapy for

Table 1 Clinicopathologic characteristics of FPLC and SPLC

Variable	FPLC, n (%)	SPLC, n (%)	*P* value
Number of patients	997	997	
Age, median (IQR)	67(61,73)	70(63,75)	**< 0.001**
Sex			> 0.999
Female	565(56.7)	565(56.7)	
Male	432(43.3)	432(43.3)	
Marital status			0.256
Married	594(59.6)	568(57)	
Unmarried	403(40.4)	429(43)	
Race			> 0.999
Black	70(7)	70(7)	
White	820(82.2)	820(82.2)	
Others	107(10.7)	107(10.7)	
Primary site labeled			**0.002**
Lower lobe	291(29.2)	357(35.8)	
Middle lobe	46(4.6)	59(5.9)	
Upper lobe others	643(64.5); 17(1.7)	560(56.2)	
		21(2.1)	
Laterality			0.685
Left	437(43.8)	447(44.8)	
Right	560(56.2)	550(55.2)	
Histology			0.461
Aden	643(64.5)	664(66.6)	
Squa	209(21)	206(20.7)	
Others	145(14.5)	127(12.7)	
Surgery			**< 0.001**
None	109(10.9)	241(24.2)	
Yes	888(89.1)	756(75.8)	
Radiation			**0.001**
None	845(84.8)	785(78.7)	
Yes	152(15.2)	212(21.3)	
Chemotherapy			**0.001**
No/Unknown	696(69.8)	763(76.5)	
Yes	301(30.2)	234(23.5)	
Grade			**< 0.001**
I	163(16.3)	244(24.5)	
II	449(45)	434(43.5)	
III	350(35.1)	293(29.4)	
IV	35(3.5)	26(2.6)	
Stage			**< 0.001**
I	696(69.8)	760(76.2)	
II	105(10.5)	61(6.1)	
III	196(19.7)	176(17.7)	
T stage			**< 0.001**
T1	463(46.4)	671(67.3)	
T2	394(39.5)	214(21.5)	
T3	44(4.4)	9(0.9)	
T4	96(9.6)	103(10.3)	
N stage			**0.008**
N0	788(79)	842(84.5)	
N1	95(9.5)	64(6.4)	
N2	105(10.5)	79(7.9)	
N3	9(0.9)	12(1.2)	
Tumor size, median (IQR)	25(17,39)	17(11,25)	**< 0.001**

Bold indicates statistical significance

the first time (Fig. 2F) had significantly better survival prognosis than other patients. Patients with Grade I tumors had the best prognosis (Fig. 2I). American College of Chest Physicians (ACCP) guidelines on multiple lung tumors indicate that patients with an interval greater than 4 years and less than 4 years should be sorted as synchronous DPLC and metachronous DPLC, respectively, without systemic metastasis [16]. No significant difference was seen in CSS prognosis for DPLC patients based on the interval months ($P = 0.49$, Fig. 2H).

Univariate and multivariate Cox regression analyses were utilized to evaluate the factors for the prognosis of DPLC patients and assess the association between patient characteristics and risk factors (Table 2). It was observed that patients with age > 65 years (HR = 1.495, 95% CI 1.198–1.864, $P < 0.001$), male (HR = 1.443, 95% CI 1.185–1.757, $P < 0.001$), T3 stage (HR = 13.354, 95% CI 4.243–42.024, $P < 0.001$), N1–N3 stage (HR = 4.485, 95% CI 1.942–10.358, $P < 0.001$; HR = 2.562, 95% CI 5.191, $P = 0.009$; HR = 3.153, 95% CI 1.126–8.829, $P = 0.029$), and tumor volume > 25 mm (HR = 1.515, 95% CI 1.15–1.994, $P = 0.003$) had an increased risk of CSS prognosis. Compared to patients with both primary LCs being adenocarcinoma, patients with DPLC being adenocarcinoma-squamous cell carcinoma had a higher risk (HR = 1.87, 95% CI 297–2.697, $P = 0.001$). In terms of treatment, patients who underwent surgical treatment (yes/no, HR = 0.388, 95% CI 0.247–0.61, $P < 0.001$; yes/yes, HR = 0.38, 95% CI 0.254–0.567, $P < 0.001$) and chemotherapy (yes/no, HR = 0.719, 95% CI: 0.522–0.989, $P = 0.043$) had reduced survival risk. The model with the lowest AIC was selected as the final model, and the forest plot of the final model is shown in the supplementary materials (Figure S1).

