RESEARCH ARTICLE

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Development and Internal Validation of the SPR-HCC Score System: A Prognostic Tool for Survival Prediction in Hepatocellular Carcinoma in a Resource-Limited Setting

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Abstract

Background: Hepatocellular carcinoma (HCC) is a heterogeneous disease, in which survival is influenced by various factors beyond tumor characteristics. Although many prognostic models have been developed, they often have limitations, and the models do not include data from Thai patients. This study aimed to develop and internally validate a prognostic scoring system (SPR-HCC) using routinely available clinical and laboratory parameters. **Methods:** This retrospective cohort study analyzed 484 HCC patients diagnosed between October 2018 and April 2023 at a Thai tertiary center. Clinical, laboratory, and treatment data were extracted from electronic records. Independent mortality predictors were identified via multivariable Cox regression. Model performance was evaluated using Harrell's C-statistic, calibration plots, bootstrap resampling, and decision curve analysis. **Results:** Among 484 patients, 399 (82.4%) had died. The median overall survival (mOS) was 4.73 months (95% CI: 3.68–6.51). Eight independent predictors were identified: ECOG performance status, Child-Pugh class, tumor size >5 cm, bone metastasis, ALP >120 IU/L, AFP ≥400 ng/mL, PLR ≥150, and treatment aim. The final SPR-HCC model demonstrated strong discrimination (C-statistic = 0.797) and good calibration. Patients were stratified into low- (0–5 points), intermediate- (5.5–9.5 points), and high-risk (≥10 points) groups, with corresponding mOS of 29.12, 6.24, and 1.51 months (log-rank $p < 0.001$). Bootstrap validation showed minimal optimism (0.0000442) and a shrinkage factor of 0.9995. DCA indicated net clinical benefit across a threshold probability range of 0.15–0.60, with optimal benefit between 0.25–0.45. **Conclusions:** The model demonstrated good performance in stratifying patients into three risk groups with significantly different survival. This scoring system may be applied to clinical decision-making by providing risk group stratification for HCC patients.

Keywords: Hepatocellular carcinoma- prognostic models- survival analysis- Cox Proportional Hazards Models

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Introduction

Hepatocellular carcinoma (HCC) is a major global health burden and the third leading cause of cancer-related death in Thailand [1]. As with other malignancies, clinical staging systems are essential for guiding treatment decisions and prognostication [2]. However, HCC survival is influenced by multiple factors beyond tumor burden, including liver function [3, 4], underlying disease etiology [5-8], access to screening programs [9, 10], physical performance status [11], tumor biology [12] and treatment modality [13-16].

While many prognostic models exist, many have limitations. The American Joint Committee on Cancer (AJCC) TNM system focuses solely on tumor characteristic [2]. Others models such as the Okuda system[17] , Japan Integrated Staging (JIS) score [18], Cancer of the Liver Italian Program (CLIP) [19] and Model to Estimate Survival in Ambulatory HCC Patients (MESIAH) [20] incorporate liver function or cirrhosis severity but often exclude physical performance status, a strong predictor of survival. The Barcelona Clinic Liver Cancer (BCLC) staging system considers both tumor and patient characteristics and serves as a treatment guideline, but it was not primarily designed for prognostication [21, 22]. Accurate survival prediction remains challenging due to the clinical heterogeneity of HCC, its complex etiologies, and differences in healthcare resources between high- and low-income settings. To address this gap, the present study aims to develop the HCC Survival Scoring system—a prognostic tool intended to estimate survival at diagnosis and support personalized treatment planning.

Materials and Methods

Study design and data collection

This retrospective cohort study was conducted within the medical oncology unit of Sawanpracharak Hospital,

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Thailand, following approval from the institutional Human Research Ethics Committee (certificate approval no. 24/2567). The study included patients diagnosed with HCC (ICD-O-C22) between October 2018 and April 2023. Patient through the hospital's cancer registry. Sawanpracharak Hospital is a tertiary care center serving the lower northern region of Thailand. HCC diagnoses were confirmed either pathology proven or by imaging criteria using radiographic evidence by multi-phase computed tomography (CT) or magnetic resonance imaging (MRI) demonstrating characteristic features as defined by the American Association for the Study of Liver Diseases (AASLD) guidelines [23].

