Prognostic nomogram for hepatocellular carcinoma with fibrosis of varying degrees: a retrospective cohort study

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Background: Hepatocellular carcinoma (HCC) is a common and biologically aggressive malignancy linked to cirrhotic and pre-cirrhotic changes in the liver. We analyzed degrees of fibrosis in affected patients as indices of survival, to establish an effective prognostic nomogram.

Methods: Eligible patients with HCC and hepatic fibrosis, of varying degrees, were selected from the Surveillance, Epidemiology, and End Results (SEER) database for propensity score matching (PSM). The prognostic value of data was determined using Kaplan-Meier and Cox proportional hazards model. A nomogram based on variables derived from multivariate analyses was established and subjected to internal validation. Its predictive accuracy was tested by concordance index (C-index) and calibration plots.

Results: In this propensity score-matched cohort, advanced fibrosis/cirrhosis (*vs.* none-to-moderate fibrosis) correlated with poorer survival [hazard ratio (HR): 1.131, 95% confidence interval (CI): 1.032–1.240; P=0.009]. Multivariate analysis identified the following as independent risk factors for HCC: age >63 years, higher fibrosis score, American Joint Cancer Committee (AJCC) stages T3–4, distant metastasis (M1), tumor size >1 cm, major vascular invasion, and elevated alpha-fetoprotein (AFP) level. A nomogram that integrated these factors offered a superior prognostic prediction for HCC patients (C-index: 0.749, 95% CI: 0.7485–0.7495) relative to conventional tumor staging the AJCC tumor-node-metastasis (TNM) staging system (0.730). In calibration plots, optimal agreement between nomogram-predicted and observed survival was evident.

Conclusions: Increased fibrosis was an independent risk factor for survival of HCC patients. A prognostic nomogram integrating fibrosis score and other independent risk factors offered more accurate depictions in this regard.

Keywords: Hepatocellular carcinoma (HCC); fibrosis; nomogram; prognosis

Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer, accounting for up to 10% of cancer-related mortality worldwide and carrying a 70–100% cumulative risk of recurrence within 5 years after surgery (1-3). In the vast majority of cases (70–90%), HCC arises within advanced fibrosis and cirrhosis as a consequence of various etiologic insults (4). Fibrosis is a protective wound healing

Page 2 of 11

Zhang et al. Prognostic nomogram for HCC with fibrosis of varying degrees

response to chronic liver damage that progresses to fibrous scarring or cirrhosis if injurious conditions persist (5). Often associated with hepatic dysfunction, fibrosis and cirrhosis are considered premalignant states that heighten the risk of developing HCC (6).

The American Joint Cancer Committee (AJCC) tumor-node-metastasis (TNM) staging system (7th ed.) is commonly used for tumor classification and remains the prognostic standard in this setting (7). Nonetheless, its practical application is not entirely satisfactory, especially in patients with advanced disease (8). One possible explanation for inconsistencies lies in the heterogeneity of patient backgrounds and its failure to include other clinicopathological characteristics (such as demographics and tumor profiles) that are important to predict survival. As effective and convenient statistical tools, nomograms incorporate all prognostic variables and have been generated for a variety of cancer types (9-11).

Using Surveillance, Epidemiology, and End Results (SEER) analysis, we established a prognostic nomogram that integrated fibrosis scores and other independent variables to predict patient survival as a function of hepatic fibrosis. This model offers greater accuracy that may aid clinicians in routine practice.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-3267).

Methods

Patients selection and data extraction

We performed a retrospective cohort analysis by querying the SEER-18 regs research data (November 2017 submission) (https://seer.cancer.gov/) for patients diagnosed with HCC [International Classification of Diseases for Oncology (3rd ed., ICD-O-3): HCC, histologic codes 8170-8175; liver, site code C22.0] between 2004 and 2015. Ethics approval and informed consent were waived because SEER data are freely available and our investigation was retrospective in nature.