Construction and validation of the CSS nomogram

According to the Cox proportional hazards model from the previous chapter, chemotherapy, tumor size, sex, age, T stage, histological type, N stage, and surgery were identified as risk factors of CSS in DPLC patients. By integrating these factors, a nomogram for the study cohort was built to predict 1-, 3-, and 5-year CSS in DPLC patients (Fig. 3). The C-index of the training set was 0.671, and the C-index of the testing set was 0.644. ROC curve showed that AUC values for 1-, 3-, and 5-year survival times in the training set were 0.84 (95% CI 0.79–0.88), 0.78 (95% CI 0.74–0.82), and 0.74 (95% CI 0.71–0.78), respectively (Fig. 4A). AUC values in the testing set were 0.72 (95% CI 0.65–0.80), 0.74 (95% CI 0.69–0.80), and 0.75 (95% CI 0.70–0.81), respectively (Fig. 4B), indicating the good predictive ability of the nomogram. Furthermore, calibration curves of the training and testing sets were close to diagonal, suggesting high-quality predictions of the nomogram results (Fig. 4C, D). Additionally, DCA results for the training and testing sets indicated that the nomogram tool provided significant net benefits across different risk thresholds. Notably, the model's decision-making ability was most pronounced when the risk threshold was between 0.1 and 0.3, demonstrating the strong decision-making capability of the nomogram (Fig. 4E, F).

Discussion

The detection rate of MPLC keeps rising due to the quick advancement of medical technology, the rise in living standards, and the prolonged survival of LC patients. In recent years, the survival prognosis of MPLC has garnered increasing attention. However, as the main subtype of MPLC, clinical characteristics and prognostic variables of DPLC CSD are poorly understood. Therefore, there is an urgent need for clear clinical features and accurate prediction models to effectively assess them, thus enabling targeted treatments. We retrospectively analyzed the clinical characteristics of DPLC patients extracted from the SEER database from 1992 to 2020. Univariate and multivariate Cox regression analyses were utilized to investigate clinically significant factors and establish a prognostic model. In our study, age, sex, histological type, surgery, chemotherapy, T stage, N stage, and tumor size were important factors for CSS in DPLC patients. These results are generally consistent with other studies investigating prognostic factors for OS in DPLC patients [6, 17], indicating the significant impact of the prognostic factors on the survival prognosis of DPLC patients. However, Song et al. have found that race and primary tumor location are factors for OS in DPLC patients [6], whereas, in our current study, race and primary tumor location did not significantly affect the CSS of DPLC patients. The reasons for these differences may be attributed to the focus of this study on CSS, which emphasizes the impact of relevant prognostic factors of DPLC on cancer itself, excluding deaths unrelated to DPLC. Therefore, compared to OS, CSS may better reflect the impact of treatment on cancer survival, leading to some data discrepancies. Additionally, differences in sample selection and size among these studies may also introduce selection bias.

Aging is a significant driving factor for increased LC-specific death [18]. Studies have shown that advancing age further impacts the mortality of LC [19]. Mortality of LC patients rapidly worsen with increasing age, reaching its peak in the population aged 65–74 (https://seer.cancer.gov/statfacts/html/lungb.html). Advanced age is considered a risk factor for poorer prognosis in LC patients [20]. Similarly, in our work, age was identified as an independent risk factor of CSS in DPLC patients, with a

