

Supplementary

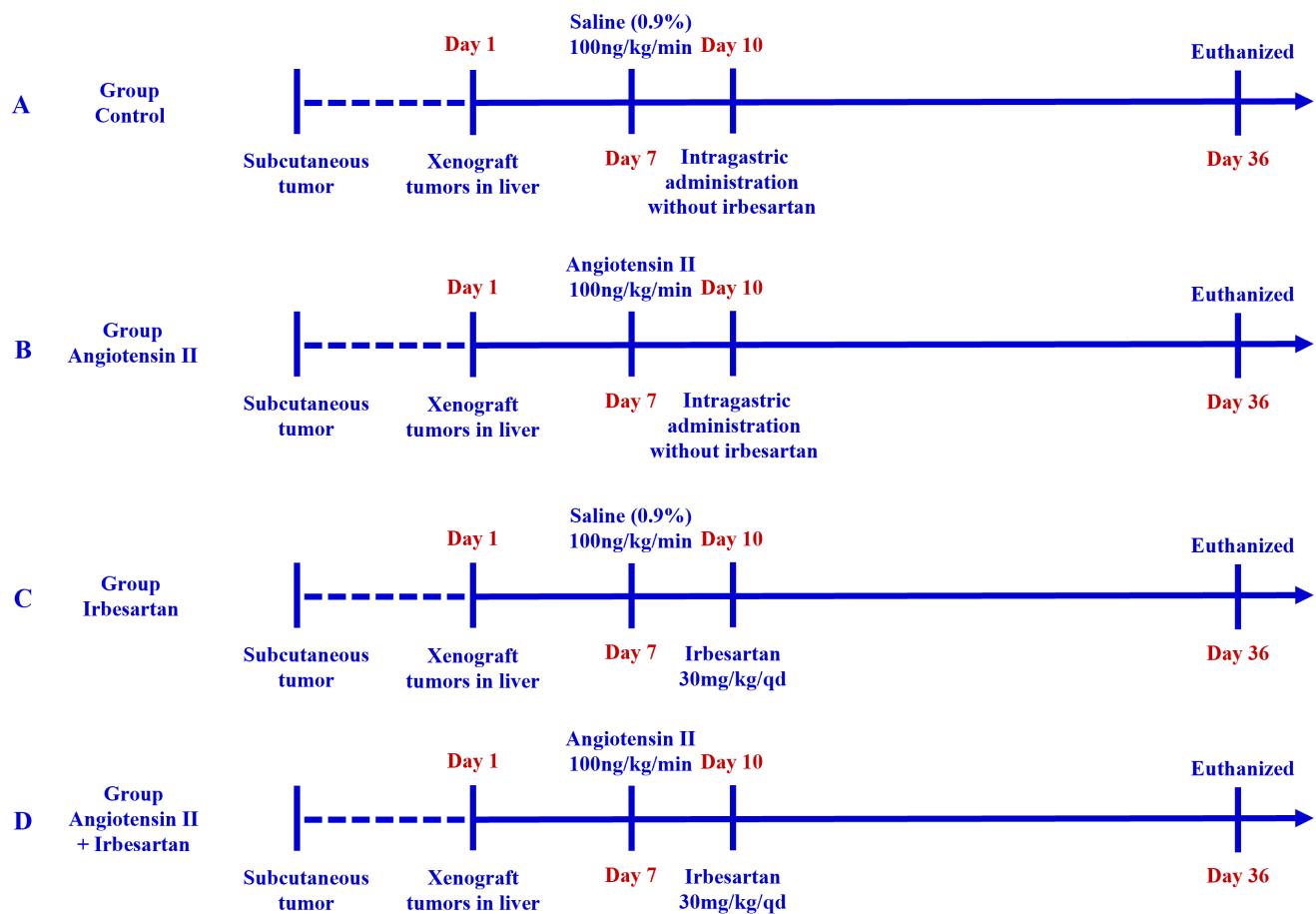


Figure S1 The groups and time axes of animal experiments (Orthotopic tumor xenograft model).