The following exclusion criteria were applied to HCC patients in this study: (I) age <18 years, (II) voids in survival time or fibrosis score, (III) ID number duplication, (IV) diagnosis prior to 2004, and (V) no evidence of primary cancer. Fibrosis (or Ishak) scores were categorized as F0–4 (code 0, none-to-moderate) or F5–6 (code 1, severe fibrosis or cirrhosis), to compare these subsets in terms of patient survival. Alpha-fetoprotein (AFP) levels were likewise grouped as positive/elevated (code 10), negative/normal or within normal limits (code 20), or unclear results. Most tumors (90%) were <1 cm; therefore, the related groupings were ≤1 cm (code 0–991), >1 cm (code 992–996), or unclear. Vascular invasion was recorded as absent, minor (codes 200/350/370/380/400/520/550), major (codes 630/635/660), or unclear. Data on age, sex, AJCC TNM stage, fibrosis score, AFP level, tumor size, vascular invasion, and survival (months) were ultimately extracted from the SEER database.

Statistical analysis

As previously described (12), 1:1 propensity score matching (PSM) was implemented to minimize selection bias and balance baseline covariates in F0–4 and F5–6 subsets of hepatic fibrosis. No overt covariate imbalances emerged in pertinent testing, supporting the adequacy of execution. Statistical analysis of SEER data relied on standard software (SPSS v19.0; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) values and analyzed via unpaired t-tests. Chi-square or the Fisher's exact test was used to compare categorical variables. Survival curves were generated by Kaplan-Meier method (log-rank test). Factors significantly impacting survival in the univariable analysis were further tested by multivariate Cox proportional hazards model. Due to unclear data recorded for some variables, four sensitivity analyses were undertaken to gauge the robustness of their influence (after PSM) on overall survival (OS), repeating all statistical maneuvers to accommodate the following adjustments: (I) all unclear T stages classified as T1–2; (II) all unclear T stages classified as T3–4; (III) all unclear M stages classified as M0; and (IV) all unclear M stages classified as M1. The prognostic nomogram utilized variables of multivariate analyses and was constructed in R software (rms package; R Foundation for Statistical Computing, Vienna, Austria). The predictive accuracy and discriminative ability were determined by concordance index (C-index) and calibration curves. Statistical significance was set at P<0.05.

Results

Clinicopathologic characteristics

A total of 8,119 patients listed in the SEER database met our eligibility criteria, each diagnosed with HCC between
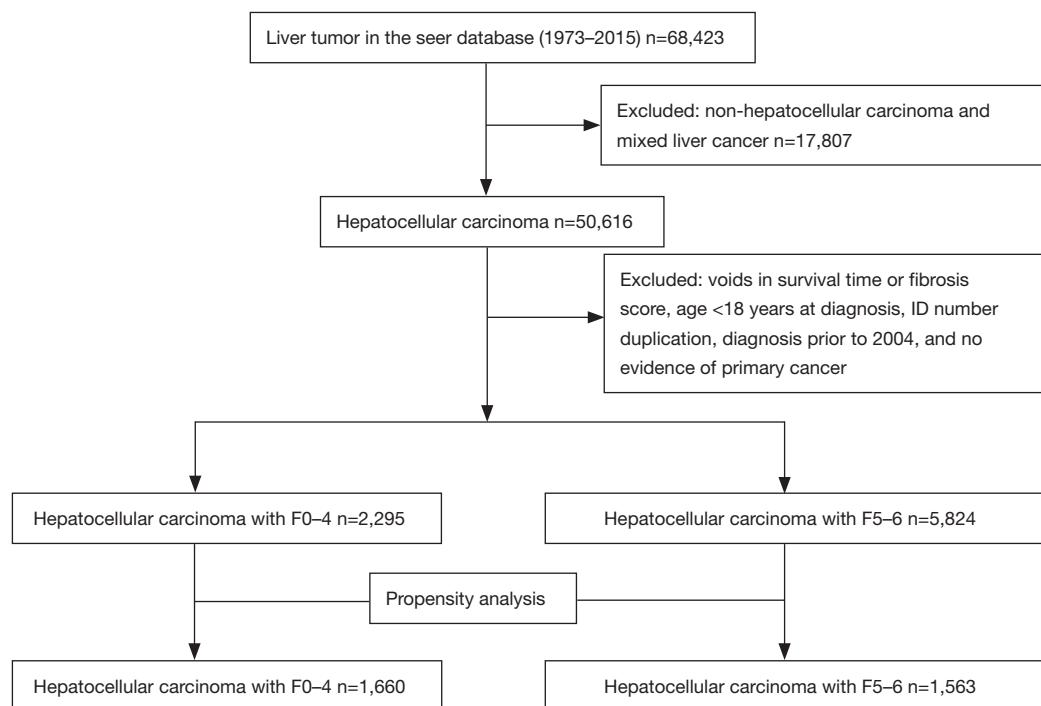
Figure 1 Flowchart of selecting patients with HCC using SEER database. HCC, hepatocellular carcinoma; SEER, Surveillance, Epidemiology, and End Results.

