Original Article

Development and validation of nomogram-based models for personalized survival assessment in pediatric hepatoblastoma patients

Weiming Chen[#], Ling Zhang[#], Bing Zhang, Yifan Fang, Yuanbin He

Department of General Surgery, Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou, China

Contributions: (I) Conception and design: W Chen, L Zhang, Y He; (II) Administrative support: Y Fang, B Zhang; (III) Provision of study materials or patients: W Chen; (IV) Collection and assembly of data: W Chen, L Zhang; (V) Data analysis and interpretation: W Chen, L Zhang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Yuanbin He, MD. Department of General Surgery, Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, 966 Hengyu Road, Fuzhou 350011, China. Email: heyb1989@fjmu.edu.cn.

Background: Hepatoblastoma (HB) is a prevalent form of liver cancer in pediatric patients, characterized by an embryonal malignant tumor. In the current study, a clinical prediction model was developed; that can effectively assess the likelihood of a patient's survival with HB.

Methods: Data from the Surveillance, Epidemiology, and End Results (SEER) database for cases of HB between 2010 and 2019 were used in this retrospective research. Information on clinicopathologic characteristics, therapeutic interventions, and survival outcomes were included in the data. The HB patients were randomly assigned to the training or validation cohort in a 7:3 ratio. Using univariate and multivariate Cox proportional hazards regression models, the prognostic indicators for overall survival (OS) and cancer-specific survival (CSS) were identified. The area under the receiver operating characteristic curve (AUC-ROC), calibration plots, and concordance index (C-index) were used to evaluate the accuracy and calibration of these models. The clinical utility of the models was examined using decision curve analysis (DCA).

Results: The multivariate Cox regression analysis revealed multiple autonomous prognostic determinants for the OS and CSS, including age, surgical interventions, and chemotherapy administration. Significantly, tumor size was found to be a strong predictor of OS. AUC values of 0.915, 0.846, and 0.847 for 1-, 3-, and 5-year OS, respectively, indicated that the nomogram-based models were highly accurate at predicting outcomes. Similarly, the AUC values for CSS were 0.871, 0.814, and 0.825. The C-index measurements, which quantify the discriminatory performance of the models, produced CSS values of 0.836 and OS values of 0.864. Furthermore, the calibration plots accurately represented the actual survival rates. Concurrently, the DCA had validated the clinical relevance of the nomogram-based models.

Conclusions: The present study successfully developed and validated user-friendly nomogram-based models, allowing for accurate assessment of OS and CSS in pediatric HB patients. These tools enable personalized survival predictions, enhance risk stratification, and strengthen clinical decision-making for managing HB.

Keywords: Hepatoblastoma (HB); prognostic factors; nomogram; cancer-specific survival (CSS); overall survival (OS)

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Introduction

Hepatoblastoma (HB) is the predominant hepatic cancer observed in pediatric patients, accounting for around 1% of all malignancies in those below 15 years. It represents a substantial 80% of primary liver malignancies, with a notable predisposition for children aged under 3 years (1,2). The annual incidence rate of HB is around 1.5 cases per one million individuals and has exhibited a consistent annual increase of 4.3% (3,4). Recent advancements in therapy have resulted in notable enhancements in the prognosis of pediatric patients diagnosed with HB. Integrating surgical and chemotherapeutic interventions has yielded noteworthy 5-year overall survival (OS) and disease-free survival rates, attaining 88.9% and 80.8%, respectively (5,6). The achievement of total elimination of liver tumors is of utmost importance in ensuring the efficacy of the treatment (7). To enhance the potential of attaining this significant goal, medical practitioners commonly employ preoperative or postoperative chemotherapy, diminishing the probability of tumor reoccurrence (8,9).

The prognosis of HB is connected with several parameters, including age, levels of α-fetoprotein (AFP) upon diagnosis, clinical subtype, and the occurrence of distant metastases (10-13). Nevertheless, despite the acknowledgment of these characteristics, a widely acknowledged risk categorization method for HB is yet to be established. The Children's Oncology Group (COG) in North America introduced the postoperative COG Evans staging system. This staging approach emphasizes the prognostic importance of postoperative tumor residue and histopathological type. The pretreatment extent of disease (PRETEXT) staging method, created by the International Childhood Liver Tumor Strategy Group, evaluates the extent of pediatric liver tumors before initiating therapy. This takes into account the presence of tumors and examines the influence of distant metastasis on the overall prognosis. The establishment of the Children's Hepatic Tumors International Collaboration-Hepatoblastoma Stratification (CHIC-HS) occurred in 2016 through a collaborative effort, including many research institutions operating under the auspices of CHIC (14). The current state of knowledge on the predictive efficacy of this risk stratification method for children with HB is still uncertain. A study by Huang *et al.* showed a comparative analysis of the COG and CHIC-HS risk stratification methods, and their findings led them to conclude that the CHIC-HS method has more accuracy in predicting survival outcomes (15). In contrast, Hsu *et al.* observed no statistically significant variation in survival rates between children classified as intermediate-risk and high-risk when using the CHIC-HS risk stratification method (16). Despite the endeavors mentioned above, the established prognostic variables and the generally recognized staging methods need to offer an ideal framework for accurately evaluating individual patient survival probability.

To address this gap, the utilization of nomograms emerges as a potentially beneficial strategy. Nomograms, regarded as robust statistical tools, effectively incorporate all independent prognostic variables into a graphical representation for predicting event rates. Nomograms have demonstrated clinical utility in several cancer types, including neuroblastoma, pancreatic cancer, and lung cancer, has been shown in earlier research (17-19). Nomograms are renowned for their capacity to offer precise, personalized prognostic estimates, exceeding conventional tumor staging standards. Nevertheless, previous studies have only conducted limited investigations to explore the potential of developing a nomogram-based prediction model for precise forecasts of the OS of patients with HB (20,21). In addition, previous studies have not shown specially tailored nomograms to forecast cancer-specific survival (CSS) within patients with HB.

Highlight box

Key findings

- The first nomogram for cancer-specific survival of hepatoblastoma was derived using commonly available clinicopathological factors.

What is known and what is new?

- Hepatoblastoma (HB) is the predominant hepatic cancer observed in pediatric patients. Previous studies have identified various factors associated with HB prognosis, including age, α-fetoprotein levels at diagnosis, pathological subtype, and the presence of distant metastases.
- We combined the specific clinicopathologic factors to create the first prediction model to evaluate the cancer-specific survival of HB patients.