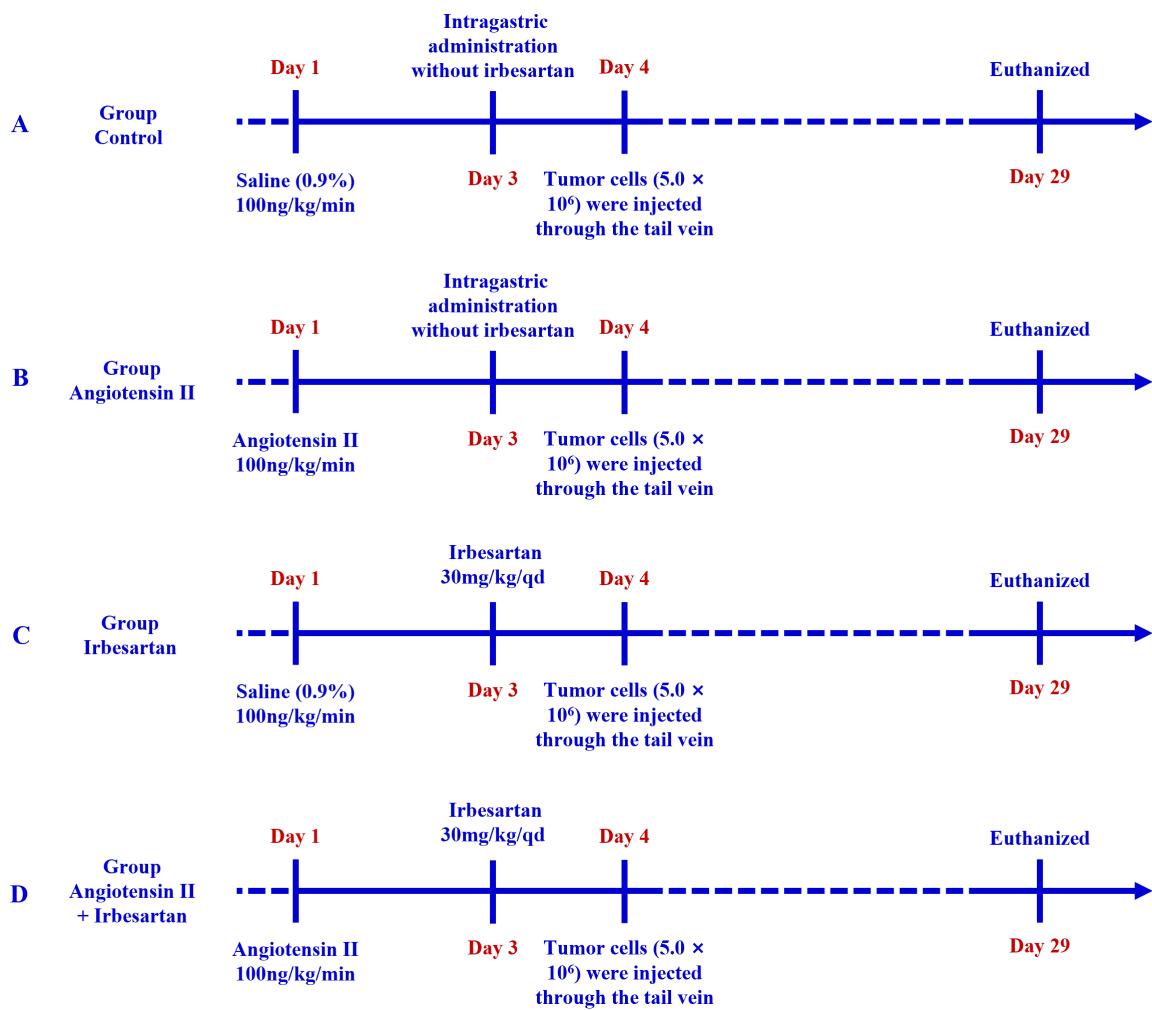


Figure S2 The groups and time axes of animal experiments (Lung metastasis model).

