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EDITORIAL OFFICE
Xiu-Xia Song, Director
*World Journal of Hepatology*
Baishideng Publishing Group Inc
7901 Stoneridge Drive,
Suite 501, Pleasanton, CA 94588, USA
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LETTERS TO THE EDITOR

# Usefulness of the MESH score in a European hepatocellular carcinoma cohort

Xavier Adhoute, Guillaume Pénaranda, Jean-Luc Raoul, Marc Bourlière

Xavier Adhoute, Marc Bourlière, Department of Hepato-Gastro-enterology, Hôpital Saint-Joseph Marseille, 13008 Paris, France

Guillaume Pénaranda, AlphaBio Laboratory Marseille, 13008 Paris, France

Jean-Luc Raoul, Department of Hepato-Gastroenterology and Digestive Oncology, Institut Paoli-Calmette Marseille, 13008 Paris, France

Author contributions: Adhoute X, Raoul JL and Bourlière M are in charge of the patients; Bourlière M, Raoul JL and Adhoute X collected the data; Pénaranda G proceeded to statistical analysis; Adhoute X, Bourlière M, Raoul JL and Pénaranda G write the manuscript.

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Correspondence to: Dr. Xavier Adhoute, Department of Hepato-Gastroenterology, Hôpital Saint-Joseph, 26 Bd de Louvain Marseille, 13008 Paris, France. adhoute.xavier@neuf.fr

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## Abstract

The Barcelona Clinic Liver Cancer classification is the most widely - used hepatocellular carcinoma (HCC) staging system because it is simple, precise and linked to a treatment algorithm based on randomized studies. But each group includes a broad spectrum of tumors, with limited therapeutic options, particularly for intermediate and advanced stages. Consequently, different additional scoring systems have been proposed to refine the prognosis and/or to improve the management. But until now, there is no consensus. Liu *et al* proposes a new scoring system, based on a large HCC cohort, with patients at different stages, treated using diverse modalities. This score includes six parameters used in current practice. It is simple to calculate, reliable, with an ability to predict survival superior to other systems, which also works with our European HCC cohort. The MESH score may be especially useful to differentiate subgroups with different prognosis for each treatment modality.

**Key words:** Hepatocellular carcinoma; Barcelona Clinic Liver Cancer; Scoring system; MESH; NIACE



**Core tip:** The Barcelona Clinic Liver Cancer system has become the reference classification for hepatocellular carcinoma (HCC). But it has been criticized; each group includes a broad spectrum of tumors with limited therapeutic options. For this reason, different additional scoring systems have been proposed to improve the management. Liu *et al* proposes the MESH score, based on a large HCC cohort. It includes six parameters used in current practice, and in a European HCC cohort, this new score appears to be simple, reliable and useful to differentiate subgroups with different prognosis for each treatment modality.

Adhoute X, Pénaranda G, Raoul JL, Bourlière M. Usefulness of the MESH score in a European hepatocellular carcinoma cohort. *World J Hepatol* 2017; 9(15): 711-714 Available from: URL: http://www.wjgnet.com/1948-5182/full/v9/i15/711.htm DOI: http://dx.doi.org/10.4254/wjh.v9.i15.711

## TO THE EDITOR

Hepatocellular carcinoma (HCC) staging system is still a controversial issue, and we have read with interest the article by Hsu *et al*[1] who proposed a new survival prognostic score for HCC called MESH. This score has been determined by multivariate analysis within a large HCC cohort ($n$ = 1591) mainly related to viral B hepatitis, mostly treated (44%) with curative strategy (surgery or radiofrequency ablation). The MESH score demonstrated a good predictive survival value, superior to other known staging and scoring systems [Barcelona Clinic Liver Cancer (BCLC), Hong Kong Liver Cancer (HKLC), Cancer of the Liver Italian Program (CLIP), Taipei Integrated Scoring system] within a large validation cohort ($n$ = 1591), with a lower Akaike information criterion (AIC) value, a higher homogeneity; within each BCLC stage and whatever treatment strategy (curative or palliative).