What is the implication, and what should change now?

- The nomogram-based models exhibited innovation and have undergone rigorous validation, showcasing remarkable prediction accuracy. These models evaluate personalized cancer-specific survival and overall survival in individuals diagnosed with HB. The aforementioned technologies exhibit a high degree of user-friendly interface and provide considerable promise in computing individualized survival probability, facilitating risk classification, and enhancing the clinical decision-making process.

As HB is relatively uncommon, there is a lack of availability of prospective data and large-scale clinical trials. Given the current situation, the Surveillance, Epidemiology, and End Results (SEER) program was employed, offering an extensive dataset encompassing various cancer types within the American population to address this limitation. Employing this useful source, the treatment outcomes, clinical characteristics, and prognostic factors of HB in the pediatric population were investigated. The present investigation accurately identified independent prognostic parameters for CSS and OS in HB patients. Furthermore, a nomogram was developed while incorporating these characteristics to facilitate the prognostication of CSS and OS. The prediction accuracy of this nomogram was systematically and thoroughly assessed. We present this article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1786/rc).

Methods

Selection of patients and study design

The research employed the SEER database from the National Cancer Institute (NCI). The data collected encompassed the baseline characteristics and clinicopathologic parameters, including gender (male or female), age, race (White or others), the North American Association of Central Cancer Registries Hispanic Identification Algorithm (NHIA) (Non-Spanish-Hispanic-Latino or Spanish-Hispanic-Latino), summary stage (localized, regional or distant), tumor size, surgery of the tumor (yes or no surgery), chemotherapy of the tumor (yes or no radiotherapy), systemic therapy of tumor (yes or no systemic therapy), lung metastasis (yes or no), OS, and CSS. In this study, systemic therapy is defined as the administration of chemotherapy combined with surgical treatment, irrespective of the order in which they were given. The SEER* Stat 8.4.1 program was utilized for data analysis. The individuals who satisfied the predetermined criteria for eligibility were clinically diagnosed with HB *via* a thorough examination of histological samples. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). As per the ethics guidelines, since public and anonymous data were utilized, neither informed consent nor approval of an ethics committee was necessary.

This led to the inclusion of a total of 409 individuals who had complete data and follow-up information between 2004 and 2019. A random partitioning approach was employed to achieve dataset balance, with a 7:3 ratio. This approach resulted in forming two distinct cohorts: a training cohort comprising 286 patients and a separate validation cohort comprising 123 patients. The development of nomograms for predicting CSS and OS was undertaken using training data. These nomograms were subsequently subjected to a rigorous validation process using an independent validation cohort. To stratify patients based on age and tumor size, we relied on the X-tile program, a tool from Yale University. The program accurately determined the precise cutoff points, leading to the classification of age into two distinct groups: those under 2 years old and those aged 2 years or older. Similarly, tumor size was categorized into two groups: tumors measuring less than 123 mm and those measuring 123 mm or larger (*Figure 1*). This systematic approach improved our analysis, ultimately increasing the precision of our results.

Study outcomes and nomogram construction

The investigation was primarily focused on CSS and OS. The CSS was defined as the duration between the initial diagnosis of HB and HB-specific mortality. In contrast, OS was described as the duration between the initial diagnosis of HB to the mortality from any reason or the date of the patient's last follow-up.

In order to validate and assess the precision of the nomogram, we initially identified predictors associated with both OS and CSS by the implementation of multivariate and univariate Cox proportional hazard regression models. Subsequently, a thorough and detailed construction of a survival outcomes nomogram was conducted, utilizing the insights from the multivariate Cox regression models. The validity of the nomogram was confirmed by employing a bootstrap resampling technique, and its prediction accuracy was assessed using the concordance index (C-index). Calibration plots were employed to contrast predicted survival estimates with actual probabilities. In addition, the model's effectiveness was determined by computing the area under the receiver operating characteristic curve (AUC-ROC). Moreover, decision curve analysis (DCA) was utilized to evaluate the prediction model's clinical usefulness by quantifying the benefits of including the nomogram in