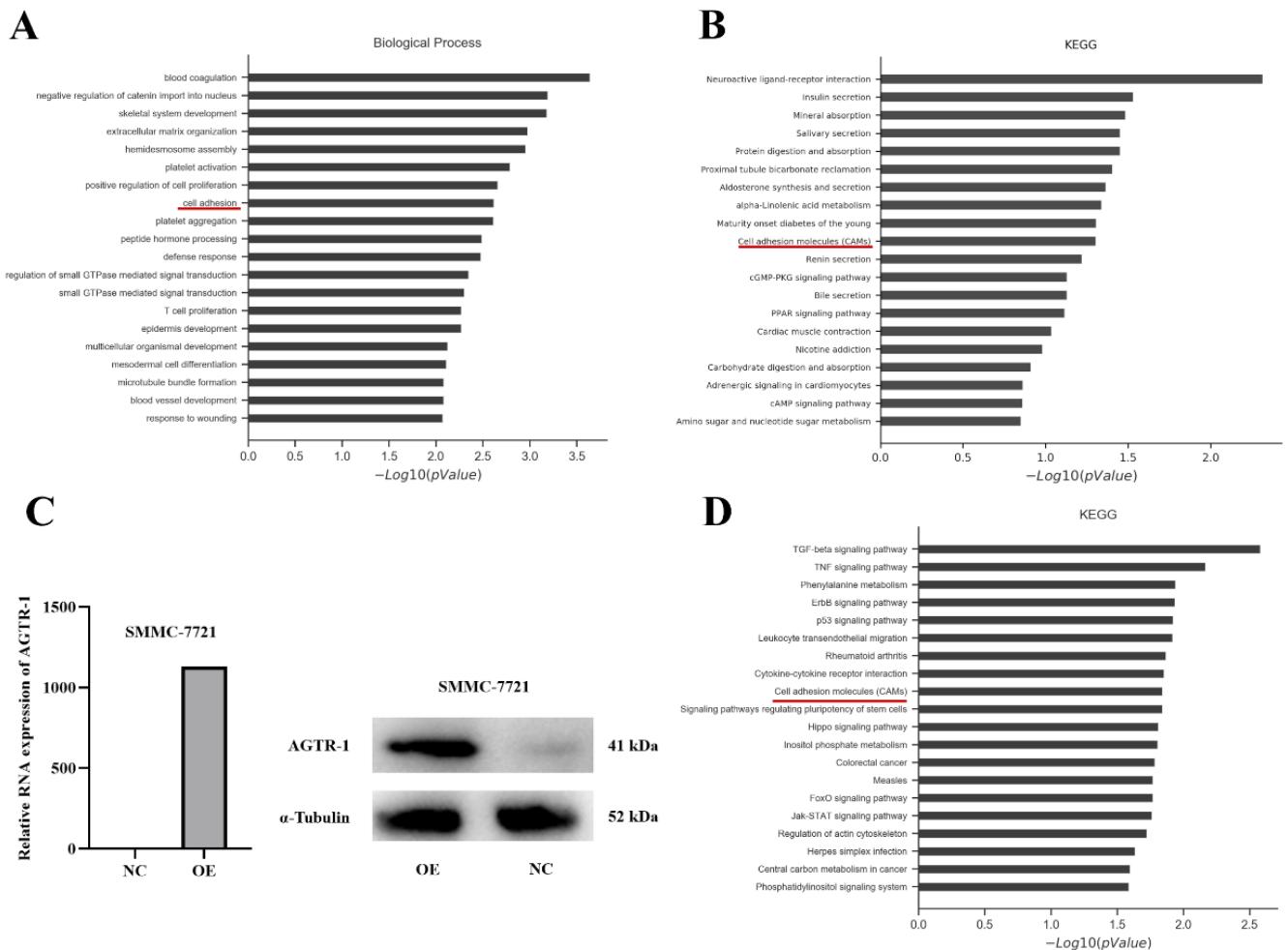


Figure S3 Human gene expression microarray: Ang II could affect the expression of adhesion molecules in HCC cells. (A) Biological behavior analysis on Ang II-treated HMHCC97-H cells and control HMHCC97-H cells. (B) Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis on Ang II-treated HCCLM3 cells and control HCCLM3 cells. (C) Real-time PCR and Western blot: verification of AGTR-1 overexpression in SMMC-7721 cells. (D) KEGG analysis on SMMC-7721-AGTR-1-overexpressed cells and SMMC-7721-Control cells. NC, control group; OE, AGTR-1 overexpression group.