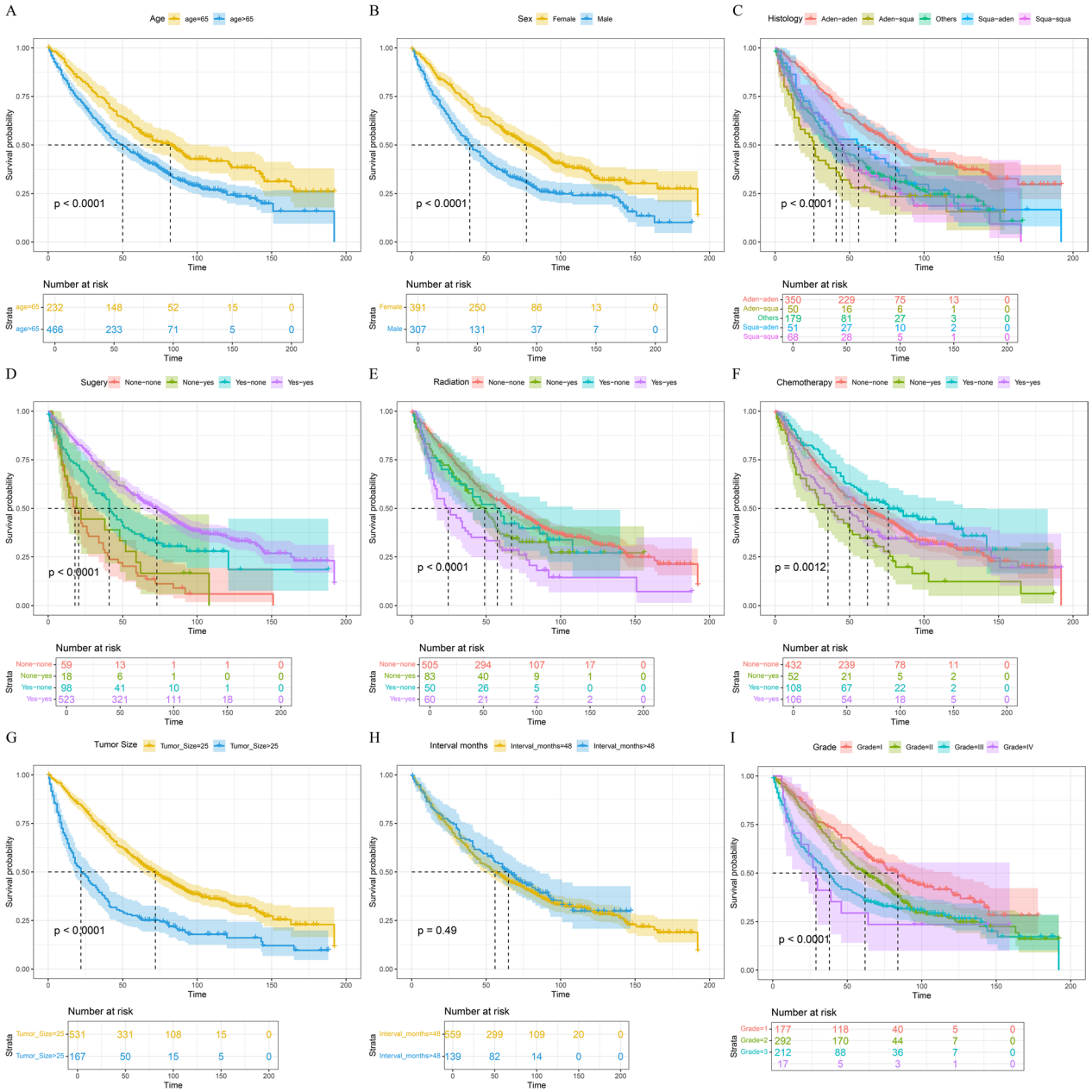

Fig. 2 Kaplan–Meier survival analysis results for CSS in patients with DPLC based on different risk factors. **A** Effect of age on CSS. **B** Effect of sex on CSS. **C** Effect of histological type on CSS. **D** Effect of surgery on CSS. **E** Effect of radiotherapy on CSS. **F** Effect of chemotherapy on CSS. **G** Effect of tumor size on CSS. **H** Effect of interval months on CSS. **I** Effect of tumor grade on CSS. Note: The unit of the horizontal axis "Time" is in "months"