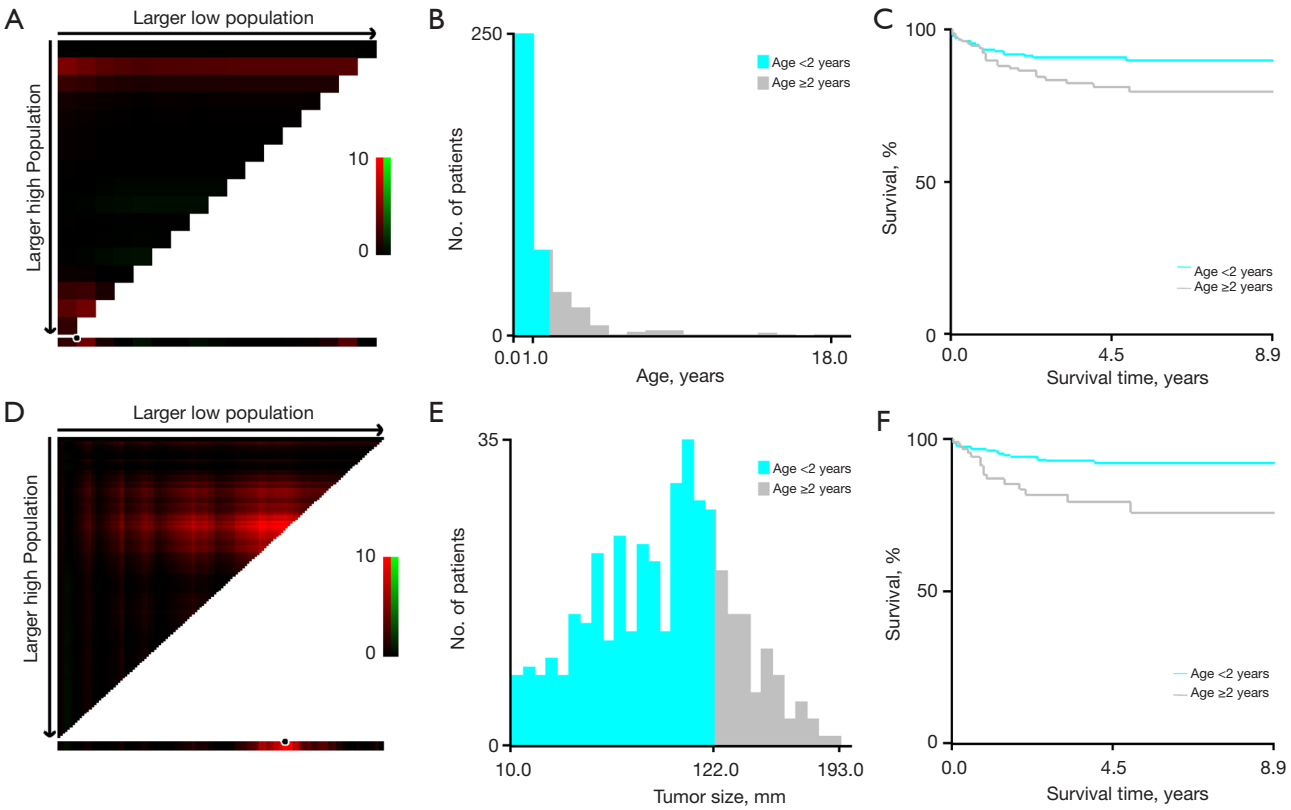

Figure 1 The optimal cutoff values of age and tumor size identified by X-tile. (A,B) The optimal cutoff value of age. (C) The Kaplan-Meier curves for the subgroups of age (<2, ≥2 years) for overall survival. (D,E) The cutoff value of tumor size. (F) The Kaplan-Meier curves for the subgroups of tumor size (<123, ≥123 mm) for overall survival.

the decision-making process.

Statistical analysis

Statistical methods such as Fisher exact tests or Chi-square tests were utilized to compare the training and validation cohorts in relation to categorical clinicopathologic variables. The evaluation of continuous variables was conducted by the utilization of *t*-tests or Mann-Whitney U-tests. The examination of survival disparities between subgroups was performed using Kaplan-Meier analysis and log-rank testing. The statistical analyses were executed using IBM SPSS version 26.0 and R software version 4.2.0 (www.r-project.org). A $P<0.05$ was considered as statistical significance.

Results

Baseline characteristics of HB patients

The present retrospective analysis examined the clinicopathological and demographic characteristics of 409 patients with HB according to the predefined inclusion criteria (*Figure 2*). The patients were randomly distributed into two groups: a training group comprising 286 patients and a validation group comprising 123 patients. The random allocation was done at a ratio of 7:3 between the years 2010 and 2019. *Table 1* provides an overview of the baseline patient characteristics for both cohorts. Notably, the clinical characteristics had a consistent uniform distribution and were comparable across both groups. In the total cohort, a significant proportion of patients were under the age of 2

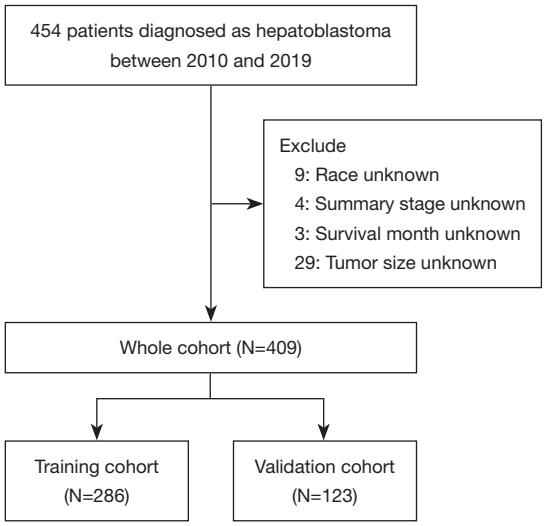

Figure 2 Flowchart of the selection process of included patients.

(61.6%), identified as male (60.6%), belonged to the White ethnic group (73.6%), and were classified as Non-Spanish-Hispanic-Latino (66.7%). The study yielded promising results, indicating that a significant proportion of patients, around 89.5%, had surgical intervention. Additionally, it was observed that a substantial majority, around 92.9%, of individuals diagnosed with HB received adjuvant chemotherapy. The investigation included a cohort of pediatric patients with HB, having a median duration of follow-up of 54 months. The OS rates at 1, 3, and 5 years were 92.1%, 88.0%, and 85.8%, respectively. Similarly, the corresponding CSS rates were 94.3%, 90.4%, and 88.8%, respectively. Among the pediatric cohort, a notable proportion of individuals, around 15.6%, presented with distant metastases, with the lungs being the primary site of metastasis. In this subset, the one-year OS and CSS rates were 75.8% and 77.2%, respectively. *Figure 3* presents a graphical representation of the survival curves, which explored the impact of variables such as age, summary stage, surgery, chemotherapy, systemic therapy, tumor size, and lung metastasis on the prognosis of HB. This study was conducted *via* the Kaplan-Meier method and the $P<0.05$ was considered statistically significant.

Predictor selection

Multivariate and univariate Cox regression analyses were performed to ascertain independent prognostic markers for CSS and OS. The entire findings from these studies are presented in *Tables 2,3*. The final multivariate analysis solely included the prognostic variables deemed relevant based on the prior univariate study. A multivariate study demonstrated that patient age, surgery, chemotherapy, and tumor size (*Table 2*) significantly influenced OS in individuals diagnosed with HB. Furthermore, the research revealed that age, surgery, and chemotherapy were significant predictors of CSS, as indicated in *Table 3*.

Construction of nomograms

The nomograms were developed for CSS and OS based on multivariate Cox analysis by incorporating the independent prognostic variables into the assessment. Nomograms are presented in *Figure 4*, where they provided predictions for 1-, 3-, and 5-year intervals. Combining the scores associated with each selected variable was necessary to determine the likelihood of an HB patient's survival. As an example, a patient of age three, diagnosed with a tumor measuring 15 cm and possessing a medical background involving chemotherapy and surgical procedures, would obtain a cumulative score of 102 and 52 in the OS and CSS nomograms, respectively. These findings provided projected 1-, 3-, and 5-year OS rates of 90%, 81%, and 77%, respectively; in addition to this, the corresponding CSS rates of 1-, 3-, and 5-year were about 96%, 93%, and 91%, respectively.

