cancers

MDPI

Supplementary Materials

Plasma hPG80 (Circulating Progastrin) as a Novel Prognostic Biomarker for Hepatocellular Carcinoma

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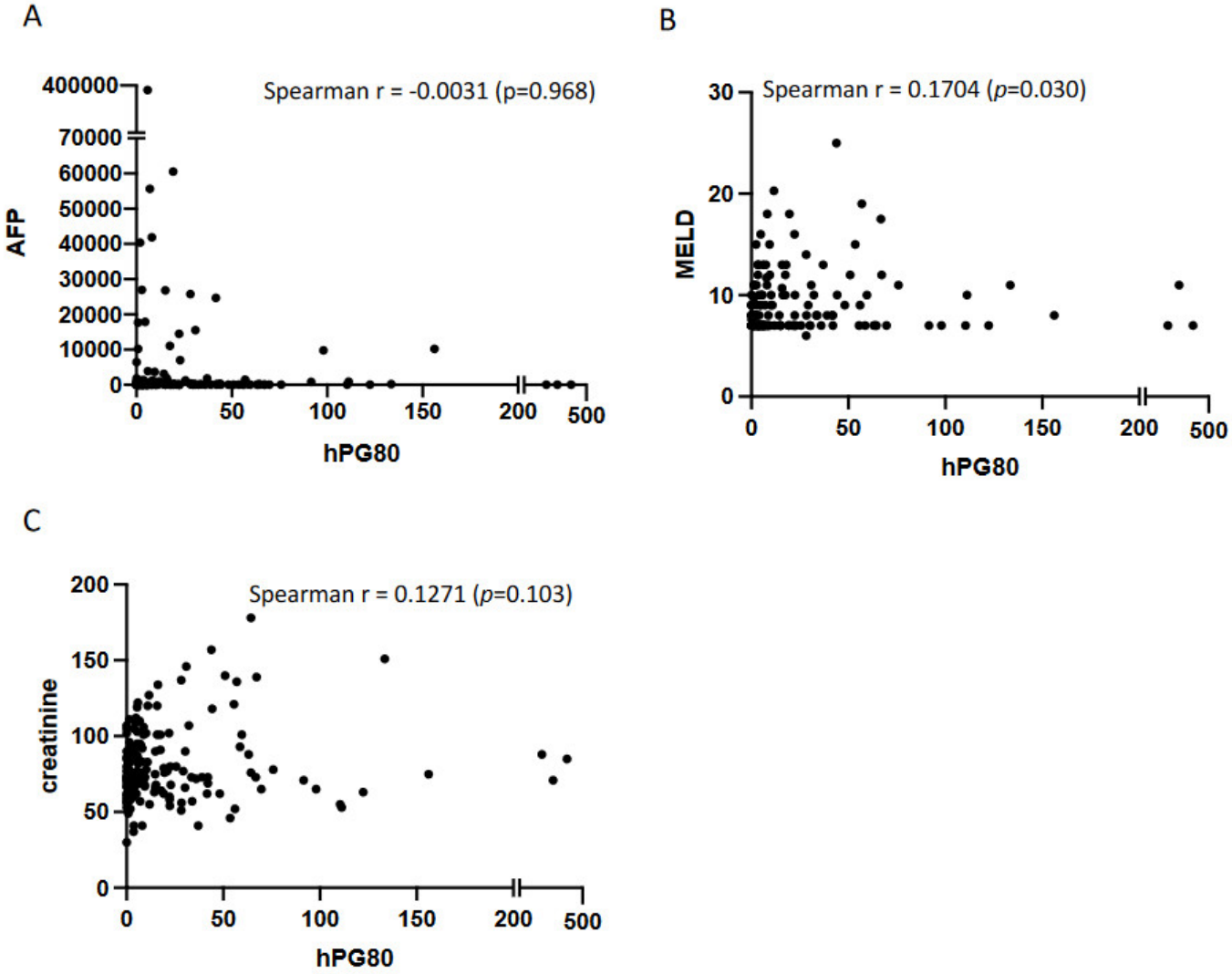
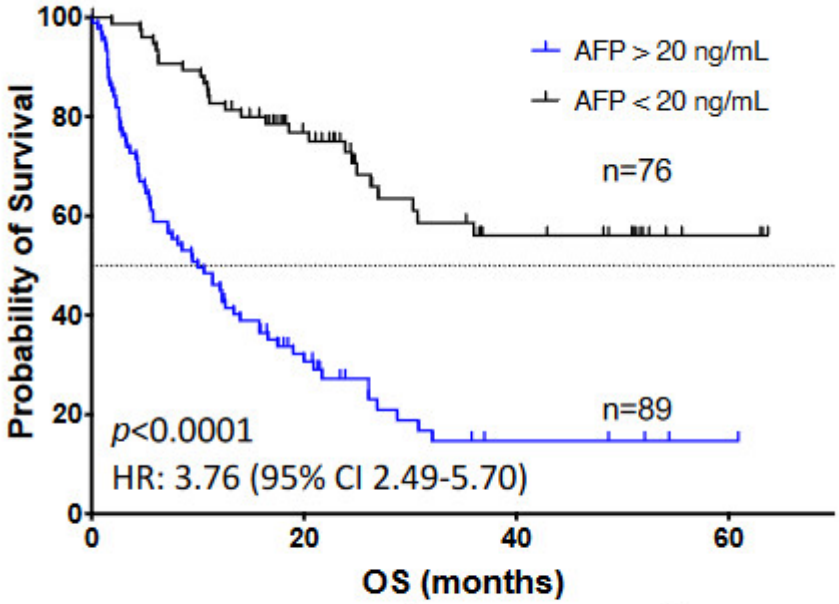