2004 and 2015. Follow-up intervals ranged from 0–143 (median, 15) months. The F0–4 and F5–6 fibrosis subsets accounted for 2,295 and 5,824 patients, respectively (*Figure 1*). Those with advanced fibrosis and cirrhosis were more apt to be younger (61.76±9.54, P<0.001) and male (P=0.027), with T1–2 tumors (P<0.001), no nodal metastasis (P=0.0065), no distant metastasis (P=0.0002), and elevated AFP levels (P<0.001). Those with none-to-moderate fibrosis were more often older and female, with T3–4 tumors and no AFP elevations. Because differing degrees of hepatic fibrosis may be confounded by differences in baseline patient characteristics, we used PSM to distinguish 1:1 matched pairs (F0–4, 1,660; F5–6, 1,563). Covariates of the two groups were thus well balanced and demonstrated no significant differences at baseline (P>0.05 for all; *Table 1* and Figure S1).

Progression of fibrosis correlates with worse prognosis in patients with HCC

Prior to matching, patients of the F0–4 (*vs.* F5–6) subset displayed significantly higher cumulative 1-, 3-, and 5-year OS rates (65.8%, 44.5%, and 33.9% *vs.* 62.3%, 41.2%,

and 32.0%, respectively). The prognosis in those with advanced fibrosis/cirrhosis was significantly worse (P=0.029) (*Figure 2A*), and the median OS was significantly lower (23 *vs.* 27 months, P=0.029). After 1:1 PSM, the 1-, 3-, and 5-year cumulative OS rates still diverged (F0–4, 70.6%, 49.6%, and 37.6% *vs.* F5–6, 65.8%, 47.7%, and 34.7%, respectively). In these patients, the median OS was again significantly lower (28 *vs.* 36 months, P=0.028), and patient prognosis was significantly worse in those with advanced fibrosis/cirrhosis (P=0.028) (*Figure 2B*). In univariate analysis of all matched patients, age (P<0.001), sex (P=0.008), primary tumor (P<0.001), nodal metastasis (P<0.001), distant metastasis (P<0.001), vascular invasion (P<0.001), AFP level (P<0.001), fibrosis score (P=0.028), and tumor size (P<0.001) were closely associated with OS (*Table 2*). Multivariate Cox proportional hazards analyses, using factors proven significant by univariate analysis, identified advanced fibrosis/cirrhosis [hazard ratio (HR): 1.131, 95% confidence interval (CI): 1.032–1.240; P=0.009], age >63 years (HR: 1.365; P<0.001), T3–4 staging (HR: 1.810; P<0.001), distant metastasis (M1) (HR: 3.460; P<0.001), tumor size >1 cm (HR: 2.536; P<0.001), major vascular invasion (HR: 2.321; P<0.001), and elevated AFP level (HR:

Table 1 The baseline characteristics of patients with HCC of different fibrosis scores

Variables	Before PSM			After PSM		
	F0–4 (n=2,295)	F5–6 (n=5,824)	P value	F0–4 (n=1,660)	F5–6 (n=1,563)	P value
Age, mean ± SD	63.84±12.13	61.76±9.54	<0.001	63.54±9.62	63.43±9.24	0.248
Sex, n			0.027			0.614
Male	1,742	4,555		1,320	1,254	
Female	553	1,269		340	309	
AJCC T, 7th ed., n			<0.001			0.755
T1–T2	922	2,707		729	705	
T3–T4	361	762		201	180	
Unclear	1,012	2,355		730	678	
AJCC N, 7th ed., n			0.0065			0.721
N0	1,211	3,283		909	869	
N1	72	197		19	14	
Unclear	1,012	2,344		732	680	
AJCC M, 7th ed., n			0.0002			0.950
M0	1,175	3,250		890	844	
M1	143	387		47	46	
Unclear	977	2,187		723	673	
AFP, n			<0.001			0.749
Positive/elevated	1,217	3,531		958	911	
Negative	648	1,411		432	413	
Unclear	430	882		270	239	
Tumor size, n			0.347			0.896
≤1 cm	2,091	5,262		1,583	1,492	
>1 cm	7	12		0	0	
Unclear	197	550		77	71	
Vascular invasion, n			<0.001			0.909
Absent	920	2,219		761	713	
Minor	284	399		138	120	
Major	185	475		91	87	
Unclear	906	2,731		670	643	