worse prognosis for DPLC patients over 65. Additionally, sex has a significant impact on CSS in DPLC patients. A previous study has shown that females have higher survival rates than males in primary LC patients [21]; our results also indicated that male DPLC patients had worse CSS compared to females. The differential distribution of EGFR mutations between sexes may be a reason for the better survival prognosis in female LC patients. EGFR mutations occur more frequently in females [22, 23]. EGFR mutations and overexpression are considered important mechanisms in NSCLC occurrence and development and are pivotal targets for cancer treatment in clinical practice [24]. In recent years, with ongoing research, EGFR-TKIs targeting EGFR mutations have shown good clinical efficacy in the treatment of NSCLC [25].

Table 2 Determination of CSS risk factors in patients with DPLC based on Cox regression

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value
Age (%)				**< 0.001**
≤ 65	1(reference)		1(reference)	
> 65	1.533(1.253–1.875)	< 0.001	1.495(1.198–1.864)	
Sex (%)				**< 0.001**
Female	1(reference)		1(reference)	
Male	1.705(1.42–2.047)	< 0.001	1.443(1.185–1.757)	
Race (%)				
Black	1(reference)			
White	0.838(0.587–1.196)	0.331		
Others	0.796(0.512–1.239)	0.313		
Marital status (%)				
Married, married	1(reference)			
Married, unmarried	0.888(0.588–1.34)	0.572		
Unmarried, married	0.79(0.452–1.381)	0.408		
Unmarried, unmarried	1.043(0.86–1.265)	0.667		
Primary site (%)				
Lower lobe	1(reference)			
Middle lobe	0.822(0.557–1.211)	0.321		
Upper lobe others	0.843(0.694–1.024)	0.085		
	0.973(0.528–1.79)	0.929		
Primary site labeled				
Different lobe	1(reference)			
Same lobe	0.928(0.765–1.125)	0.445		
Laterality				
Bilateral	1(reference)			
Ipsilateral	0.923(0.762–1.118)	0.413		
Histology				
Aden-aden	1(reference)		1(reference)	
Aden-squa	2.352(1.667–3.319)	< 0.001	1.87(1.297–2.697)	**0.001**
Squa-aden	1.58(1.124–2.222)	0.009	1.294(0.906–1.846)	0.156
Squa-squa	1.93(1.424–2.616)	< 0.001	1.351(0.967–1.889)	0.078
Others	1.757(1.411–2.189)	< 0.001	1.474(1.154–1.882)	**0.002**
Surgery				
None, none	1(reference)		1(reference)	
None, yes	0.79(0.452–1.379)	0.407	0.862(0.455–1.632)	0.648
Yes, none	0.494(0.346–0.706)	< 0.001	0.388(0.247–0.61)	**< 0.001**
Yes, yes	0.317(0.237–0.424)	< 0.001	0.38(0.254–0.567)	**< 0.001**
Radiation				
None, none	1(reference)		1(reference)	
None, yes	1.362(1.027–1.807)	0.032	1.214(0.834–1.766)	0.311
Yes, none	1.2(0.838–1.718)	0.319	1.129(0.726–1.757)	0.590
Yes, yes	2(1.479–2.705)	< 0.001	0.921(0.608–1.395)	0.697
Chemotherapy				
No, no	1(reference)		1(reference)	
No, yes	1.646(1.194–2.269)	0.002	0.825(0.556–1.225)	0.340
Yes, no	0.778(0.59–1.026)	0.076	0.719(0.522–0.989)	**0.043**
Yes, yes	1.165(0.902–1.505)	0.242	0.775(0.576–1.041)	0.091

Table 2 (continued)