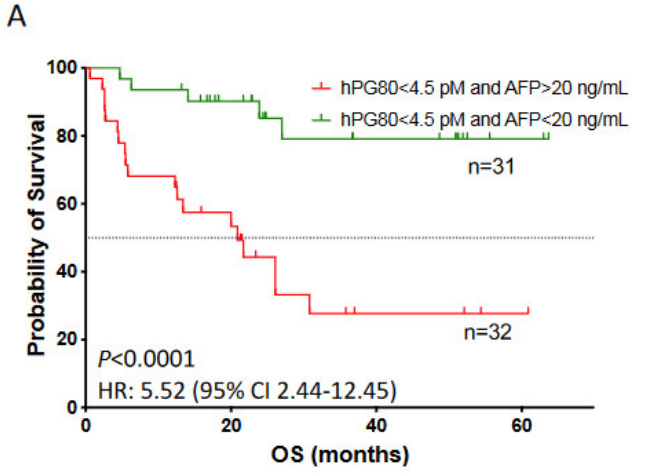
Figure S1. Scatter plots of hPG80 and AFP, MELD and creatinine in HCC patients. (**A**) Correlation between hPG80 and AFP levels in HCC patients was evaluated by the Spearman correlation coefficient. (**B**) Correlation between hPG80 and MELD levels in HCC patients was evaluated by the

Spearman correlation coefficient. (**C**) Correlation between hPG_{80} and creatinine levels in HCC patients was evaluated by the Spearman correlation coefficient.

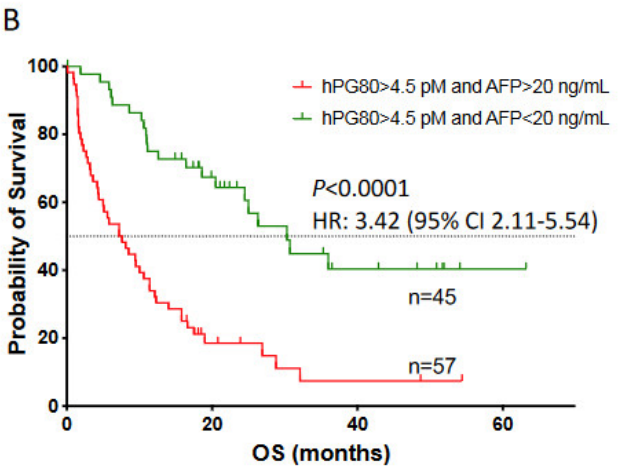


	AFP < 20 ng/ml	AFP > 20 ng/ml
Median OS (months)	Not reached	10.0

Figure S2. Overall survival of HCC patients according to AFP levels. Kaplan-Meier analysis of OS for HCC patients according to AFP levels (cutoff: 20 ng/mL; AFP < 20 ng/mL: $n = 76$; AFP > 20 ng/mL: $n = 89$). The p values, hazard ratios (HR) and 95% confidence intervals are indicated.