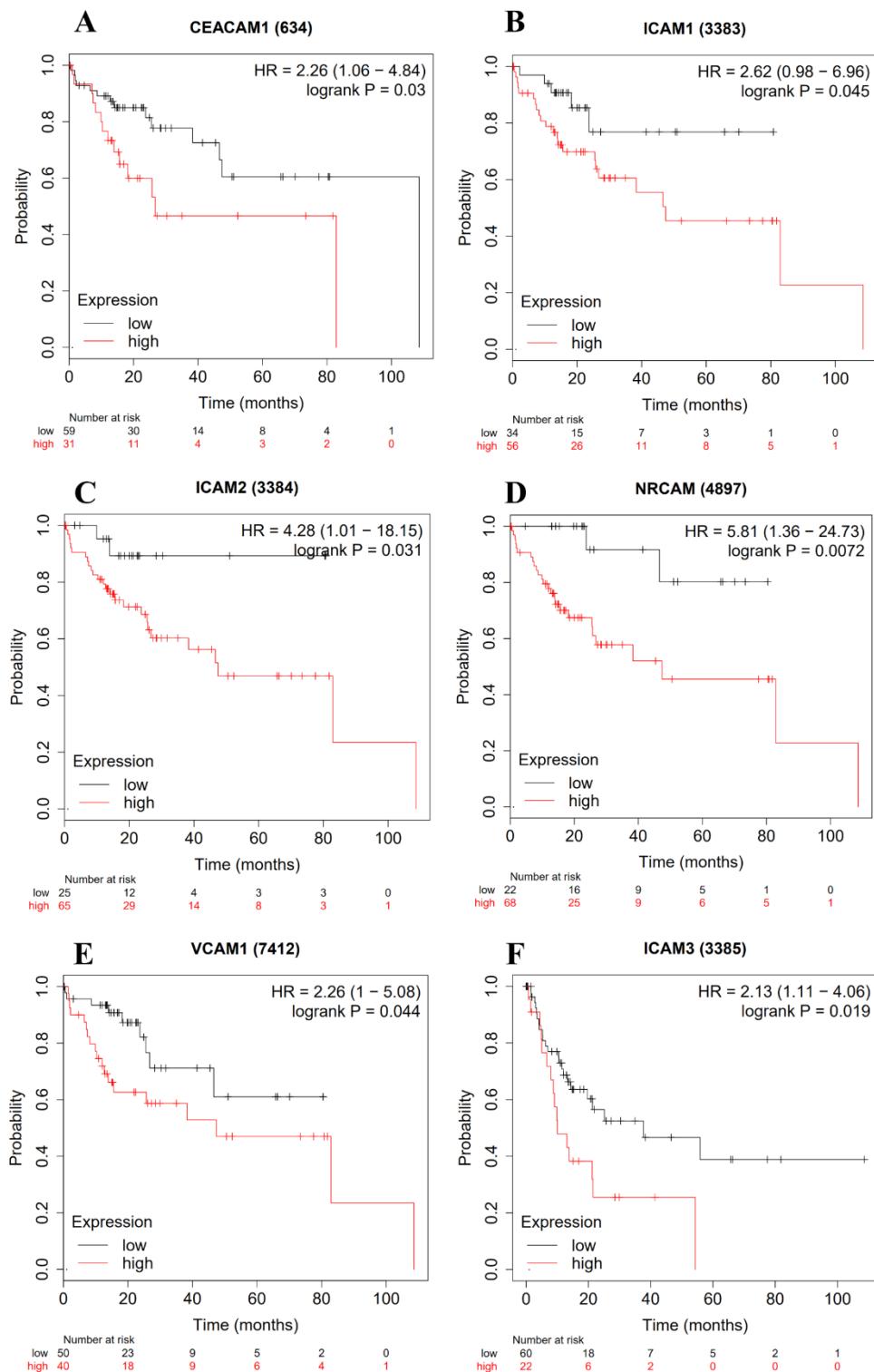


Figure S4 The relationships between the expression of six adhesion molecules in HCC tissues and prognosis in HCC patients with microvascular invasion (KM-Plotter public database, n=90). (A) CEACAM-1, overall survival; (B) ICAM-1, overall survival; (C) ICAM-2, overall survival; (D) NRCAM, overall survival; (E) VCAM-1, overall survival; (F) ICAM-3, recurrence.