Validation of nomograms

The training set yielded C-index values of 0.864 for OS and 0.836 for CSS, indicating a strong discriminative capacity. The results obtained in the validation set were also strong, as evidenced by the C-index values of 0.762 for OS and 0.791 for CSS. The predictive ability of the nomograms was further validated using the ROC curves. The training set exhibited exceptional performance regarding 1-, 3-, and 5-year OS, as evidenced by the area AUC values of 0.915, 0.846, and 0.847, respectively (*Figure 5A*). The AUC of the validation set were 0.795, 0.713, and 0.666 (*Figure 5B*). *Figure 5C-5H* for OS provided additional evidence between the predicted and observed survival probabilities in the training and validation datasets. Similarly, the AUC for 1-, 3-, and 5-year CSS were found to be 0.871, 0.814, and 0.825 in the training set, as depicted in *Figure 6A*. In the validation set, the corresponding AUCs were 0.914, 0.734, and 0.710, as illustrated in *Figure 6B*. *Figure 6C-6H* for CSS provided additional evidence between the predicted and observed survival probabilities in the

Table 1 Baseline characteristics across the entire dataset, the training dataset, and the validation dataset

Characteristics	Whole cohort (N=409)	Training cohort (N=286)	Validation cohort (N=123)	P
Age (years)				>0.99
<2	252 (61.6)	176 (61.5)	76 (61.8)	
≥2	157 (38.4)	110 (38.5)	47 (38.2)	
Gender				>0.99
Male	248 (60.6)	173 (60.5)	75 (61.0)	
Female	161 (39.4)	113 (39.5)	48 (39.0)	
Race				0.903
White	301 (73.6)	211 (73.8)	90 (73.2)	
Others	108 (26.4)	75 (26.2)	33 (26.8)	
NHIA				>0.99
Non-Spanish-Hispanic-Latino	273 (66.7)	191 (66.8)	82 (66.7)	
Spanish-Hispanic-Latino	136 (33.3)	95 (33.2)	41 (33.3)	
Summary stage				0.204
Localized	224 (54.8)	163 (57.0)	61 (49.6)	
Regional	121 (29.6)	77 (26.9)	44 (35.8)	
Distant	64 (15.6)	46 (16.1)	18 (14.6)	
Surgery				0.727
No	43 (10.5)	29 (10.1)	14 (11.4)	
Yes	366 (89.5)	257 (89.9)	109 (88.6)	
Chemotherapy				>0.99
No/unknown	29 (7.1)	20 (7.0)	9 (7.3)	
Yes	380 (92.9)	266 (93.0)	114 (92.7)	
Systemic therapy				0.766
No	63 (15.4)	43 (15.0)	20 (16.3)	
Yes	346 (84.6)	243 (85.0)	103 (83.7)	
Tumor size (mm)				0.307
<123	315 (77.0)	216 (75.5)	99 (80.5)	
≥123	94 (23.0)	70 (24.5)	24 (19.5)	
Lung metastasis				>0.99
No	352 (86.1)	246 (86.0)	106 (86.2)	
Yes	57 (13.9)	40 (14.0)	17 (13.8)	

Data are presented as n (%). NHIA, North American Association of Central Cancer Registries Hispanic Identification Algorithm.

Table 2 Univariate and multivariate Cox analyses evaluating variables for predicting overall survival in the training cohort

Characteristics	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age (years)						
<2		Reference			Reference	
≥2	3.237	1.505–6.962	0.003	2.973	1.215–7.273	0.017
Gender						
Male		Reference				
Female	1.470	0.710–3.046	0.300			
Race						
White		Reference				
Others	1.819	0.859–3.851	0.118			
NHIA						
Non-Spanish-Hispanic-Latino		Reference				
Spanish-Hispanic-Latino	0.769	0.341–1.736	0.527			
Summary Stage						
Localized		Reference			Reference	
Regional	3.103	1.203–8.005	0.019	1.260	0.430–3.691	0.674
Distant	6.172	2.392–15.926	<0.001	1.133	0.132–9.726	0.909
Surgery						
No		Reference			Reference	
Yes	0.070	0.034–0.146	<0.001	0.025	0.004–0.165	<0.001
Chemotherapy						
No/unknown		Reference			Reference	
Yes	0.265	0.101–0.695	<0.001	0.052	0.011–0.255	<0.001
Systemic therapy						
No		Reference			Reference	
Yes	0.108	0.052–0.224	<0.001	4.702	0.679–32.566	0.117
Tumor size (mm)						
<123		Reference			Reference	
≥123	5.550	2.643–11.650	<0.001	4.649	1.677–12.891	0.003
Lung metastasis						
No		Reference			Reference	
Yes	3.909	1.815–8.416	<0.001	1.226	0.139–10.800	0.854

HR, hazard ratio; CI, confidence interval; NHIA, North American Association of Central Cancer Registries Hispanic Identification Algorithm.

Table 3 Univariate and multivariate Cox analyses assessing variables for predicting cancer-specific survival in the training cohort

Characteristics	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age (years)						
<2		Reference			Reference	
≥2	4.145	1.718–9.998	0.002	3.995	2.418–7.768	0.011
Gender						
Male		Reference				
Female	1.127	0.501–2.537	0.773			
Race						
White		Reference			Reference	
Others	2.524	1.130–5.635	0.024	2.210	0.708–1.971	0.080
NHIA						
Non-Spanish-Hispanic-Latino		Reference				
Spanish-Hispanic-Latino	0.675	0.268–1.701	0.850			
Summary stage						
Localized		Reference			Reference	
Regional	3.147	1.029–9.622	0.044	1.453	0.420–2.482	0.567
Distant	8.627	2.996–24.837	<0.001	1.867	1.572–8.126	0.590
Surgery						
No		Reference			Reference	
Yes	0.064	0.028–0.143	<0.001	0.056	1.061–2.404	0.017
Chemotherapy						
No/unknown		Reference			Reference	
Yes	0.278	0.095–0.814	0.020	0.123	0.138–0.772	0.027
Systemic therapy						
No		Reference			Reference	
Yes	0.095	0.042–0.213	<0.001	1.959	0.835–1.577	0.596
Tumor size (mm)						
<123		Reference			Reference	
≥123	5.539	2.453–12.510	<0.001	3.004	1.035–1.961	0.068
Lung metastasis						
No		Reference			Reference	
Yes	5.308	2.354–11.970	<0.001	1.539	1.035–1.961	0.707

HR, hazard ratio; CI, confidence interval; NHIA, North American Association of Central Cancer Registries Hispanic Identification Algorithm.