HCC, hepatocellular carcinoma; PSM, propensity score matching; AJCC, American Joint Cancer Committee; AFP, alpha-fetoprotein.
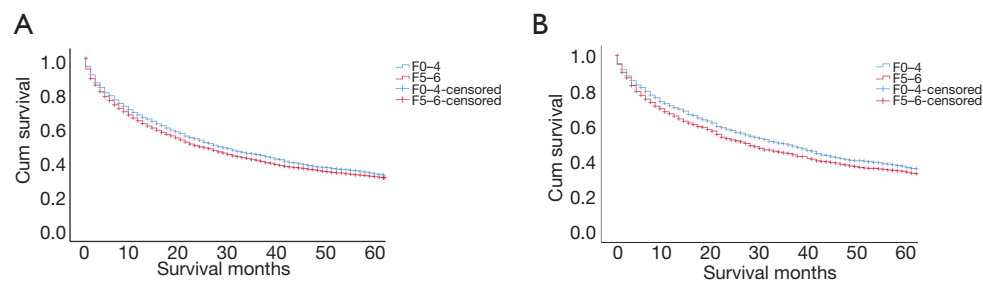
Figure 2 Analyses of patient survival in F0–4 and F5–6 subsets of hepatic fibrosis (A) before and (B) after PSM, underscoring related prognostic ramifications. PSM, propensity score matching.

1.511; P<0.001) as independent risk factors for increased mortality (*Table 3*).

Predictors of survival in patients with advanced fibrosis/cirrhosis patients

Using multivariate analysis, predictors of survival among patients with advanced fibrosis/cirrhosis patients were assessed. As shown in *Table 4*, survival worsened significantly at an older age (>63 years) in patients with advanced fibrosis/cirrhosis (HR: 1.480, 95% CI: 1.297–1.689; P<0.001), and in the presence of advanced fibrosis/cirrhosis patients, T3–4 staging (HR: 1.900, 95% CI: 1.477–2.444; P<0.001), distant metastasis (M1) (HR: 3.270, 95% CI: 2.297–4.655; P<0.001), tumor size >1 cm (HR: 2.809, 95% CI: 2.152–3.668; P<0.001), and major vascular invasion (HR: 2.457, 95% CI: 1.819–3.319; P<0.001). Patient survival was also significantly better in the absence (*vs.* presence) of AFP elevation (HR: 0.702, 95% CI: 0.594–0.831; P<0.001).

Construction and internal validation of prognostic nomogram

Our prognostic nomogram integrated all significant independent factors determined by multivariate analyses, achieving a C-index of 0.749 (95% CI: 0.7485–0.7495) for predicting survival (*Figure 3A*). Calibration plots for probabilities of survival at 1, 3, and 5 years also indicated optimal agreement between predictions by nomogram and actual observations (*Figure 3B*). A portion of the cohort (30%) was then selected at random for internal validation using R open-source software. The C-index of internal validation for this nomogram was 0.761 (95% CI: 0.759–0.763), and the calibration curves indicated good agreement between the nomogram-predicted and observed OS at 1, 3,

and 5 years (*Figure 3C*). Hence, the integration of fibrosis score and other factors (i.e., age, AJCC T stage, distant metastasis, tumor size, vascular invasion, and AFP level) in our nomogram provided a reliable means to predict survival in patients with HCC.