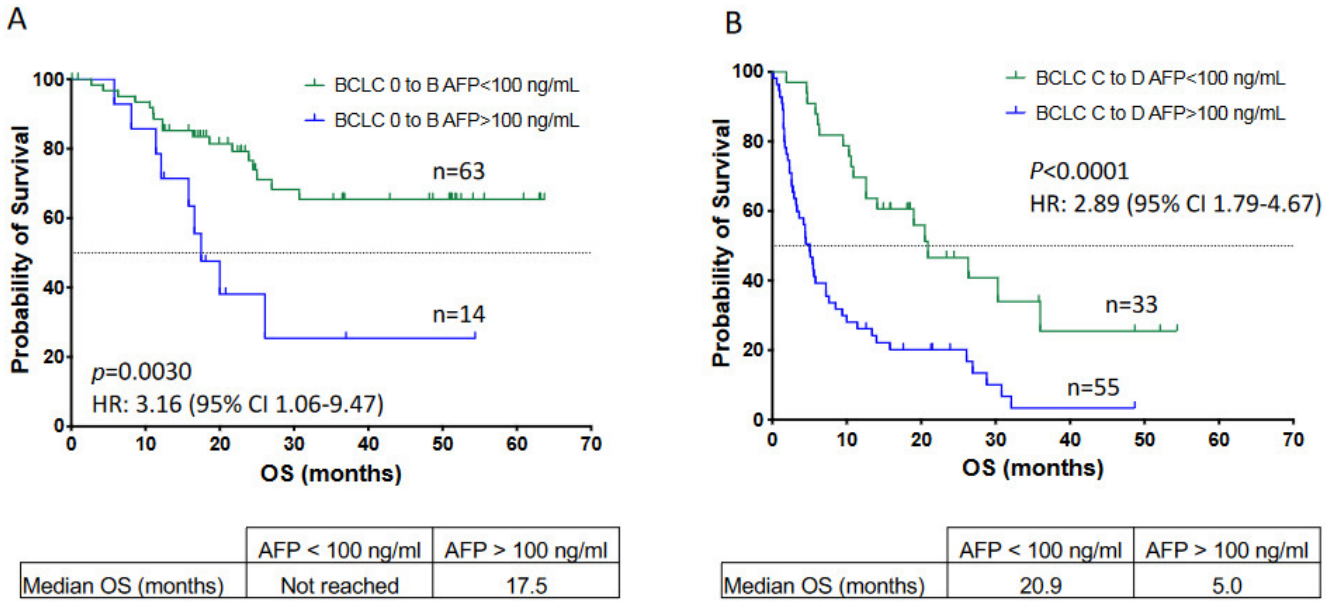
	AFP<20 ng/mL	AFP>20 ng/mL
Median OS (months)	Not reached	20.9



	AFP<20 ng/mL	AFP>20 ng/mL
Median OS (months)	30.30	7.60

Figure S3. Overall survival of HCC patients based on combined hPG_{80} and AFP levels. (**A**) Kaplan-Meier analysis of OS for HCC patients with low hPG_{80} levels ($hPG_{80} < 4.5$ pM; $n = 63$) according to AFP levels (cutoff: 20 ng/mL; AFP < 20 ng/mL: $n = 31$; AFP > 20 ng/mL: $n = 32$). (**B**) Kaplan-Meier

analysis of OS for HCC patients with high hPG_{80} levels (hPG_{80} > 4.5 pM; *n* = 102) according to AFP levels (cutoff: 20 ng/mL; AFP < 20 ng/mL: *n* = 45; AFP > 20 ng/mL: *n* = 57). The *p* values, hazard ratios (HR) and 95% confidence intervals are indicated.