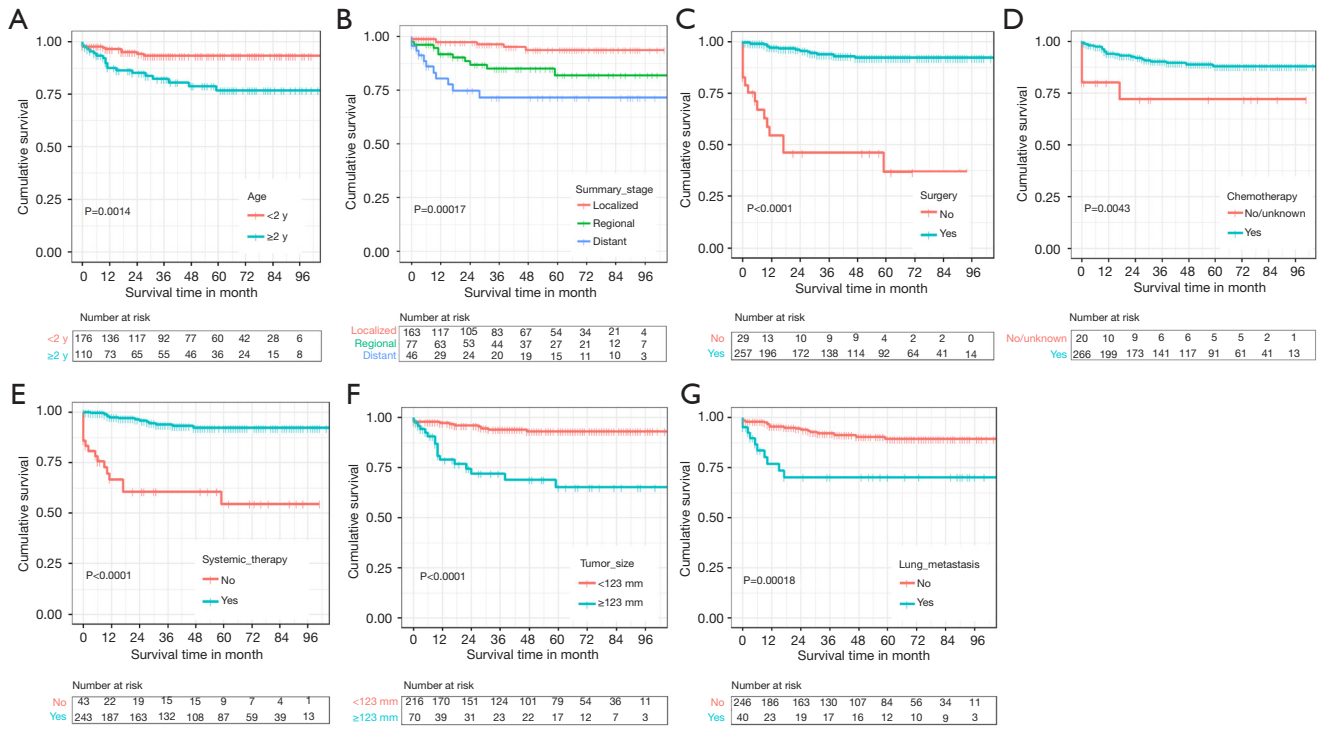

Figure 3 Kaplan-Meier curves illustrating overall survival. (A) Age. (B) Summary stage. (C) Surgery. (D) Chemotherapy. (E) Systemic therapy. (F) Tumor size. (G) Lung metastasis.

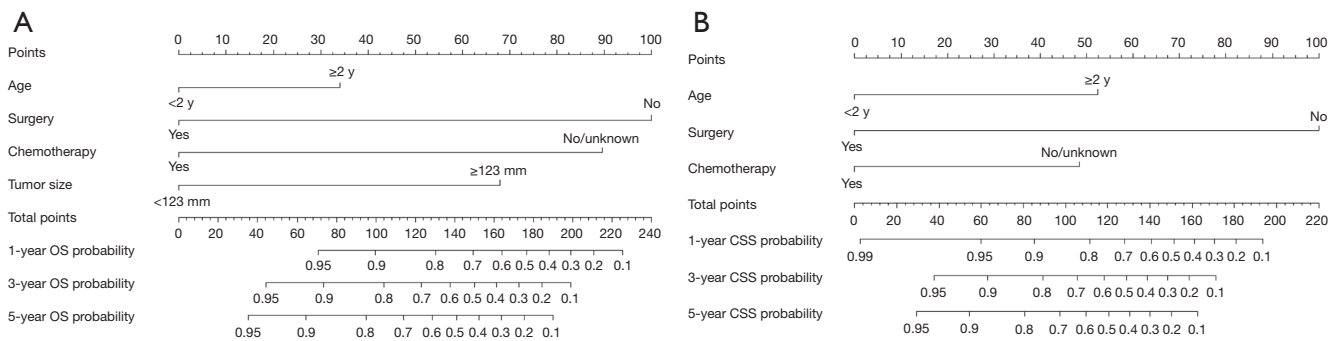

Figure 4 Nomogram for predicting 1-, 3-, and 5-year OS (A) and CSS (B) in hepatoblastoma patients. OS, overall survival; CSS, cancer-specific survival.

training and validation datasets. The clinical utility of the nomogram-based models for predicting survival at different time intervals (1 year, 3 years, and 5 years) was proven by the DCA presented in *Figure* 7.