Performance of nomogram vs. independent prognostic factors or conventional staging

The high C-indices recorded for our model underscore its predictive accuracy. In the cohort overall, the C-index for predicting survival by nomogram was 0.749 (95% CI: 0.7485–0.7495), which exceeded that of conventional staging AJCC TNM (0.730), tumor size (0.506), vascular invasion (0.509), AFP level (0.55), or patient age (0.536). Internal validation of the nomogram produced a C-index of 0.761 (95% CI: 0.759–0.763) again outperforming conventional staging AJCC TNM (0.742), tumor size (0.502), vascular invasion (0.520), AFP level (0.539), or patient age (0.534). It appears that the nomogram we generated is a useful and reliable model for predicting survival in patients with HCC, surpassing independent prognostic factors and AJCC TNM staging in this regard.

Sensitivity analyses in the propensity score-matched cohort

To check the robustness of our results, a series of sensitivity analyses were performed. As already elaborated, age, sex, primary tumor, nodal metastasis, distant metastasis (M1), vascular invasion, AFP level, fibrosis score, and tumor size proved to be closely associated with OS. Advanced fibrosis/cirrhosis, age >63 years, T3–4 staging, distant metastasis (M1), tumor size >1 cm, major vascular invasion, and AFP level further emerged as independent risk factors for increased mortality in multivariate Cox proportional hazards analysis. However, once adjustments were made (unclear T

Page 6 of 11

Zhang et al. Prognostic nomogram for HCC with fibrosis of varying degrees

Table 2 Univariate analysis of prognostic factors for OS

Variables	Before PSM			After PSM		
	All patients	Survival time (months), median (95% CI)	P value	All patients	Survival time (months), median (95% CI)	P value
Group			0.029			0.028
F0–4	2,295	27 (23.999–0.001)		1,660	36 (32.191–39.809)	
F5–6	5,824	23 (21.465–24.535)		1,563	28 (24.265–31.735)	
Age			<0.001			<0.001
≤63	4,695	30 (27.516–32.484)		1,692	40 (35.293–44.707)	
>63	3,424	20 (18.51–21.49)		1,531	25 (22.395–27.605)	
Sex			0.025			0.008
Male	6,297	24 (22.491–25.509)		2,574	30 (26.955–33.045)	
Female	1,822	27 (23.862–30.138)		649	37 (29.635–44.365)	
AJCC T, 7th ed.			<0.001			<0.001
T1–T2	3,629	44 (39.689–48.311)		1,434	56	
T3–T4	1,123	7 (6.046–7.954)		381	9 (7.077–10.923)	
Unclear	3,367	19 (17.365–20.635)		1,408	22 (19.305–24.695)	
AJCC N, 7th ed.			<0.001			<0.001
N0	4,494	32 (29.665–34.335)		1,778	42 (37.736–46.264)	
N1	269	4 (3.095–4.905)		33	4 (1.908–6.092)	
Unclear	3,356	20 (18.367–21.633)		1,412	22 (19.307–24.693)	
AJCC M, 7th ed.			<0.001			<0.001
M0	4,425	33 (30.567–35.433)		1,734	42 (37.38–46.62)	
M1	530	3 (2.494–3.506)		93	4 (3.191–4.809)	
Unclear	3,164	21 (19.190–22.81)		1,396	23 (20.243–25.757)	
Vascular invasion			<0.001			<0.001
Absent	3,139	52 (47.312–56.688)		1,474	59 (49.969–68.031)	
Minor	683	30 (25.482–34.518)		258	36 (24.221–47.779)	
Major	660	4 (3.281–4.719)		178	7 (4.961–9.039)	
Unclear	3,637	17 (15.722–18.278)		1,313	17 (14.85–19.15)	
AFP			<0.001			<0.001
Positive/elevated	4,748	19 (17.785–20.215)		1,869	23 (20.536–25.464)	
Negative	2,059	47 (41.161–52.839)		845	57 (48.156–65.844)	
Unclear	1,312	21 (17.714–24.286)		509	25 (19.72–30.28)	
Tumor size			<0.001			<0.001
≤1 cm	7,353	30 (28.238–31.762)		3,075	35 (32.288–37.712)	
>1 cm	19	13 (0–27.348)		0	–	
Unclear	747	2 (1.568–2.432)		148	2 (1.069–2.931)	

OS, overall survival; PSM, propensity score matching; CI, confidence interval; AJCC, American Joint Cancer Committee; AFP, alpha-feto-protein.