	AFP < 100 ng/ml	AFP > 100 ng/ml
Median OS (months)	Not reached	17.5

	AFP < 100 ng/ml	AFP > 100 ng/ml
Median OS (months)	20.9	5.0

Figure S4. Overall survival of HCC patients depending on the BCLC stages according to AFP levels. (**A**) Kaplan-Meier analysis of OS for HCC patients with very early to intermediate BCLC stages (BCLC 0 to B, *n* = 77) according to AFP levels. Patients were divided into two groups based on AFP levels (cutoff: 100 ng/mL; AFP < 100 ng/mL: *n* = 63; AFP > 100 ng/mL: *n* = 14). (**B**) Kaplan-Meier analysis of OS for HCC patients with advanced to terminal BCLC stages (BCLC C to D, *n* = 88) according to AFP levels. Patients were divided into two groups based on AFP levels (cutoff: 100 ng/mL; AFP < 100 ng/mL: *n* = 33; AFP > 100 ng/mL: *n* = 55).

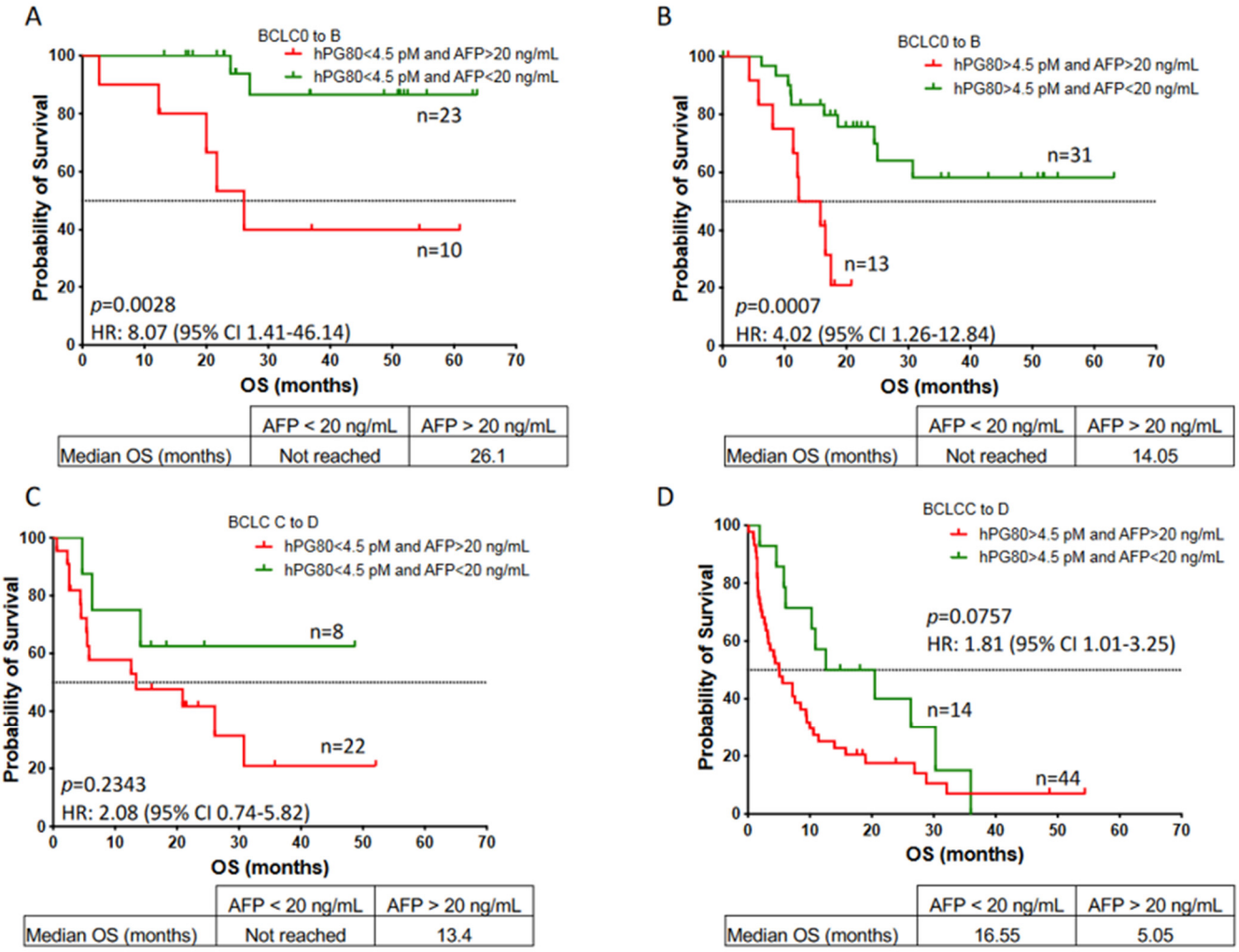


Figure S5. Overall survival of HCC patients with early to intermediate BCLC stages (BCLC 0 to B) and with advanced to terminal BCLC stages (BCLC C to D) according to hPG_{80} alone or in combination with AFP levels at 20 ng/mL. (**A**) Kaplan-Meier analysis of OS for HCC patients with BCLC 0 to B and low hPG_{80} levels (hPG_{80} < 4.5 pM) (n = 33) according to AFP levels. Patients were divided into two groups based on AFP levels (cutoff: 20 ng/mL; AFP < 20 ng/mL: n = 23; AFP > 20 ng/mL: n = 10). (**B**) Kaplan-Meier analysis of OS for HCC patients with BCLC 0 to B and high hPG_{80} levels (hPG_{80} > 4.5 pM) (n = 44) according to AFP levels. Patients were divided into two groups based on AFP levels (cutoff: 20 ng/mL; AFP < 20 ng/mL: n = 31; AFP > 100 ng/mL: n = 13). (**C**) Kaplan-Meier analysis of OS for HCC patients with BCLC C