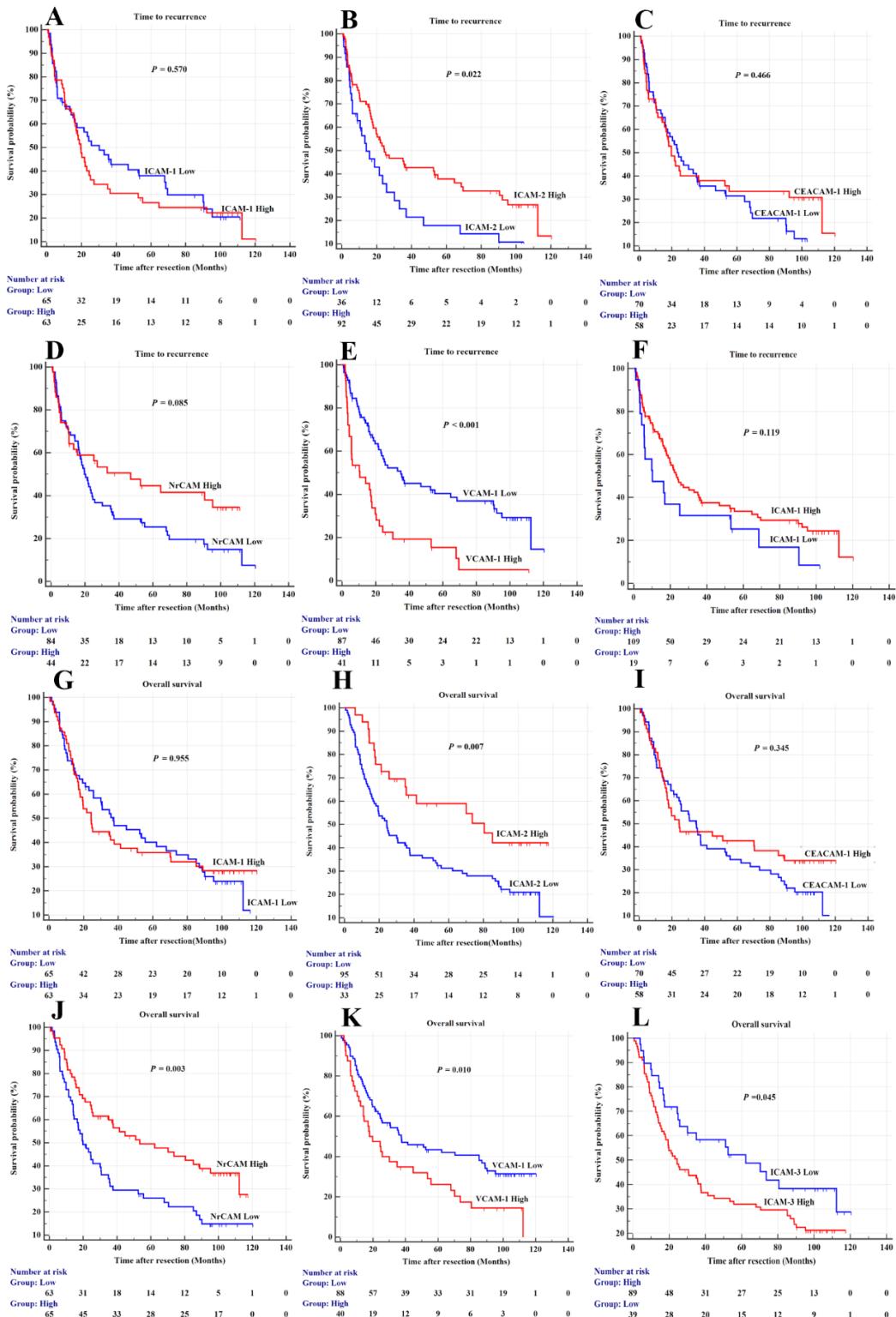


Figure S5 The relationships between the expression of five adhesion molecules in HCC tissues and overall survival in HCC patients with microvascular invasion (clinical cases from our hospital, n=128). Recurrence: (A) CEACAM-1; (B) ICAM-1; (C) ICAM-2; (D) NRNCAM; (E) VCAM-1; (F) ICAM-3. Overall survival: (G) CEACAM-1; (H) ICAM-1; (I) ICAM-2; (J) NRNCAM; (K) VCAM-1; (L) ICAM-3.

Table S1 PCR primers and sequences

Name	Primer	Sequences (5'→3')
AGTR-1	Forward	CACTGGCTGACTTATGCTTTT
AGTR-1	Reverse	TAGAAACACACTAGCGTACAGG
VCAM-1	Forward	CAGGCTGGAGATAGACTTACTG
VCAM-1	Reverse	CCTCAATGACAGGAGTAAAGGT
CEACAM-1	Forward	CCACAGTCAGACGATCATAGT
CEACAM-1	Reverse	TCATCTGTTAGGTGGTCATT
ICAM-1	Forward	TGCAAGAAGATAGCCAACCAAT
ICAM-1	Reverse	GTACACGGTGAGGAAGGTTTA
ICAM-2	Forward	ATGAGACTCTGCACTATGAGAC
ICAM-2	Reverse	GCTGAGTGTGAAAGATGT
NRCAM	Forward	CGGAGCTGCAGTTCTAATAAC
NRCAM	Reverse	TGCAGGGAAAGTACTAAAGACTG

AGTR-1, angiotensin II type 1 receptor; VCAM-1, vascular cell adhesion molecule-1; CEACAM-1, CEA cell adhesion molecule-1; ICAM-1, intercellular cell adhesion molecule-1; ICAM-2, intercellular cell adhesion molecule-2; NRCAM, neuronal cell adhesion molecule.