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value
Interval months				
≤ 48	1(reference)			
> 48	0.919(0.724–1.166)	0.486		
Grade				
I	1(reference)		1(reference)	
II	1.346(1.058–1.712)	0.016	1.188(0.917–1.54)	0.192
III	1.764(1.371–2.271)	< 0.001	1.17(0.885–1.547)	0.270
IV	1.978(1.109–3.528)	0.021	1.183(0.632–2.215)	0.600
Stage				
I	1(reference)		1(reference)	
II	2.21(1.589–3.073)	< 0.001	0.454(0.189–1.091)	0.078
III	1.626(1.289–2.051)	< 0.001	0.679(0.313–1.472)	0.327
T stage				
T1	1(reference)		1(reference)	
T2	1.781(1.438–2.207)	< 0.001	1.308(0.982–1.741)	0.066
T3	7.119(2.92–17.359)	< 0.001	13.354(4.243–42.024)	**< 0.001**
T4	1.35(1.002–1.819)	0.048	1.552(0.773–3.114)	0.216
N stage				
N0	1(reference)		1(reference)	
N1	2.279(1.659–3.132)	< 0.001	4.485(1.942–10.358)	**< 0.001**
N2	2.359(1.733–3.21)	< 0.001	2.562(1.265–5.191)	**0.009**
N3	3.045(1.439–6.441)	0.004	3.153(1.126–8.829)	**0.029**
Tumor size				**0.003**
≤ 25	1(reference)		1(reference)	
> 25	2.214(1.811–2.707)	< 0.001	1.515(1.15–1.994)	

Bold indicates statistical significance

The clinical and pathological manifestations of different histological types significantly affect the CSS of DPLC patients. This study observed a significant increase in the risk trend of DPLC with adenocarcinoma-squamous cell carcinoma compared to adenocarcinoma. Two main subtypes of LC are NSCLC and SCLC. NSCLC accounts for over 85% of all LC cases, and lung squamous cell carcinoma (LUSC) is a histological subtype that exists in NSCLC, second only to lung adenocarcinoma [26, 27]. LUSC is a malignant tumor associated with high mortality. Compared to adenocarcinoma, its treatment progress is not optimistic due to the lack of specific mutation targets [28]. Currently, chemotherapy remains the cornerstone of treatment for advanced LUSC patients [29]. Although immunotherapy combined with chemotherapy has become the standard treatment for first-line therapy in advanced LUSC patients, it has significant limitations, and only a few patients benefit from it [30–33]. Surgical resection is the predominant method to extend the survival of most MPLC patients [34, 35]. Our study indicated that DPLC patients undergone two surgical treatments, and the first surgery had a longer survival time. However, surgical treatment for SPLC had poor efficacy. This may be related to the stage detected at the time of diagnosis. Surgical resection is a preferred method for early-stage LC, but most patients present at an advanced stage and require systemic treatment, and complete surgical resection is no longer the first choice [36, 37]. For patients who preclude surgery or do not want surgery, radiotherapy and chemotherapy are effective alternative methods [38, 39]. A previous study displayed that only chemotherapy could prolong the survival time of DPLC patients, and radiotherapy is not an independent prognostic factor for DPLC patients [17], which is consistent with our results. Future research could explore the integration of MRI data or the application of advanced analytical methods such as machine learning to develop multimodal predictive models. This approach has the potential to further enhance the predictive accuracy of the models while increasing their applicability in clinical practice, thereby providing