Data were extracted from electronic medical records, encompassing demographics, clinical features, comorbidities, hepatitis serology, laboratory results, diagnosis date, cancer stage, and treatment details. Liver function was assessed using the Child-Pugh (CP) score, incorporating serum albumin, bilirubin, international normalized ratio (INR), ascites, and hepatic encephalopathy. Patients were classified into CP-A (5–6 points), CP-B (7–9 points), and CP-C (10–15 points). Date of death was ascertained from the Thailand Civil Registration data bases. Overall survival was defined as the interval between diagnosis and either death or the date of a comprehensive survival census date of Mar 31, 2025 based on the National Registry of Deaths.

Statistical analysis

The required sample size for developing was calculated using pmsampsize, based on the criteria proposed by Riley et al. [24]. Assigning an event rate of 0.8, considering 8 potential predictors, and a targeting C-statistic of 0.8, the estimated a total sample size of 351 individuals with 281 events.

Continuous data were presented as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on distribution, and compared using t-test or rank-sum test. Categorical variables were described as frequencies and percentages. Survival was analyzed using the Kaplan-Meier method, with the log-rank test used to identify prognostic factors. Variables with $p < 0.1$ were entered into a Cox proportional hazards regression model using backward elimination (Supplementary Table 1).

The final prediction model was constructed using the regression of selected predictors. Discriminative performance was evaluated using Harrell's concordance index (C-index) and calibration was assessed using calibration plots to verify the accuracy of scoring system. Internal validation was performed using bootstrapping resampling to estimate optimism and shrinkage. Clinical utility was assessed using decision curve analysis (DCA). Analyses were conducted using STATA version 16 (StataCorp LLC, College Station, TX, USA).

Results

A total of 484 patients with HCC were analyzed, of whom 399 (82.4%) had died. The median overall survival (mOS) was 4.73 months (95%CI:3.68 - 6.51). Deceased patients were more likely to be male (79.20% vs 67.06%, $p = 0.022$) and had significantly poorer performance status, with 76.94% having ECOG 0–2 compared to 98.8% among survivors ($p < 0.001$). Alcohol consumption was more frequent in deceased patients (39.45% vs. 25.88%, $p = 0.019$), while HCC detection through surveillance was more common among survivors (32.14% vs. 15.33%, $p = 0.001$). Viral etiology was not significantly associated with survival ($p = 0.593$). Survivors had better liver function, with a higher proportion classified as Child-Pugh A (83.33% vs. 41.52%, $p < 0.001$). Symptoms such as weight loss, abdominal pain, jaundice, and ascites were significantly less common among survivors (all $p < 0.001$). Tumor burden was lower in survivors, with smaller median tumor size (3.20 vs. 7.85 cm, $p < 0.001$), fewer multifocal liver lesions (31.76% vs. 71.68%, $p < 0.001$), and lower rates of main portal vein invasion (2.35% vs. 35.43%, $p < 0.001$), lung metastasis (2.35% vs. 15.54%, $p < 0.001$), and tumor rupture (3.53% vs. 11.28%, $p = 0.028$). Laboratory profiles also more favorite in survivors, with significant lower levels of ALP, AFP, WBC, neutrophils, platelet counts, INR, NLR, and PLR (all $p < 0.001$), and higher hemoglobin ($p= 0.001$; the as Table 1).

All candidate variables were initially entered into a multivariable regression analysis, yielding a c-statistic of 0.803. Multivariable Cox regression with stepwise selection identified ECOG 3–4 was associated with increased mortality (HR: 1.577; 95% CI: 1.166–2.134), as were Child-Pugh class B (HR: 1.604; 95% CI: 1.229–2.092) and class C (HR: 2.987; 95% CI: 2.075–4.300) compared to class A. Tumor size >5 cm (HR: 1.684; 95% CI: 1.288–2.201) and bone metastasis (HR: 1.738; 95% CI: 1.021–2.960) also predicted worse survival. Laboratory markers including ALP >120 IU/L (HR: 2.265; 95% CI: 1.721–2.980), AFP ≥400 ng/mL (HR: 1.370; 95% CI: 1.067–1.757), and PLR ≥150 (HR: 1.476; 95% CI: 1.167–1.867) were independent predictors of mortality in patients with HCC. These predictors were incorporated into the prognostic model with assigned scores summarized in Table 2.

For risk stratification, total scores derived from the SPR-HCC model were used to categorize patients into three risk groups: low (0–5 points), intermediate (5.5–9.5 points), and high (≥10 points). Kaplan-Meier survival curves showed significant separation among the groups (log-rank $p < 0.001$) as Figure 1. The low-risk group had a mOS of 29.12 months, compared to 6.24 months in the intermediate-risk group (HR: 4.03; 95% CI: 2.89–5.63; $p < 0.001$) and 1.51 months in the high-risk group (HR: 14.25; 95% CI: 10.07–20.19; $p < 0.001$) the as Table 3.