Table S2 Seventeen adhesion molecules and prognosis of hepatocellular carcinoma with microvascular invasion after resection (KM-plotter public database)

Number	Adhesion molecules	Abbreviation	OS (n=90)	RFS (n=90)
1	Activated leukocyte cell adhesion molecule	ALCAM	-	-
2	Basal Cell Adhesion Molecule	BCAM	-	-
3	CEA cell adhesion molecule-1	CEACAM-1	↑	↓
4	Epithelial Cell Adhesion Molecule	EpCAM	↓	-
5	Epithelial cadherin	E-Cadherin	-	-
6	Intercellular cell adhesion molecule-1	ICAM-1	↑	-
7	Intercellular cell adhesion molecule-2	ICAM-2	↑	-
8	Intercellular cell adhesion molecule-3	ICAM-3	-	↑
9	Neuronal cell adhesion molecule-1	NCAM-1	-	-
10	Neuronal cell adhesion molecule	NRCAM	↑	↓
11	Placental-cadherins	P-Cadherin	-	↓
12	Platelet endothelial cell adhesion molecule-1	PECAM-1	-	↓
13	Endothelial selectin	E- Selectin	-	-
14	Leukocyte selectin	L-Selectin	-	-
15	Platelet selectin	P-Selectin	-	-
16	Vascular cell adhesion molecule-1	VCAM-1	↑	-
17	Vascular endothelial cadherin	VE-Cadherin	↓	-

OS, overall survival; RFS, recurrence free survival; MVI, microvascular invasion; “↑”, High expression is associated with poor prognosis; “↓”, Low expression is associated with poor prognosis; “-”, no difference in prognosis.

Table S3 Univariate analysis of clinicopathological parameters associated with recurrence and survival in hepatocellular carcinoma patients with microvascular invasion

Clinicopathological parameters	Number	Time to recurrence		Overall survival P values
			P values	
Gender (Man/Female)	113/15		0.137	0.696
Age (Year)	128		0.662	0.637
Transfusion (Yes/No)	15/113		0.342	0.529
HBsAg (Positive/Negative)	19/109		0.004	0.044
Pringle maneuver (Yes/No)	38/90		0.867	0.651
AFP >20 µg/L (Yes/No)	93/35		0.564	0.047
CA19-9 >40 µ/mL (Yes/No)	27/101		0.732	0.799
ALT >50 U/L (Yes/No)	35/93		0.333	0.499
AST >50 U/L (Yes/No)	24/104		0.349	0.863
GGT >60 U/L (Yes/No)	77/51		0.027	0.065
ALP >135 U/L (Yes/No)	18/110		0.529	0.616
Total bilirubin (µmol/L)	128		0.365	0.470
Albumin (g/L)	128		0.693	0.426
Hemoglobin (g/L)	128		0.691	0.354
Platelet (10 ⁹ /L)	128		0.099	0.382
Prothrombin time (second)	128		0.642	0.252
Size (cm)	128		0.270	0.014
Singe nodule (Yes/No)	81/47		0.999	0.123
Intact capsule (Yes/No)	53/75		0.524	0.269
Differentiation (I-II/III-IV)	70/58		0.643	0.093
Cirrhosis (Yes/No)	74/54		0.221	0.057
Satellite nodules (Yes/No)	26/102		0.268	0.055
Tumor thrombus (Yes/No)	30/98		0.541	0.048
ICAM-1 (High/Low)	63/65 (63/65) †		0.570	0.955
ICAM-2 (High/Low)	92/36 (33/95) †		0.022	0.007
ICAM-3 (High/Low)	19/109(39/89) †		0.118	0.045
CEACAM-1 (High/Low)	58/70 (58/70) †		0.466	0.345
NRCAM (High/Low)	44/84 (65/63) †		0.085	0.003
VCAM-1 (High/Low)	41/87 (40/88) †		0.001	0.010

†, group of overall survival. ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, γ -glutamyl transpeptidase; ICAM-1, Intercellular cell adhesion molecule-1; ICAM-2, Intercellular cell adhesion molecule-2; ICAM-3, Intercellular cell adhesion molecule-3; CEACAM-1, CEA cell adhesion molecule-1; NRCAM, Neuronal cell adhesion molecule; VCAM-1, Vascular cell adhesion molecule-1.