Table 3 Multivariate analysis of factors predictive of patients' OS

Variables	Before PSM		After PSM	
	HR (95% CI)	P value	HR (95% CI)	P value
Group, F5–6 (*vs.* F0–4)	1.111 (1.042–1.185)	0.001	1.131 (1.032–1.240)	0.009
Age, >63 (*vs.* ≤63)	1.447 (1.366–1.533)	<0.001	1.365 (1.243–1.498)	<0.001
Sex, female (*vs.* male)	0.917 (0.856–0.983)	0.014		
AJCC T, 7th ed., T3–4 (*vs.* T1–2)	1.683 (1.517–1.867)	<0.001	1.810 (1.517–2.159)	<0.001
AJCC N, 7th ed., N1 (*vs.* N0)	1.364 (1.168–1.594)	<0.001		
AJCC M, 7th ed., M1 (*vs.* M0)	2.328 (2.068–2.621)	<0.001	3.460 (2.705–4.424)	<0.001
Tumor size, >1 cm (*vs.* ≤1 cm)	1.417 (0.837–2.399)	0.194	2.536 (2.096–3.068)	<0.001
Vascular invasion, minor (*vs.* absent)	1.267 (1.132–1.418)	<0.001	1.202 (1.000–1.445)	0.050
Vascular invasion, major (*vs.* absent)	2.401 (2.134–2.701)	<0.001	2.321 (1.885–2.857)	<0.001
AFP, negative (*vs.* positive/elevated)	0.670 (0.622–0.721)	<0.001	0.662 (0.587–0.746)	<0.001

OS, overall survival; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; AJCC, American Joint Cancer Committee; AFP, alpha-fetoprotein.

Table 4 Multivariate analysis of predictors of survival among patients with advanced fibrosis/cirrhosis patients

Variables	HR (95% CI)	P value
Age, >63 (*vs.* ≤63)	1.480 (1.297–1.689)	<0.001
Derived AJCC T, 7th ed., T3–4 (*vs.* T1–2)	1.900 (1.477–2.444)	<0.001
Derived AJCC M, 7th ed., M1 (*vs.* M0)	3.270 (2.297–4.655)	<0.001
Tumor size, >1 cm (*vs.* ≤1 cm)	2.809 (2.152–3.668)	<0.001
Vascular invasion, minor (*vs.* absent)	1.200 (0.918–1.569)	0.181
Vascular invasion, major (*vs.* absent)	2.457 (1.819–3.319)	<0.001
AFP, negative (*vs.* positive/elevated)	0.702 (0.594–0.831)	<0.001

HR, hazard ratio; CI, confidence interval; AJCC, American Joint Cancer Committee; AFP, alpha-fetoprotein.

stages classified as T1–2; unclear M stages classified as M1), minor vascular invasion was identified as an independent risk factor of OS (Tables S1-S6). Consequently, the association between minor vascular invasion and OS is not particularly robust and requires caution in its interpretation.

Discussion

Findings of the present study have demonstrated that advanced fibrosis/cirrhosis is independently associated with survival of patients with HCC. We used this information to generate an internally validated fibrosis score-based prognostic nomogram. This predictive model is reliable and compelling, with practical ramifications in a clinical setting.

HCC is an aggressive malignancy closely linked to hepatic fibrosis and end stage cirrhosis. Nearly all affected patients (~80–90%) harbor some underlying fibrotic changes, roughly one in three patients with cirrhosis are likely to develop HCC in their lifetime. In patients with advanced hepatic fibrosis/cirrhosis, the 5-year incidence of HCC ranges from 5–30% (6,13). However, the prognostic impact of fibrosis scores in conjunction with HCC, has yet to be fully explored (14-17). A better understanding of the role that fibrosis plays in this setting and the use of a nomogram that includes fibrosis score, may yield a more accurate prediction for patient survival.