to D and low hPG_{80} levels (hPG_{80} < 4.5 pM) (n = 30) according to AFP levels. Patients were divided into two groups based on AFP levels (cutoff: 20 ng/mL; AFP < 20 ng/mL: n = 8; AFP > 20 ng/mL: n = 22). (**D**) Kaplan-Meier analysis of OS for HCC patients with very BCLC C to D and high hPG_{80} levels (hPG_{80} > 4.5 pM) (n = 58) according to AFP levels. Patients were divided into two groups based on AFP levels (cutoff: 20 ng/mL; AFP < 20 ng/mL: n = 14; AFP > 20 ng/mL: n = 44). The p values, hazard ratios (HR) and 95% confidence intervals are indicated.

Table S1. Clinical and pathological characteristics for the training and validation cohorts.

		Training Cohort N (%) *n* = 84	**Validation Cohort N(%) *n* = 84**
Age, years	Median (range)	66 (27–85)	68 (45–84)
Gender	Male	74 (88.1%)	75 (89.3%)
	Female	10 (11.9%)	9 (10.7%)
Laboratory values			
hPG_{80}	Median (IQR), pM	8.79 (2.93–21.94)	6.31 (2.40–31.85)
	Mean (SE), pM	16.77 (2.26)	34.27 (7.92)
AFP	Median (IQR), ng/mL	27.80 (5.00–825.50)	41.05 (6.39–479.50)
	Mean (SE), ng/mL	7006 (4663)	3196 (975)
Etiology			
NASH	Y	9 (10.7%)	22 (26.2%)
	N	75 (89.3%)	62 (73.8%)
Alcohol consumption	Y	52(61.9%)	55 (65.5%)
	N	32 (38.1%)	29 (34.5%)
Hepatitis B virus	Y	8 (9.5%)	5 (6.0%)
	N	76 (90.5%)	79 (94.0%)
Hepatitis C virus	Y	28 (33.3%)	17 (20.2%)
	N	56 (66.7%)	67 (79.8%)
Cirrhosis	Y	73 (86.9%)	65 (77.4%)
	N	11 (13.1%)	19 (22.6%)
BCLC	0	9 (10.7%)	1 (1.25%)
	A	18 (21.4%)	16 (19.0%)
	B	17 (20.2%)	18 (21.4%)
	C	38 (45.2%)	48 (57.1%)
	D	2 (2.5%)	1 (1.25%)

Abbreviations, AFP: alpha-fetoprotein; IQR: interquartile range; SE: standard error; BCLC: Barcelona Clinic Liver Center; NASH: nonalcoholic steatohepatit.