Model Performance and validation

The final model demonstrated C-statistic of 0.797. The calibration curve demonstrated fine agreement between observed and predicted survival probabilities (Figure 2). The internal validation with bootstrap resampling showed yielded an optimism 0.0000442 and shrinkage factor was 0.99950113.

Clinical use

The DCA (Figure 3) demonstrated a net clinical benefit of the SPR-HCC scoring model across a threshold

Table 1. Patient Characteristic

	Total		Death		Alive		p-value
	N	Result	N	Result	N	Result	
Male, %	484	77.07	316	79.2	57	67.06	0.022
Age-year, mean ± SD	484	61.33±10.19	399	61.42±10.28	85	60.92±9.78	0.686
BMI, median (IQR)	458	22.14 (20.10, 24.66)	373	22 (20.08, 24.22)	85	22.65 (20.19,25.78)	0.091
ECOG, %							<0.001
0-2	391	80.79	307	76.94	84	98.82	
3-4	93	19.21	92	23.06	1	1.18	
Viral associated, %							0.593
Non-viral	59	12.32	47	11.93	12	14.12	
HCV	141	29.44	112	28.43	29	34.12	
HBV	256	55.32	223	56.6	42	49.41	
HBV and HCV	14	2.92	12	3.05	2	2.35	
Alcohol, %	179	37.06	157	39.45	22	25.88	0.019
Surveillance, %	88	18.26	61	15.33	27	32.14	0.001
Underlying disease, %							
HIV	8	1.66	5	1.26	3	3.53	0.151
Diabetic mellitus	90	18.62	75	18.8	15	17.86	1
IHD	9	1.86	8	2.01	1	1.18	1
CVD	16	3.31	14	3.52	2	2.35	0.749
Dyslipidemia	88	18.18	73	18.3	15	17.65	1
Child Pugh, %							<0.001
A	234	48.85	164	41.52	70	83.33	
B	268	35.07	154	38.99	14	16.67	
C	77	16.08	77	19.49	0	0	
Weight loss, %	201	41.53	185	46.37	16	18.82	<0.001
Abdominal pain, %	258	53.31	230	57.63	28	32.94	<0.001
Jaundice, %	68	4.05	66	16.54	2	2.35	<0.001
Ascites, %	133	27.48	124	31.08	9	10.59	<0.001
GIB, %	53	10.95	45	11.28	8	9.41	0.705
Hepatomegaly	128	26.35	117	29.32	11	12.94	0.002
Main PV, %	143	29.61	141	35.43	2	2.35	<0.001
Rupture, %	48	9.92	45	11.28	3	3.53	0.028
Size-cm, median (IQR)	481	7 (3.5, 11.3)	396	7.85 (4.5, 11.9)	85	3.2 (1.9, 5.8)	<0.001
Multifocal liver lesion, %	313	64.67	286	71.68	27	31.76	<0.001
Lung metastasis, %	64	13.22	62	15.54	2	2.35	<0.001
Peritoneal metastasis, %	8	1.65	7	1.75	1	1.18	1
Bone metastasis, %	18	3.72	18	4.51	0	0	0.053
BCLC, %							<0.001
0	4	0.83	1	0.25	3	3.53	
A	61	12.6	27	6.77	34	40	
B	147	30.37	104	26.07	43	50.59	
C	167	34.5	162	40.6	5	5.88	
D	105	21.69	105	26.32	0	0	
Treatment, %							<0.001
Curative surgery	7	1.66	3	0.85	4	5.8	
RFA	37	8.77	14	3.97	23	33.33	
TACE	83	19.67	53	15.01	30	43.48	
Palliative TKI	6	1.42	6	1.7	-	-	
Palliative CMT	34	8.06	31	8.78	3	4.35	
Palliative surgery	5	1.18	4	1.13	1	1.45	
Palliative radiation	4	0.95	4	1.13	-	-	
Best supportive care	246	58.29	238	67.42	8	11.59	
Total bilirubin (mg/dl), median (IQR)	480	1.2 (0.6, 2.3)	395	1.3 (0.7, 2.8)	85	0.8 (0.5, 1.3)	<0.001