According to the AJCC, fibrosis (or Ishak) scores are categorized as either none-to-moderate or severe fibrosis/
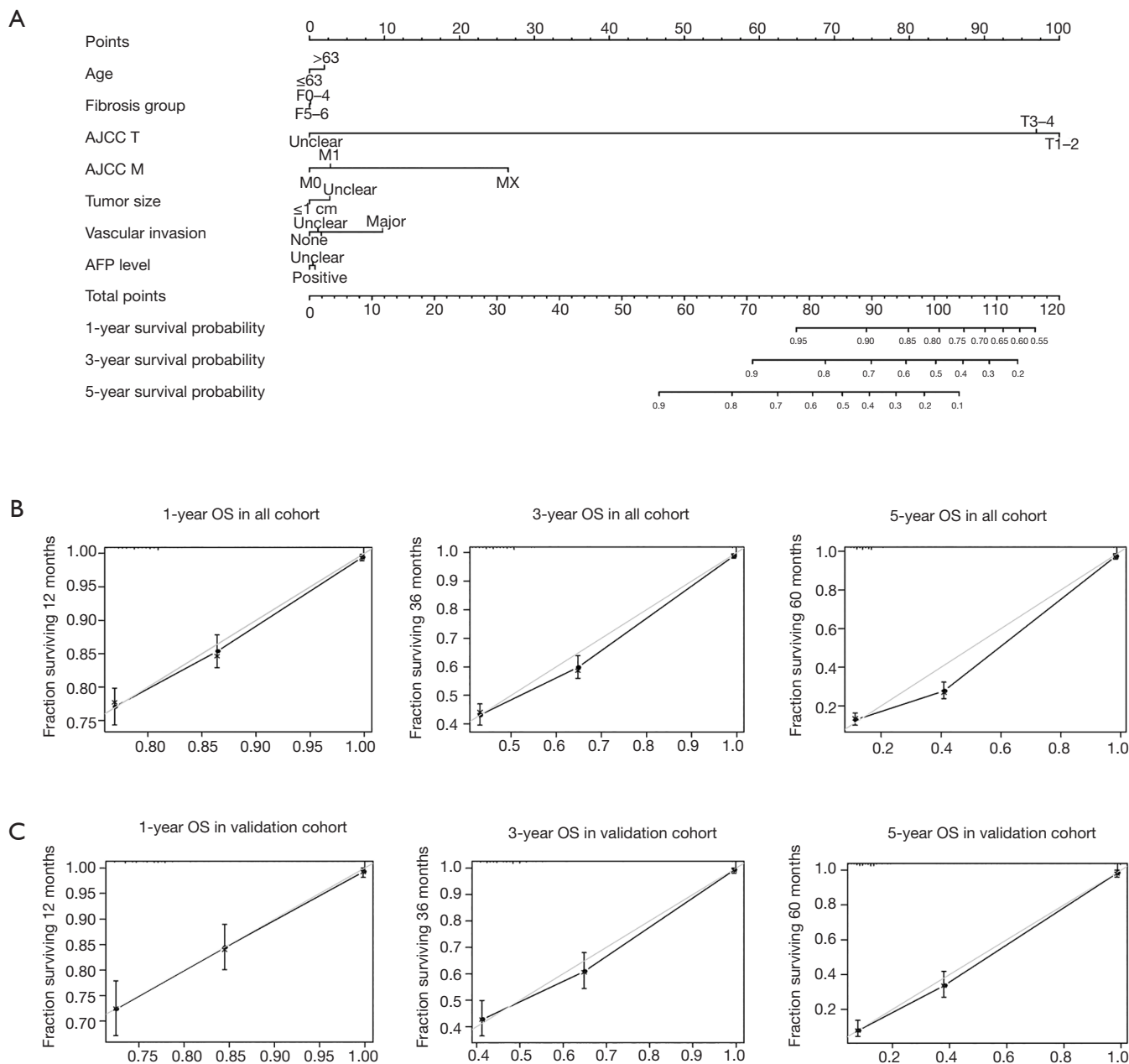
Page 8 of 11

Zhang et al. Prognostic nomogram for HCC with fibrosis of varying degrees

A

B

C

Figure 3 HCC survival nomogram and calibration curves. (A) Prognostic nomogram integrating fibrosis score and other independent risk factors for predicting OS and (B,C) calibration curves for predicting patient survival at 1, 3, and 5 years in all patients and in a validation cohort. HCC, hepatocellular carcinoma; OS, overall survival; AJCC, American Joint Cancer Committee; AFP, alpha-fetoprotein.

