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A model to estimate survival in ambulatory patients with hepatocellular carcinoma: Can it predict the natural course of hepatocellular carcinoma?

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ABSTRACT

Background: Several hepatocellular carcinoma (HCC) staging systems are available including the newly developed staging system, the Model to Estimate Survival in Ambulatory HCC patients (MESIAH); however, whether these staging systems could predict the natural course of HCC is largely unknown.
Methods: 1013 patients with history of HCC treatment and 111 patients without any history of treatment till death or last follow-up at a single tertiary hospital were included.
Results: The MESIAH score showed a better discrimination ability, with a C-statistic of 0.835 [95% confidence interval (CI), 0.810–0.861] in the group of treated patients compared to the Barcelona Clinic Liver Cancer (BCLC) staging system [0.739 (95% CI, 0.709–0.769)] before propensity score matching. However, the MESIAH score failed to stratify patients according to their risk of death in the group of untreated patients unlike the BCLC staging system. Propensity score matching analysis confirmed that the MESIAH score was most strongly influenced by whether treatment was given or not.
Conclusions: Although the MESIAH score provided better prognostic stratification than other staging systems in treated HCC patients, it was not helpful in predicting the natural course of HCC. Since the treatment affects patient outcome and prognosis, it is necessary to develop a new staging system that can also reflect the natural course of HCC.

1. Introduction

Accurate cancer staging is mandatory to predict survival outcome and to determine optimal treatment strategies. Hepatocellular carcinoma (HCC) is different from other solid tumors in that the prognosis is decided not only by the tumor extent but also by overall liver function. Therefore, many staging systems had been built on relevant prognostic factors for both the tumor extent and overall liver function. Moreover, since the preferred staging system and treatment strategy for HCC is diversified by various factors, the accurate prediction for the outcome of untreated HCC can give more valuable clinical information compared to other types of cancers. Up to the minute, the most reliable and widely adopted methods for staging HCC, which is endorsed by American and European liver societies, is the Barcelona Clinic Liver Cancer (BCLC) staging system [1,2]. A recent study shows that BCLC system had a superior predictive ability over other staging systems for the prediction of the outcome of untreated HCC [3]. However, more convincing studies are required in that BCLC staging system has the main downside that it includes subjective factors including the performance status and the Child-Pugh score. Moreover, which staging system is the best remained still controversial.

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Table 1A
Comparison of the covariates between the two groups before and after propensity score matching.