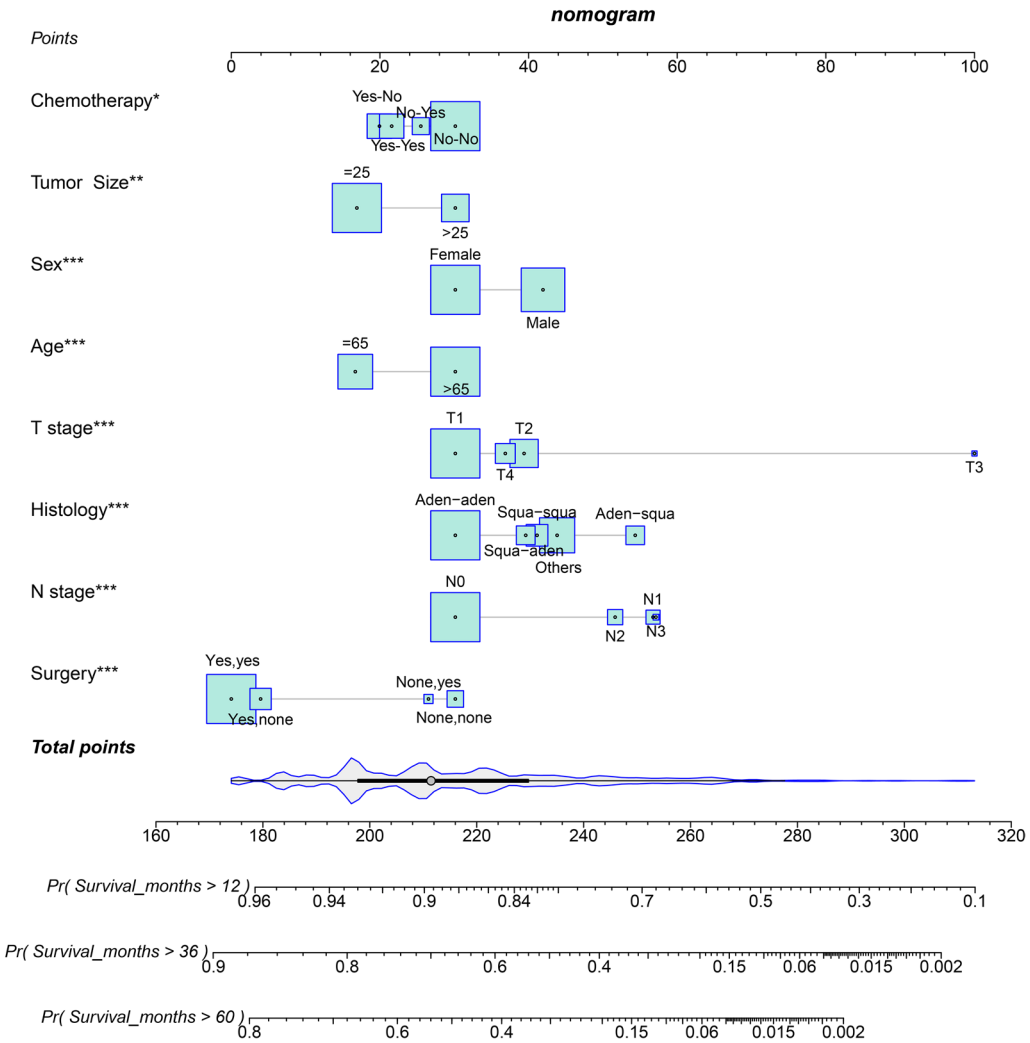

Fig. 3 Survival nomogram for 1-year, 3-year, and 5-year prognosis in patients with DPLC. Note: The size of the squares represents the sample size

stronger support for personalized diagnosis and treatment [40, 41].

In LC patients, TNM staging is a critical prognostic factor that drives treatment and monitoring decisions [42]. Similar to a previous study [43], we found that N staging and T staging are independent prognostic factors for CSD in DPLC patients, and higher T and N staging are implicated in unfavorable LC prognosis. It is noteworthy that our results indicated that the T3 stage was associated with a particularly significant risk of poor CSS in patients with DPLC. This finding may be related to the smaller sample size of T3 stage patients (Table 2), which could lead to statistical bias. Therefore, more data are needed to validate this trend for T3-stage patients and to further explore the underlying biological mechanisms. Additionally, our study found that the N1 stage presented a higher risk for CSS in DPLC patients compared to other N stages, which may be linked to the choices of treatment modalities. Postoperative chemotherapy is a commonly used treatment to improve the disease-free survival rate and OS in clinical practice [44, 45].However, existing studies have shown that postoperative chemotherapy may increase mortality in patients with N1 stage non-small cell lung cancer, thereby elevating the prognostic risk for LC patients [46, 47]. This suggests that the benefits of chemotherapy for patients at the N1 stage may require careful evaluation to balance its potential risks and advantages. Tumor size is also an important factor for CSS prognosis [48]. Our results supported the view that smaller tumors are associated with lower CSD risk [49]. In summary, our findings highlighted the significance of TNM staging, tumor size, and the selection of treatment strategies at specific stages on the CSS prognosis for patients with DPLC.