cirrhosis. While adopting these same subsets, we conducted PSM to minimize selection bias. Patients designated as such did not differ significantly by age, sex, AJCC TNM stage, AFP level, tumor size, or vascular invasion; therefore, patient distribution was well balanced. Our results indicate a worse prognosis in patients with HCC who displayed advanced fibrosis/cirrhosis, rather than those with none-to-moderate fibrotic change. Notably, Noda *et al.* found no significant relationship between hepatic fibrosis and OS in patients with HCC (P=0.1185) (18). Similarly, Suh *et al.* found no significant difference between OS and fibrosis, regardless of the fibrosis score (mild *vs.* severe;

P=0.267) (14). However, severe fibrosis/cirrhosis constituted as an independent risk factor for OS in our analysis of the data. The outcomes herein are consistent with those of a recent meta-analysis by Zhang *et al.* and another study by Toyoda *et al.* (19,20). Prior discrepancies may be partly attributable to differences in patient enrollment criteria. Noda *et al.* focused on patients with HCC of non-viral origins (18), whereas Suh *et al.* investigated Child - Pugh A status and single HCC lesions <5 cm (14). Approximately 70% of patients with HCC have viral hepatitis infections (6). Child-Pugh B status and hepatitis C viral positivity also carry poor prognoses in conjunction with HCC (21).

Aside from fibrosis score, other factors (i.e., age >63 years, T3–4 staging, M1, tumor size >1 cm, major vascular invasion, and elevated AFP level) emerged as independent predictors of poor prognosis in multivariate analyses of our patients with HCC, which is consistent with past reports (8,22-25). The fact that we did not find sex or nodal metastasis to be predictive of patient survival, is also consistent with past reports (25,26). Furthermore, patients with advanced fibrosis/cirrhosis who were older (>63 years) demonstrated worse survival. Additionally, T3–4 staging, M1, tumor size >1 cm, major vascular invasion, or elevated AFP level worsened patient survival in the presence of advanced fibrosis/cirrhosis. The prognostic nomogram that we developed (C-index: 0.749) incorporated these factors comprehensively and was internally validated (C-index: 0.761). Our prognostic nomogram also outperformed AJCC TNM staging, in both all (C-index: 0.730) and validation (C-index: 0.742) cohorts. Calibration plots for 1-, 3-, and 5-year probabilities of survival, indicated optimal agreement between predictions by nomogram and actual observations in both all and validation cohorts.

There were certain limitations of this study that might have influenced our results to some extent. The SEER database lacked any records pertaining to etiologic origins of HCC (e.g., viral hepatitis), liver function indices, Child-Pugh classifications, degrees of portal hypertension, or scoring of performance status. Thus, our nomogram and other commonly used systems, including Barcelona Clinic Liver Cancer (BCLC) staging, Hong Kong Liver Cancer (HKLC) staging, the model to estimate survival for hepatocellular carcinoma (MESH), or the Cancer of the Liver Italian Program (CLIP) score, could not be compared in terms of predictive accuracy (27-30). Some variables were also unclear or insufficiently detailed. For example, although Hsu *et al.* invoked AFP thresholds of 20 and 400 ng/mL to predict long-term outcomes of patients with HCC, the SEER database merely records AFP levels as elevated or negative (31).

It is well known that therapeutics have tremendous bearing on the clinical outcomes of patients with HCC. Use of nucleos(t)ide analogs for hepatitis B viral suppression and eradication of hepatitis C virus through direct-acting antivirals or pegylated interferon, may significantly diminish the prospect of hepatic decompensation and ultimately improve patient survival. In the absence of fibrosis, patient eligibility for curative treatment is often heightened. However, SEER-18 Regs Research data (November 2017 submission) offered no information on related treatment modalities.

Finally, the retrospective nature of this study made it difficult to avert bias from other confounding factors, despite our implementation of PSM. Further validation through multicenter prospective recruitment is clearly warranted to augment this initial assessment of our novel prognostic nomogram.

Conclusions

Based on our findings, it is evident that patients with HCC have poorer outcomes if there is advanced fibrosis/cirrhosis rather than lesser degrees of fibrosis. We have successfully generated a reliable and superior nomogram that incorporates fibrosis score and other independent risk factors to accurately predict patient prognoses in this setting.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-3267

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-3267). The authors have no conflicts of interest to declare.

Page 10 of 11

Zhang et al. Prognostic nomogram for HCC with fibrosis of varying degrees

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.

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