Table 1. Continued

	Total		Death		Alive		p-value
	N	Result	N	Result	N	Result	
Albumin (g/dl), median (IQR)	480	3.3 (2.8, 3.8)	395	3.2 (2.7, 3.7)	85	3.7 (3.2, 4.1)	<0.001
ALP (IU/L), median (IQR)	480	157 (106, 238)	395	170 (115, 257)	85	110 (83, 143)	<0.001
AFP (ng/ml), median (IQR)	443	408 (21, 6235)	361	842 (42, 11174)	81	29 (63, 371)	<0.001
Hb (g/dl), median (IQR)	478	11.0 (9.6, 12.6)	394	10.9 (9.3, 12.3)	84	11.85 (10.3, 13.3)	0.001
WBC (mm^3), median (IQR)	478	7660 (5320, 9760)	394	7960 (5600, 10260)	84	5910 (3970, 7785)	<0.001
Neutrophil (mm^3), median (IQR)	478	4955 (3010, 7140)	394	5375 (3250, 7700)	84	3360 (2145, 4900)	<0.001
Lymphocyte (mm^3), median (IQR)	478	1440 (1050, 1045)	394	1459 (1070, 3060)	84	1340 (995, 2060)	0.425
Platelet ($x10^3$), median (IQR)	478	230 (140, 459)	394	236 (146, 460)	84	178 (100, 391)	0.01
INR, median (IQR)	437	1.17 (1.07, 1.31)	360	1.19 (1.08, 1.34)	77	1.11 (1.03, 1.20)	<0.001
NLR, median (IQR)	478	3.21 (1.89, 5.73)	394	3.55 (2.15, 6.00)	84	2.16 (1.38, 5.84)	<0.001
PLR, median (IQR)	478	164.0 (92.4, 335.11)	394	172.4 (96.3, 343.4)	84	128.9 (72.3, 324.4)	0.036
GFR (mL/min/1.73 m^2), median (IQR)	479	83.3 (63.4, 98.3)	394	83.4 (63.6, 98.5)	85	83 (63.4, 95.7)	0.927

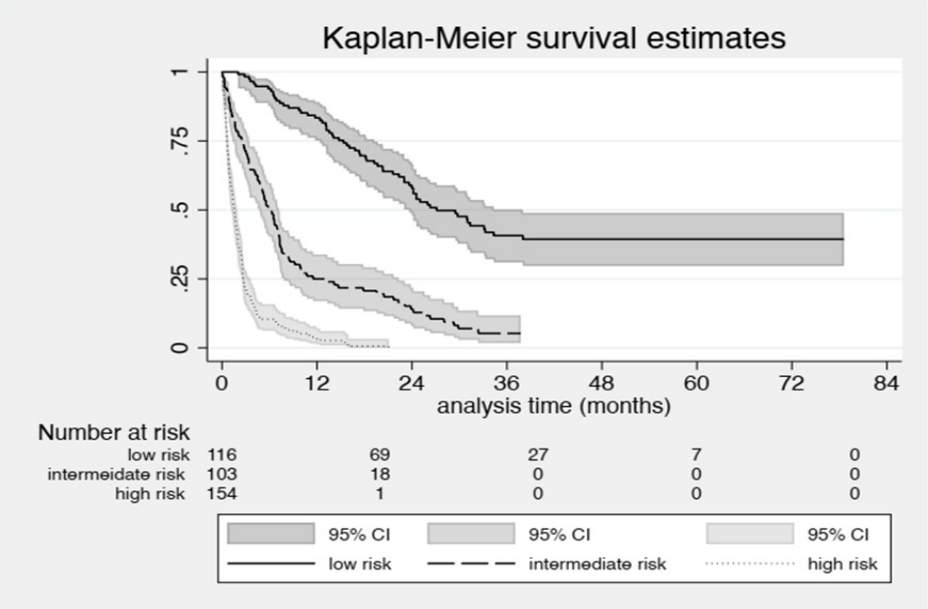

Figure 1. Kaplan Meier Survival According to Risk Group

probability range of 0.15 to 0.60. The optimal threshold appears to lie between 0.25 and 0.45, where the model's net benefit is highest compared to alternative strategies.