ACCP guidelines on MPLT indicate that patients with an interval greater than 4 years and less than 4 years

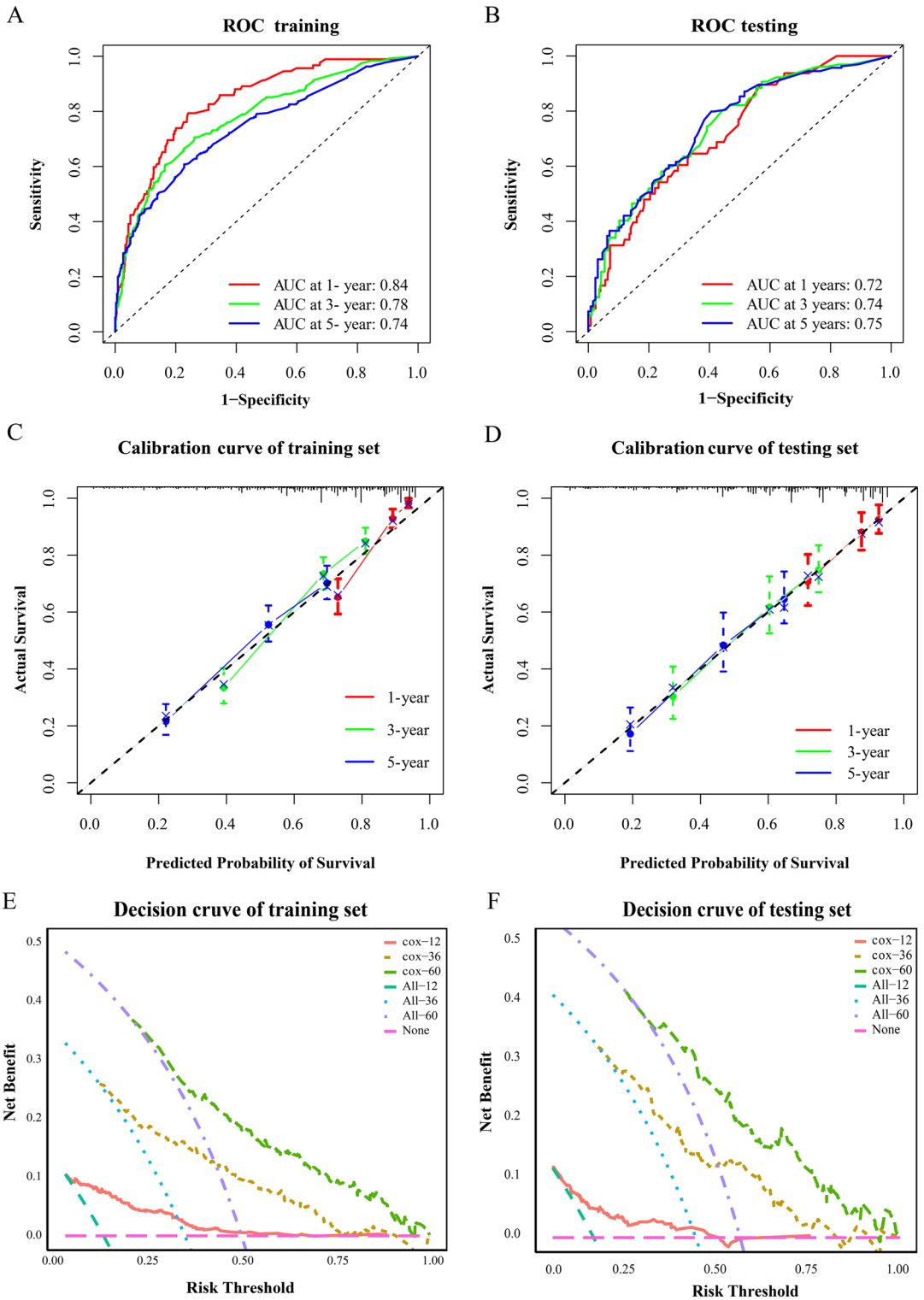

Fig. 4 Validation of the nomogram in the training and testing sets. **A** ROC curve of the training set; **B** ROC curve of the testing set; **C** Calibration curve of the training set; **D** Calibration curve of the testing set; **E** Decision curve of the training set; **F** Decision curve of the testing set

should be sorted as synchronous DPLC and metachronous DPLC, respectively [16]. The association between the time interval between FPLC and SPLC and the survival rate of DPLC patients has been a subject of debate. Some studies have suggested that longer intervals are associated with better prognosis [50]. However, other studies have observed no significant difference in long-term survival rates between synchronous and metachronous DPLC patients [51]. Our study results showed no significant association between time interval and CSS prognosis in DPLC patients.

In summary, our study represents the first attempt to use nomograms to predict CSS and prognosis in DPLC patients, constructing an effective nomogram for survival prediction. This fills a gap in existing research on CSS and aids clinicians in more accurately assessing patients' survival prognosis, thus providing personalized treatment decision support. Our study results indicated that, compared to previous research, our model was specifically developed for patients with DPLC, making it more targeted and applicable. Most existing models focus on patients with single primary LC, while our findings showed that age, sex, histological type, surgery, chemotherapy, T stage, N stage, and tumor size were independent prognostic factors affecting CSS in DPLC patients. These results align with other studies on risk factors for OS in DPLC patients, further confirming the significant impact of these prognostic factors on survival outcomes. The findings from this study can help generate testable hypotheses for rigorous clinical trials. Future research could further validate and refine our predictive model to improve its accuracy and reliability in clinical practice. Additionally, prospective studies and multi-center validations could provide a more comprehensive assessment of the model's stability and generalizability.