We have evaluated the prognostic value of the MESH score and compared it to other known staging and scoring systems [BCLC, HKLC, CLIP and NIACE: Tumor Nodularity, Infiltrative nature of the tumor, serum Alpha-fetoprotein (AFP) level, Child-Pugh stage, Eastern Cooperative Oncology Group Performance Status (ECOG PS)[2]] within a French HCC cohort including 581 patients. Demographic and clinical characteristics of the 581 patients with HCC are shown in Table 1. Our patients were mostly male (82%), with a mean age of 67 years. Cirrhosis was present in 87% of our patients, CP A (64%), CP B (36%). Underlying liver disease was mostly related to alcohol abuse (37%) or viral C hepatitis (36%). HCC were multinodular in 61% of cases and vascular invasion or distant metastasis was found in 37% and 10% of patients, respectively. Baseline ECOG PS of our population (as expression of symptomatic tumor) was as follows: PS 0 (48%), PS 1 (23%), PS 2 (24%), PS 3-4 (5%). BCLC distribution was similar to the Liu cohorts: BCLC A 31%, B 16%, C 41% and D 12%. Treatment modalities were as follows: 23% were treated by surgery or radiofrequency ablation (RFA), 30% by transarterial chemoembolization, 26% by Sorafenib and 21% have received supportive care. Mean overall survival for the entire cohort was 26.0 ± 1.3 mo, consistent with the median follow-up duration: 18.3 ± 20.3 mo. Seventy-one percent of patients died. The discriminatory ability (linear trend $\chi^2$ score), homogeneity ability (likelihood ratio test), prognostic stratification ability (AIC) and C-index were compared among scoring systems. Survivals between groups were compared using log-rank test in case of proportionality of hazards across time; generalized Wilcoxon test was used in case of non-proportionality of hazards.

**Table 1 Baseline characteristics in European hepatocellular carcinoma cohort ($n$ = 581) $n$ (%)**

| Patients characteristics | Cohort ($n$ = 581) |
|---|---|
| Age, yr, mean ± SD | 67.4 ± 11.7 |
| Male | 475 (82) |
| Etiology - HCV/HBV/Alcohol/MS/others | 209 (36)/41 (7)/215 (37)/87 (15)/29 (5) |
| Cirrhosis | 505 (87) |
| Child - Pugh stage[1] A/B | 323 (64)/182 (36) |
| Maximal tumor diameter, mean ± SD | 60.9 ± 39.1 |
| Tumor nodularities (1/2/≥ 3), $n$ (%) | 227 (39%)/76 (13%)/278 (48) |
| Infiltrative tumor | 235 (40) |
| Extrahepatic metastasis | 59 (10) |
| Vascular invasion | 213 (37) |
| Performance status 0/1/2-4 | 276 (48)/136 (23)/169 (29) |
| Laboratory values (mean ± SD) | |
| Alkaline phosphatase (IU/L) > 200 | 112 (19) |
| PT (%), mean ± SD | 78.0 ± 15.8 |
| Albumin (g/L), mean ± SD | 34.7 ± 6.1 |
| Aspartate transaminase (IU/L), mean ± SD | 68.7 ± 60.7 |
| Alpha-fetoprotein (ng/mL), mean ± SD | 5680 ± 31332 |
| Tumor stages | |
| BCLC (A/B/C/D), $n$ (%) | 181 (31)/92 (16)/241 (41)/67 (12) |
| Treatment allocation | |
| Resection or RFA, $n$ (%) | 131 (23) |
| TACE, $n$ (%) | 175 (30) |
| Sorafenib, $n$ (%) | 152 (26) |
| Supportive care, $n$ (%) | 123 (21) |
| Follow-up Time, mo, mean ± SD | 18.3 ± 20.3 |
| Deaths, $n$ (%) | 413 (71) |
| Overall Survival, mo, mean ± SD | 26.0 ± 1.3 |

[1]Cirrhotic patients. HCV: Hepatitis C virus; HBV: Hepatitis B virus; MS: Metabolic syndrom; PT: Prothrombin time; BCLC: Barcelona Clinic Liver Cancer; RFA: Radiofrequency ablation; TACE: Trans arterial chemoembolization.

Each staging system showed a significant difference in the probability of survival across the stages ($P$ < 0.0001). The MESH score determined subgroups of different survival prognosis in our cohort: MESH 0: 66 (40-68) mo, MESH 1: 37 (22-80) mo, MESH 2: 21 (13-49) mo, MESH 3: 10 (6-20) mo, MESH 4: 5 (4-9) mo, MESH 5 and 6: 4 (2-6) mo; $P$ (Wilcoxon) < 0.0001. Its predictive value on survival was higher than other scores or classifications (BCLC, HKLC and CLIP) within this cohort with a lower AIC, a higher homogeneity, a higher c-Index (Table 2). However the NIACE score obtained the best prognostic information.