Web-based survival rate calculator

To enhance accessibility, a web-based survival rate calculator (https://nbnomogram.shinyapps.io/NBnomo/) incorporating the nomogram was constructed. This tool enables healthcare professionals and individuals receiving medical care to estimate long-term OS. For example, a scenario involving a 6-month-old boy with HB and a tumor size of less than 123 mm is illustrated. The 3-year OS rate is approximately 26.6% without chemotherapy and surgical resection. However, with chemotherapy and surgical

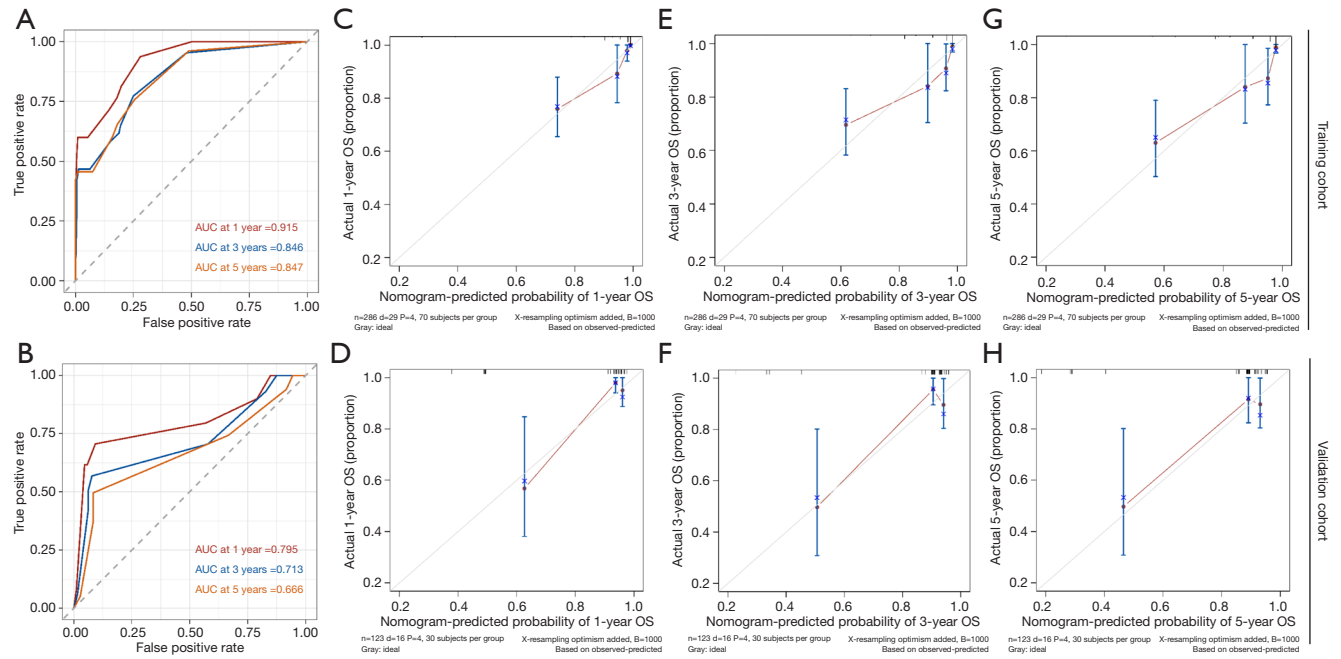

Figure 5 Validation of the nomogram-based model for OS. Time-dependent ROC curves (A,B) and calibration plots (C-H) for predicting 1-, 3-, and 5-year overall survival in the training cohort and the validation cohort. OS, overall survival; ROC, receiver operating characteristic; AUC, area under the curve.

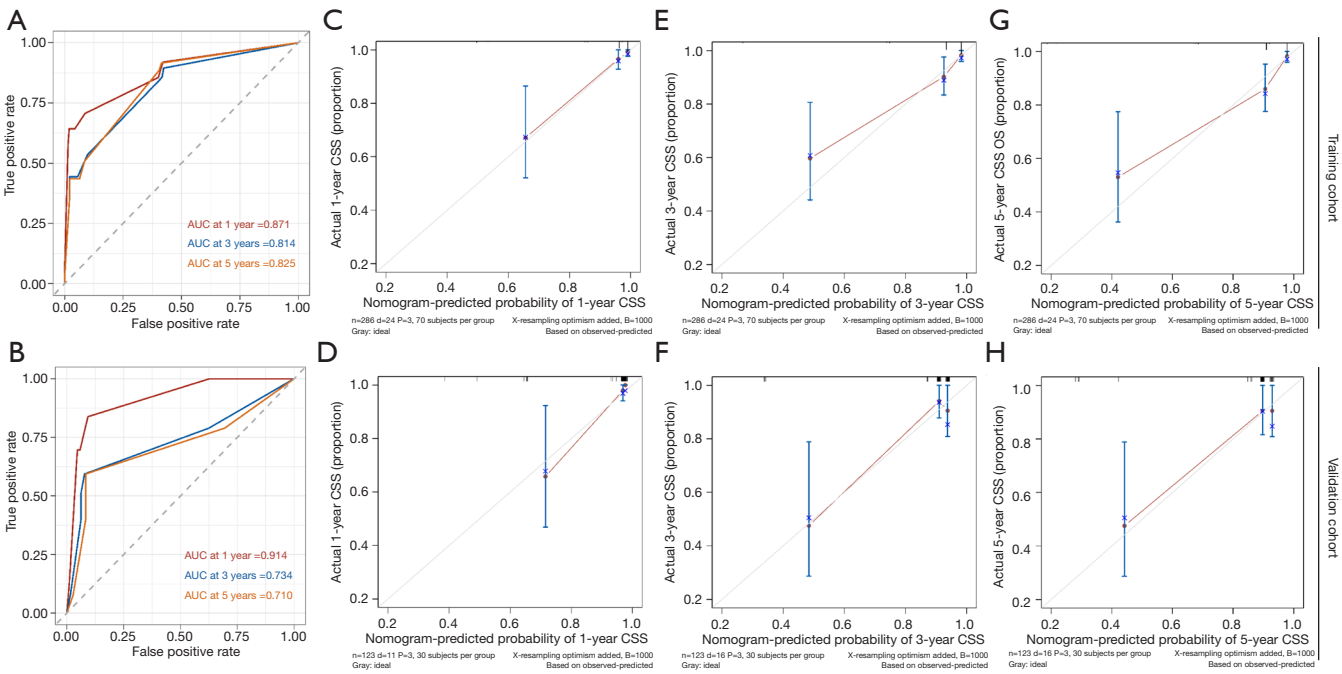

Figure 6 Validation of the nomogram-based model for CSS. Time-dependent ROC curves (A,B) and calibration plots (C-H) for predicting 1-, 3-, and 5-year CSS in the training cohort and the validation cohort. CSS, cancer-specific survival; ROC, receiver operating characteristic; AUC, area under the curve.