However, our study also has certain limitations. Firstly, due to data limitations, we did not explicitly investigate differences between synchronous DPLC and metachronous DPLC. Second, the SEER database lacks information on the time of treatment initiation to include time-dependent effects of treatment. We analyzed treatment variables as baseline characteristics and failed to account for the effect of treatment timing on survival outcomes, which may have led to estimation bias. Future studies should include more information on treatment duration to more fully assess the impact of these factors on patient outcomes. At the same time, the SEER database fails to provide information on smoking, chronic obstructive pulmonary disease, and other potentially important factors that may be risk factors for DPLC. Moreover, the nomogram was constructed based on SEER database data, which may not fully reflect the global population. Lastly, being a retrospective study, there may be selection bias. We did not implement propensity score matching to eliminate the influence of other factors on the observed outcomes. Additionally, patients with incomplete information were excluded from the study, unavoidably leading to selection bias. Considering the limitations of retrospective analysis, further prospective analysis is recommended to assess relevant prognostic factors. Despite these limitations, we believe that with further research and validation, this model will provide important support for the clinical management of DPLC patients and contribute to improving patient survival outcomes.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-025-03385-y.

Additional file 1. Fig. S1: Forest plot of variables associated with cancer-specific survival in patients with dual primary lung cancer.

Additional file 2. Table S1: Baseline characteristics of the training and testing sets.

Author contributions

Tenghao Rong: Conceptualization, Methodology, Software, Data curation, Writing—Original draft preparation. Cheng Ai: Conceptualization, Methodology, Software, Data curation, Writing- Original draft preparation. Tong Yang:Writing- Reviewing and Editing, Data curation Qingchen Wu: Visualization, Investigation, Supervision, Software, Validation Min Zhang: Visualization, Investigation, Supervision, Software, Validation.

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Data availability

The datasets generated and/or analysed during the current study are available in the [SEER database] repository.

Declarations

Ethics approval and consent to participate

Not applicable.

Competing interests

The authors declare no competing interests.

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