Discussion

This study developed and internally validated the SPR-HCC scoring system, a prognostic tool for HCC based

Table 2. Multivariable Cox Regression with Stepwise Selection and Assigned Scores (SPR-HCC Model)

Predictors	HR	95% CI	B Coefficient	Assigned Score
ECOG3-4	1.577	1.166, 2.134	0.456	1.5
Child				
A				0
B	1.604	1.229, 2.092	0.472	1.5
C	2.987	2.075, 4.300	1.094	3.5
Size >5 cm	1.684	1.288, 2.201	0.521	1.5
Bone metastasis	1.738	1.021, 2.960	0.553	2
AFP ≥400	1.37	1.067, 1.757	0.314	1
ALP >120	2.265	1.721, 2.980	0.818	2.5
PLR ≥150	1.476	1.167, 1.867	0.389	1
Palliative aim	3.657	2.630, 5.084	1.296	4

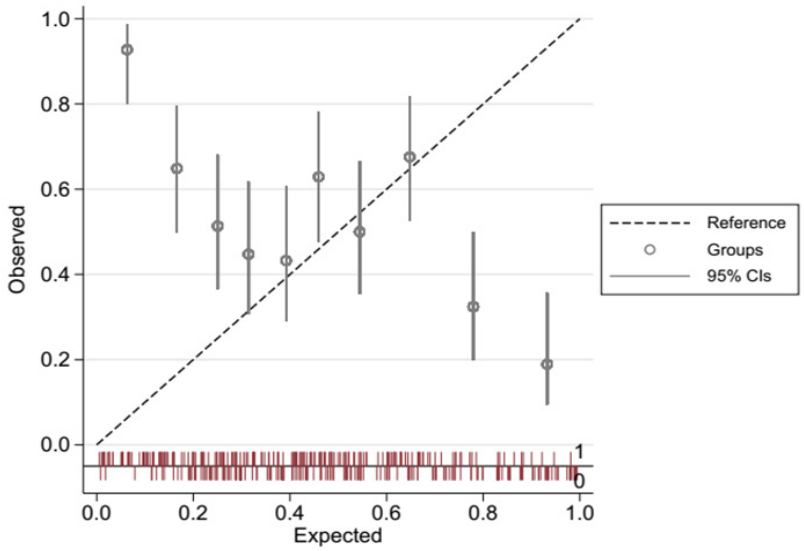

Figure 2. Calibration Plot between the Scoring Predicted Survival Probability and Observed Survival Probability

Table 3. Overall Survival among by SPR-HCC Risk Groups

Risk groups stratified by core	Subjects	mOS (month)	Hazard Ratio	95% CI	p-value
Low risk (score 0-5)	116	29.12	ref		
Intermediate risk (score 5.5-9.5)	103	6.24	4.03	2.890, 5.630	<0.001
High (risk score≥10.0)	154	1.51	14.25	10.070, 20.188	<0.001

on routinely available clinical and laboratory parameters. The model demonstrated good discriminatory ability (C-statistic = 0.797) and well calibration, effectively stratifying patients into three distinct risk groups with significantly different mOS (29.12, 6.24, and 1.51 months for low-, intermediate-, and high-risk, respectively; $p < 0.001$). These findings support its potential clinical utility for individualized survival prediction, applied to clinical-decision and prioritization management.

The final model incorporated eight independent predictors: ECOG performance status, CP score, size of tumor, Bone metastasis, AFP, ALP, PLR and treatment aim. These variables reflect key aspects of tumor burden, liver function, systemic inflammation, and physical condition factors known to influence HCC prognosis. Notably, performance status, NLR, and PLR are often excluded from widely used models such as CLIP or JIS, despite their established prognostic significance. Their inclusion may enhance the model's relevance in real-world applicability, especially in settings with limited access to advanced imaging or biomolecular profiling.