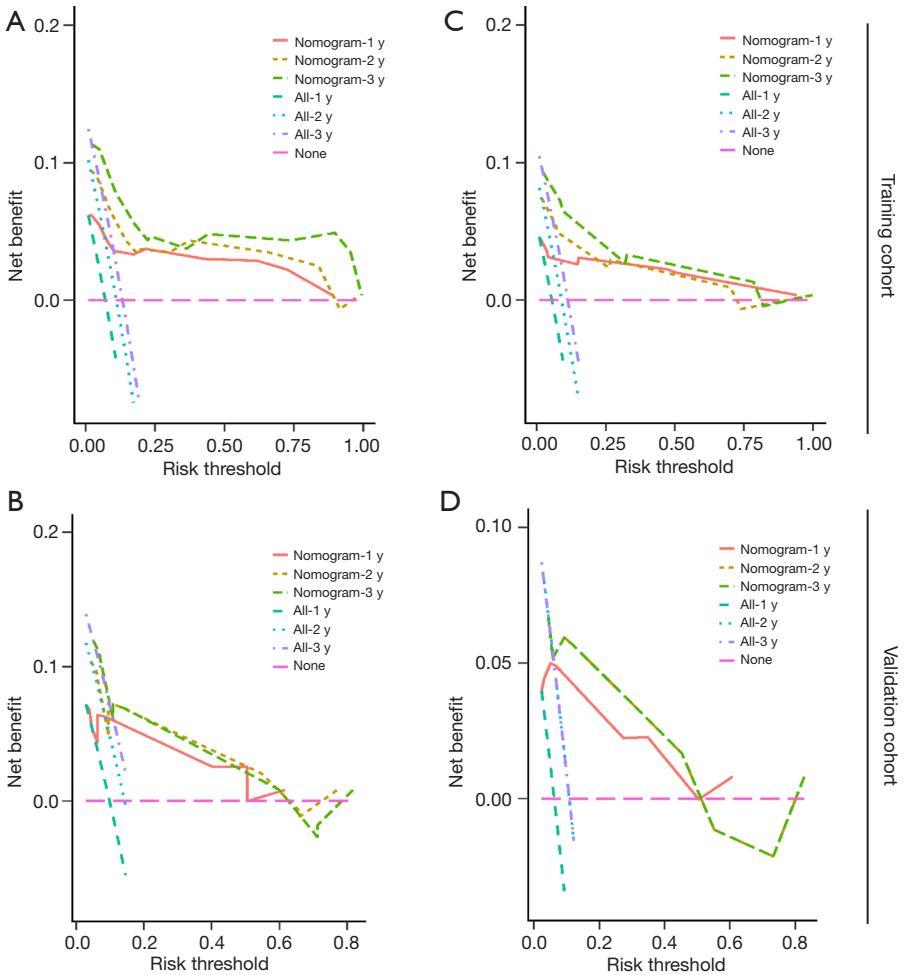

Figure 7 Decision curve analysis of the nomogram for predicting 1-, 3-, and 5-year overall survival (A,B) and cancer-specific survival (C,D) in the training cohort and the validation cohort.

resection, the 3-year OS rate significantly improves to approximately 99.0% (*Figure 8*).

Discussion

In this extensive retrospective investigation, novel nomograms were designed and validated for the prediction of the CSS and OS in a larger group of pediatric patients with HB. Nomograms can provide individualized long-term prognosis prediction, hence offering improved decision-making for clinical decisions. The construction of the nomogram was done by the utilization of multivariate Cox regression to identify prognostic markers. Moreover, the differentiation, calibration, and utility assessments conducted in our work have revealed the robust prediction capabilities of the nomograms.

Primary liver tumors in pediatric patients account for around 1% of all tumors in children and 5–6% in the abdominal region. Among these tumors, HB is the most frequently occurring tumor (22,23). HB includes various tumors arising from various hepatic precursor cells, exhibiting marked heterogeneity and varying clinical outcomes (5,24). Accurate risk stratification is essential for treatment planning, requiring the identification of prognostic risk factors. Multiple investigations have found many indicators associated with an unfavorable prognosis, including PRETEXT stages, metastasis, AFP levels ranging from 100–999 ng/L, tumor multifocality, vascular invasion, extrahepatic invasion, and older age of disease onset (25-28). The study determined that the independent predictive variables were age, chemotherapy, and surgery.