The BCLC system has become the reference classification by its simplicity, its prognostic value and a treatment algorithm based on randomized clinical trials. But each BCLC stage includes a broad spectrum of tumors of different prognosis[2-5], with one therapeutic option for stages B and C. Some stage B HCC patients could be good candidates for surgery[6,7], unlike other BCLC B

**Table 2 Comparison of performances of each scoring systems in the entire cohort**

| Score | Discriminatory ability linear trend test | | Homogeneity likelihood ratio test | | Akaike Information Criterion | C-index (95%CI) |
|---|---|---|---|---|---|---|
| | LT ($\chi^2$) | *P* value | LR ($\chi^2$) | *P* value | | |
| MESH | 145.125 | < 0.0001 | 372.4846 | < 0.0001 | 4145.284 | 0.830 |
| BCLC | 137.845 | < 0.0001 | 327.5024 | < 0.0001 | 4194.266 | 0.806 |
| HKLC | 104.966 | < 0.0001 | 387.2755 | < 0.0001 | 4146.493 | 0.811 |
| CLIP | 108.423 | < 0.0001 | 341.3485 | < 0.0001 | 4101.288 | 0.816 |
| NIACE | 144.998 | < 0.0001 | 425.6698 | < 0.0001 | 4092.099 | 0.853 |

MESH: Model to estimate survival for HCC; BCLC: Barcelona Clinic Liver Cancer; HKLC: Hong Kong Liver Cancer; CLIP: Cancer of the Liver Italian Program; NIACE: Tumor Nodularity, Infiltrative nature of the tumor, Serum Alpha-fetoprotein level, Child-Pugh stage, Eastern Cooperative Oncology Group Performance Status; LT: Linear trend; LR: Likelihood ratio.

**Table 3 Comparison of performances of each scoring systems in patients treated by surgery/radiofrequency ablation**

| Score | Discriminatory ability linear trend test | | Homogeneity likelihood ratio test | | Akaike Information Criterion | C-index (95%CI) |
|---|---|---|---|---|---|---|
| | LT ($\chi^2$) | *P* value | LR ($\chi^2$) | *P* value | | |
| MESH | 21.5588 | < 0.0001 | 23.3342 | < 0.0001 | 346.508 | 0.719 |
| BCLC | 15.5560 | < 0.0001 | 12.4538 | 0.0020 | 359.388 | 0.644 |
| HKLC | 5.9647 | 0.0146 | 18.9510 | 0.0020 | 358.891 | 0.629 |
| CLIP | 9.9391 | 0.0016 | 13.1460 | 0.0003 | 356.696 | 0.642 |
| NIACE | 19.1701 | < 0.0001 | 23.1937 | < 0.0001 | 346.648 | 0.672 |

MESH: Model to estimate survival for HCC; BCLC: Barcelona Clinic Liver Cancer; HKLC: Hong Kong Liver Cancer; CLIP: Cancer of the Liver Italian Program; NIACE: Tumor Nodularity, Infiltrative nature of the tumor, serum Alpha-fetoprotein level, Child-Pugh stage, Eastern Cooperative Oncology Group Performance Status.

HCC patients who do not benefit from the recommended treatment namely the chemoembolization[8]. Consequently, different staging or scoring systems have been proposed in the last years, in order to improve its prognostic value[1] and/or the decision making process[8,9]. A prognostic score needs to be easy to use, reliable and useful, and the MESH score fulfills these conditions. It has a good prognostic value, especially for HCC patients treated by surgery/RFA (Table 3); it is easy to use by adding up the points of each variable, and it includes six parameters used in daily clinical practice, an essential part of HCC management. Actually, it incorporates tumor-related characteristics, general conditions and liver function, as well as two easily available biological variables (AFP, alkaline phosphatase) correlated to the HCC patients' survival, absent from the BCLC and HKLC classifications.

The MESH score could be useful for HCC management. It distinguishes two different prognostic groups within BCLC A HCC patients treated by surgery/RFA in our cohort [MESH $\leqslant$ 2: 68 (44-74) mo *vs* MESH > 2: 7 (5-7) mo, *P* (Wilcoxon) = 0.0292], within BCLC B HCC patients treated by TACE [MESH $\leqslant$ 2: 20 (15-50) mo *vs* MESH > 2: 14 (7-20) mo, *P* (Log-Rank) = 0.0078], or within BCLC C HCC patients treated by Sorafenib [MESH $\leqslant$ 3: 10 (6-26) mo *vs* MESH > 3: 5 (3-8) mo, *P* (Log-Rank) < 0.0001]. Thus, it could help clinicians in the treatment decision. We observed the same findings with the NIACE score whatever HCC stages and treatment modalities[10].

The BCLC treatment recommendations are seldom followed[11,12], related to a strict treatment algorithm and great prognosis heterogeneity within each BCLC stage. In our cohort, 65% of patients have been treated according to the BCLC recommendations and for some authors other options are possible[13,14].

We have checked that the MESH score provides good prognostic information within a European HCC cohort, whatever the treatment modalities, including HCC patients treated according to the BCLC guidelines. But these findings show once again that additional variables such as AFP and/or tumor morphology may influence HCC prognosis and its therapeutic management[15]. If the BCLC system is unavoidable, there are sufficient arguments for a prospective clinical trial to validate the usefulness of this new strategy based on a combination of BCLC system and scores[16] such as NIACE or MESH, and to determine which one to use.

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