Several existing HCC prognostic models have

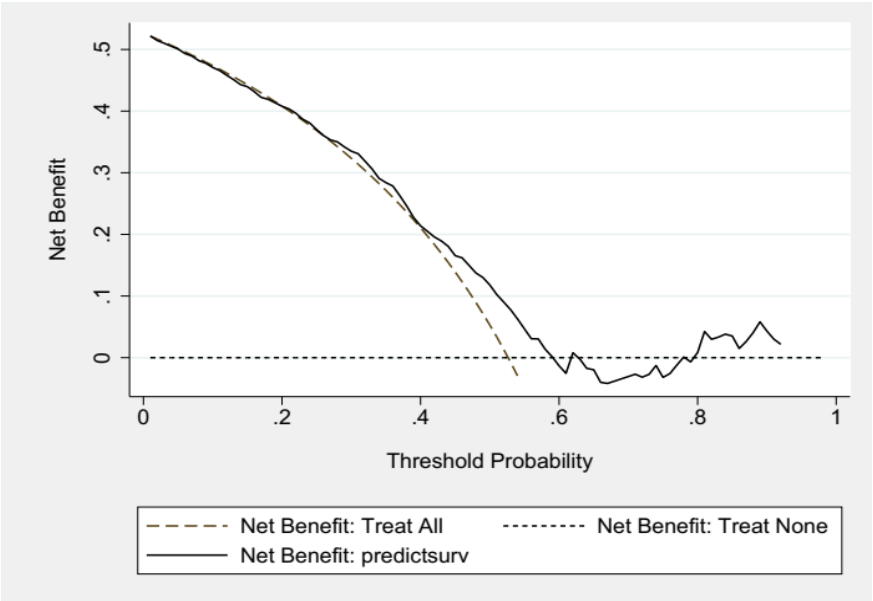

Figure 3. Decision Curve Analysis (DCA)

limitations. The TNM staging system, although standard in oncology, does not account for liver function and systemic health—both essential in HCC, where underlying cirrhosis is common [2]. The CLIP scoring-based on tumor burden, severity of cirrhosis and AFP levels- is widely used for intermediate-stage unresectable HCC and has shown superiority in discriminative performance (C-index 0.604) over TNM, Okuda, CP and ALBI [25, 26]. However, it omits performance status (PS), a key prognostic factor and essential criterion in cancer clinical trials [26, 18]. The ALBI score, although objective and liver-specific, does not consider clinical signs like ascites or encephalopathy which are reflected in the CP classification and are prognostic relevant [4]. The widely used BCLC staging system was originally designed for treatment allocation rather than prognostic tool [27] and its prognostic precision diminishes in patients with heterogeneous liver function or borderline performance status [25]. Furthermore, many existing models were developed in high-income countries and may not reflect outcomes or care realities in resource-limited settings.

ECOG remains a cornerstone in assessing patient fitness and predicting survival across malignancies [28, 29]. Tumor size at diagnosis, part of the AJCC TNM system, is associated with poorly differentiated histology [30], increased risk distant metastasis, [31] and higher mortality [32]. Although bone metastases are rare in HCC (~3.1%), they are also impair quality of life and linked to poorer survival outcomes [33, 34] consistent with the finding in this study.

AFP widely used for HCC screening and diagnosis in cirrhotic patients [35] also serves as prognostic value. Elevated AFP (≥400 ng/ml) has been associated with worse survival after hepatectomy [36, 37] and targeted therapy [38] and a prognostic value in HCC [39]. Similarly, ALP, a marker of cholestasis and biliary tract involvement, has been linked to recurrence and adverse prognosis in HCC [40, 41]. The CP score remains a validated measure of hepatic reserve and is essential for both prognosis and treatment stratification [42].

Inflammatory markers, including NLR and PLR have gained attention as prognostic tools across various cancers [43-46]. The role of proinflammatory cytokine and growth factors released by tumors and their microenvironment in promoting tumor development is well documented [47]. PLR, reflects platelet-driven tumor angiogenesis [48, 49] and both markers are considered significant contributors to tumor progression and have shown prognostic value in HCC [49, 45]. Patients receiving active HCC treatments demonstrated improved overall survival compared to those receiving palliative care. These findings are supported by studies showing that that interventions such as RFA and TACE are associated with higher response rates and prolonged time to progression Additionally, novel systemic therapies have shown survival benefits in advanced-stage HCC [15, 16, 14]. Data from western population further support improved survival in the era of advanced treatments [39]. However, limited access to these therapies in low- and middle-income countries may hinder their clinical impact, highlighting the need for models tailored to such settings.

In summary, SPR-HCC score offered a simple and accessible prognostic tool based on clinical and laboratory parameters at diagnosis, along with initial care goals. It captures key elements of tumor biology, liver function, and systemic inflammation. Another strength of this study is the use of a real-world data in a developing country, where healthcare resources, access screening, and treatment availability differ from high-income countries. Many existing models may not fully reflect the realities of resource-limited environments. The SPR-HCC model may be particularly valuable in such contexts.

However, this study has some limitations. First, it was retrospective and based on data from a single center, which may limit external validity. Second, some variables such as liver stiffness were not available in all patients, possibly affecting staging accuracy. Third, external validation in other cohorts is essential before clinical implementation. Future prospective should focus on external validation of the SPR-HCC scoring across diverse populations, particularly multi-center Asian populations, to confirm its generalizability and clinical applicability.

Author Contribution Statement

Sunee Neesanun contributed to conceptualization, methodology, data curation, data analysis, and manuscript writing. Jayanton Patumanond contributed as a research advisor and provided data analysis

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Conflict of interest

The authors declare no conflicts of interest.

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