According to the nomograms, chemotherapeutic

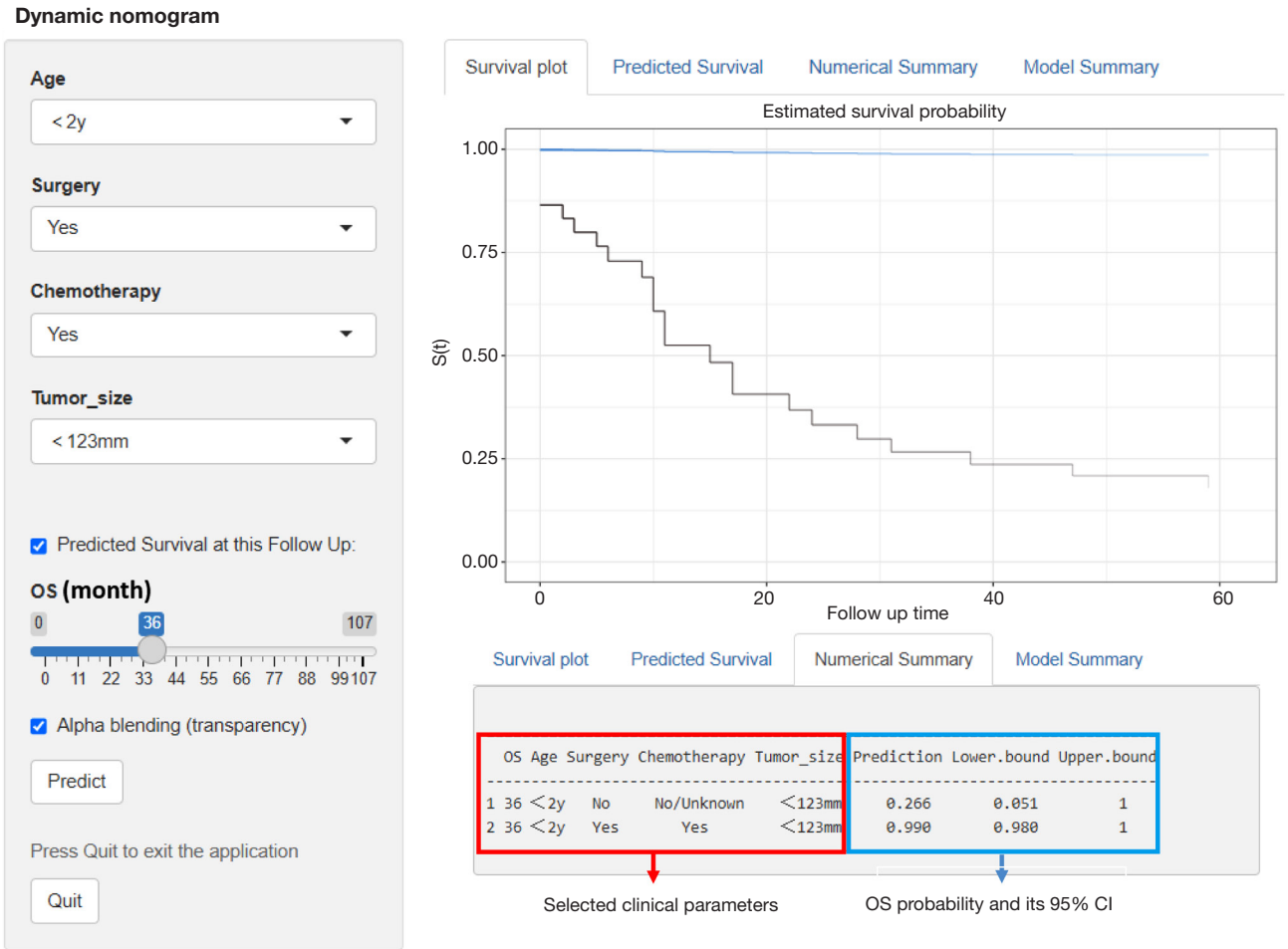

Figure 8 The interface of the web-based nomogram, survival plot, and numerical summary of the OS probability. OS, overall survival; CI, confidence interval.

treatments are the most significant prognostic indicators for both OS and CSS after surgical procedures in both point axes. Combining radical surgery and chemotherapy significantly enhances the survival rates of children diagnosed with HB. Despite the need for chemotherapy due to insufficient resection after diagnosis, surgery continues to be the primary treatment for HB (29,30). Surgery timing is still debatable, as COG recommends surgery for very-low-risk and low-risk groups (PRETEXT stages I and II) without major vessel invasion, while International Childhood Liver Tumors Strategy Group (SIOPEL) suggests chemotherapy for all patients. Therefore, timing remains a clinical concern, with some studies supporting direct surgery for very low-risk cases (31,32). For unresectable tumors at diagnosis, standard treatment involves preoperative chemotherapy, surgical resection, and postoperative chemotherapy (33). The efficacy of neoadjuvant chemotherapy in reducing tumor growth and preventing concealed metastases has been demonstrated. Furthermore, the integration of delayed surgery has notably augmented the survival percentage among pediatric patients diagnosed with HB (34).

The evaluation of chemotherapy effectiveness for solid tumors heavily relies on the measurement of tumor size, commonly represented by the maximum diameter. The assessment of therapy efficacy predominantly hinges upon alterations in tumor dimensions. The research conducted in our study revealed that around 23% of tumors had a maximum diameter ≥123 mm. The use of multifactorial Cox regression analysis revealed that children with tumors of bigger size (≥123 mm) had less favorable prognoses. Distant metastases occur in around 20% of cases of HB,

with the lungs being the most commonly affected site. As a result, the OS rates for patients with HB ranged from 25% to 50% (35,36). In the current study, it was seen that a total of 64 individuals out of the 409 participants, accounting for 15.6% of the sample, experienced the development of distant metastases. These metastases were predominantly found in the lungs, and their presence had a notable and statistically significant influence on the long-term prognosis of the affected individuals. The customary approach for managing HB with lung metastasis normally entails the administration of chemotherapy as the first treatment, with subsequent resection if residual tumors persist (37). The age of the patient significantly influences the prognosis of HB. Young children under the age of 3 generally have more positive results. Comparatively, the 8 years old or older exhibit fewer favorable prognoses. The prognostic significance of parameters such as metastatic disease, AFP levels, and tumor rupture is also influenced by age, which in turn affects chemotherapy intensity recommendations (10,27). In this study, the age of the children was classified into two groups using the X-tile tool: under two years old and two years old or older. The study's results indicated that infants under two years had more favorable survival rates.

The presence of HB poses a substantial risk to the well-being of pediatric patients, underscoring the critical need for accurate prognostic assessment of survival outcomes. Unfortunately, the existing models for this particular purpose are insufficient. The present study aims to address this knowledge deficit by proposing nomograms for OS and CSS that apply to all individuals diagnosed with HB. Their robust discriminatory and calibration capabilities evidence the efficacy of these nomograms. The research conducted in our study demonstrated a high level of reliability and dependability since it incorporated a significant sample size consisting of 409 patients. These nomograms utilized all available clinical datasets, enabling personalized survival predictions for survival outcomes of HB patients. However, the effective application of these nomograms in actual scenarios is impeded by the requirement of human computations. To tackle this matter, a user-friendly online application has been developed to forecast the survival probabilities of individuals diagnosed with HB at different points in time.

Nevertheless, it is crucial to acknowledge that this research possesses certain limitations. The retrospective analysis may be susceptible to bias. Furthermore, it should be noted that the SEER database exhibits several limitations in its inclusion of prognostic indicators. Notably, the database needs to incorporate significant variables such as tumor markers, treatment specifics, and the number of masses. The absence of these elements may hinder the precision of survival prognoses. Furthermore, it is essential to conduct a prospective validation of the process of developing and validating the nomogram in a separate dataset to establish its reliability. This is crucial since relying just on a single database has inherent limits. Notwithstanding these constraints, our research offers significant contributions and should be viewed with prudence.

Conclusions

To conclude, the nomogram-based models exhibit innovation and have undergone rigorous validation, showcasing remarkable prediction accuracy. These models evaluate personalized CSS and OS in individuals diagnosed with HB. The aforementioned technologies exhibit a high degree of user-friendly interface and provide considerable promise in computing individualized survival probability, facilitating risk classification, and enhancing the clinical decision-making process.

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Footnote

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Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). As per the ethics guidelines, since public and anonymous data were utilized, neither informed consent nor approval of an ethics committee was necessary.

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