	Before matching			After matching		
	Treated (N = 1013)	Untreated (N = 111)	P-value**	Treated (N = 108)	Untreated (N = 108)	P-value**
PS	0.25 (0.19)	0.29 (0.21)	**<0.001***	0.25 (0.19)	0.29 (0.21)	0.143
Age	58.72 (11.51)	59.44 (10.28)	**0.018***	57.86 (10.43)	59.44 (10.37)	0.266
Sex			0.423			0.140
Male	839 (82.8%)	88 (79.3%)		95 (88.0%)	86 (79.6%)	
Female	174 (17.2%)	23 (20.7%)		13 (12.0%)	22 (20.4%)	
HCC size (cm)	4.93 (1.43)	4.97 (1.55)	**<0.001***	4.92 (1.41)	4.97 (1.55)	0.846
HCC num.	2.80 (1.64)	2.72 (1.73)	**<0.001***	2.63 (1.59)	2.72 (1.72)	0.455
HCC type			**<0.001***			0.891
Nodular	857 (84.6%)	64 (57.7%)		60 (55.6%)	62 (57.4%)	
Infiltrative	156 (15.4%)	47 (42.3%)		48 (44.4%)	46 (42.6%)	
HCC location			**<0.001***			1.000
Unilobar	788 (77.8%)	40 (36.0%)		41 (38.0%)	40 (37.0%)	
Bilobar	225 (22.2%)	71 (64.0%)		67 (62.0%)	68 (63.0%)	
PVT	45 (20.0%)	66(59.5%)	**<0.001***	45 (41.7%)	63 (58.3%)	0.783
Child	6.73 (1.82)	7.17 (1.73)	**<0.001***	6.80 (1.73)	7.17 (1.75)	0.093
MELD	14.53 (5.51)	14.46 (3.25)	**<0.001***	14.11 (3.40)	14.46 (3.28)	0.125
Log (AFP)	5.51 (2.86)	5.51 (3.08)	**0.002***	5.31 (2.82)	5.51 (3.07)	0.745
BCLC			**<0.001***			0.708
0	377 (37.2%)	14 (12.6%)		14 (13.0%)	14 (13.0%)	
A	254 (25.1%)	29 (26.1%)		33 (30.6%)	28 (25.9%)	
B	224 (22.1%)	46 (41.4%)		41 (38.0%)	44 (40.7%)	
C	49 (4.8%)	22 (19.8%)		16 (14.8%)	22 (20.4%)	
D	109 (10.8%)	0 (0.0%)		4 (3.7%)	0 (0.0%)	
AJCC TNM			**<0.001***			0.993
1	519 (51.2%)	17 (15.3%)		18 (16.7%)	17 (15.7%)	
2	196 (19.3%)	8 (7.2%)		9 (8.3%)	8 (7.4%)	
3.1	78 (7.7%)	11 (9.9%)		10 (9.3%)	11 (10.2%)	
3.2	120 (11.8%)	38 (34.2%)		38 (35.2%)	37 (34.3%)	
3.3	9 (0.9%)	1 (0.9%)		1 (0.9%)	1 (0.9%)	
4.1	29 (2.9%)	11 (9.9%)		12 (11.1%)	10 (9.3%)	
4.2	62 (6.1%)	25 (22.5%)		20 (18.5%)	24 (22.2%)	
Initial treatment			–			–
Resection	198 (19.5%)	0 (0.0%)		14 (13.0%)	0 (0.0%)	
Transplantation	18 (1.8%)	0 (0.0%)		2 (1.9%)	0 (0.0%)	
TACE	593 (58.5%)	0 (0.0%)		77 (71.3%)	0 (0.0%)	
PEIT	94 (9.3%)	0 (0.0%)		4 (3.7%)	0 (0.0%)	
RFA	113 (11.2%)	0 (0.0%)		4 (3.7%)	0 (0.0%)	
Chemotherapy	10 (1.0%)	0 (0.0%)		6 (5.6%)	0 (0.0%)	

Data presented as mean (SD) or number (%).
Abbreviations: AFP, alpha fetoprotein; AJCC, American Joint Committee on Cancer; BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; PEIT, percutaneous ethanol injection therapy; PS, propensity score; PVT, portal vein thrombosis; RFA, radiofrequency ablation; TACE, trans-arterial chemoembolization.
* P-value <0.05.
** P-value of two-sample t-test or Wilcoxon's rank sum test.

Recently, new staging system, a Model to Estimate Survival in Ambulatory HCC patients (MESIAH), has been suggested to predict overall survival in ambulatory HCC patients and validated in an independent cohort [4,5]. The MESIAH showed superiority in predictive performance compared to other staging systems including BCLC [6], Cancer of the Liver Italian Program (CLIP) [7], and Japan Integrated Staging (JIS) [8]. Moreover, the MESIAH has many advantages over other staging systems including its objectivity and reproducibility; that it consists of objective and reproducible variables such as age, the model for end-stage liver disease (MELD) score, albumin, tumor size and number, and the presence of vascular invasion. However, studies of the predictive performance of the MESIAH score are scarce. Especially, whether the MESIAH score can predict survival outcome and reflect the natural course of untreated HCC patients has not been evaluated. Although development of the MESIAH score included a small portion of patients with comfort care only, it is necessary to evaluate whether the MESIAH score can also predict the natural history of HCC because the treatment itself has an influence on the survival of HCC patients, In this study, we further evaluated the predictive performance of the MESIAH score in untreated and treated HCC cohorts to evaluate whether the MESIAH score could reflect the natural course of HCC using propensity score matching analysis in comparison to the BCLC system and the seventh edition of the American Joint Committee on Cancer (AJCC) TNM staging system [9].

2. Materials and methods

2.1. Study subjects

This retrospective cohort study was approved by the Institutional Review Board of Seoul National University Hospital (Seoul, Korea) and was exempted from the requirement to obtain informed consent. The study protocol conformed to the ethical guidelines of the World Medical Association Declaration of Helsinki.

From November 2004 and March 2008, 1124 HCC patients (111 untreated and 1013 treated HCC patients) were consecutively enrolled in this study. The diagnosis of HCC was made largely

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