Supplementary

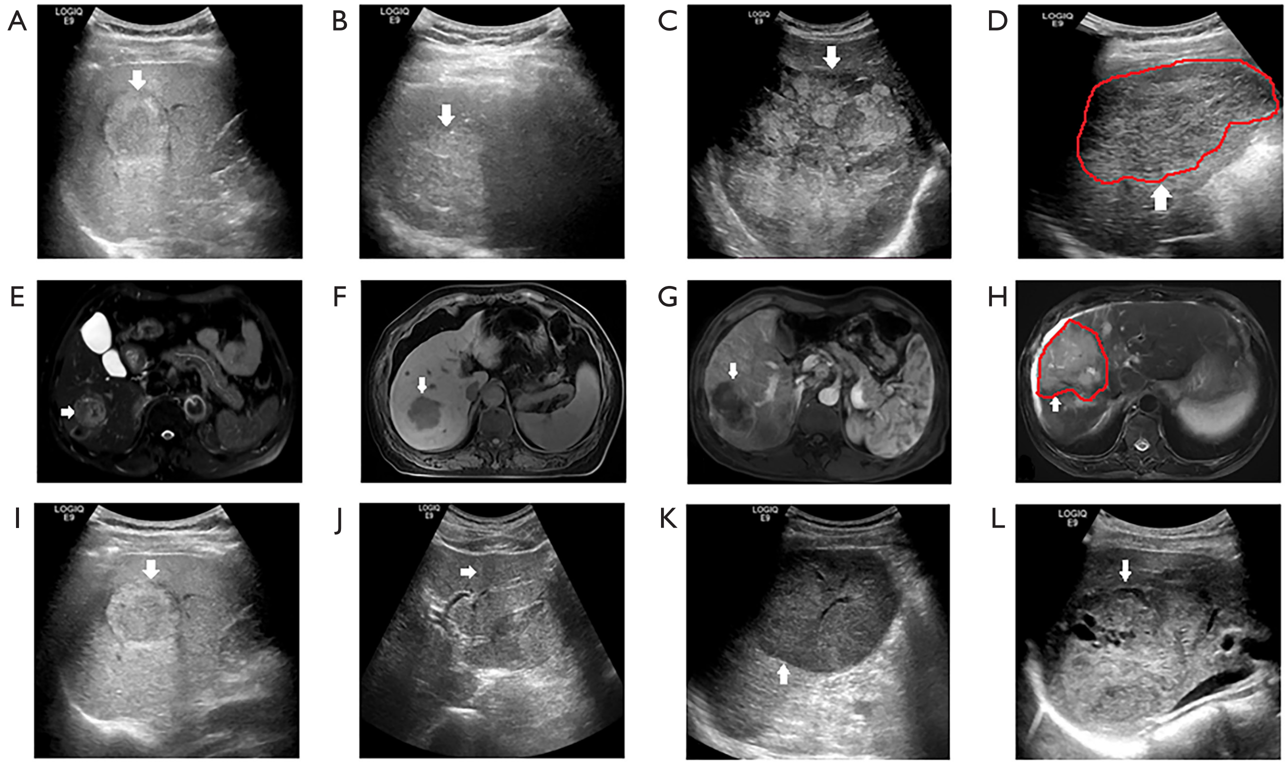

Figure S1 Image analysis in CUS and MRI. (A) Regular shape (arrow). (B-D) Irregular shape: (B) focal extranodular extension (arrow), (C) multinodular confluence appearance (arrow), and (D) focal infiltrative margin (arrow). (E-H) Tumor shape in MRI: (E) round nodular, (F) protruding nodular, (G) multiple fused nodules, and (H) irregular infiltration. (I-L) Echogenicity of the tumor: (I) hyperechoic, (J) isoechoic, (K) hypoechoic, and (L) multiple fused echo. CUS, conventional ultrasound; MRI, magnetic resonance imaging.

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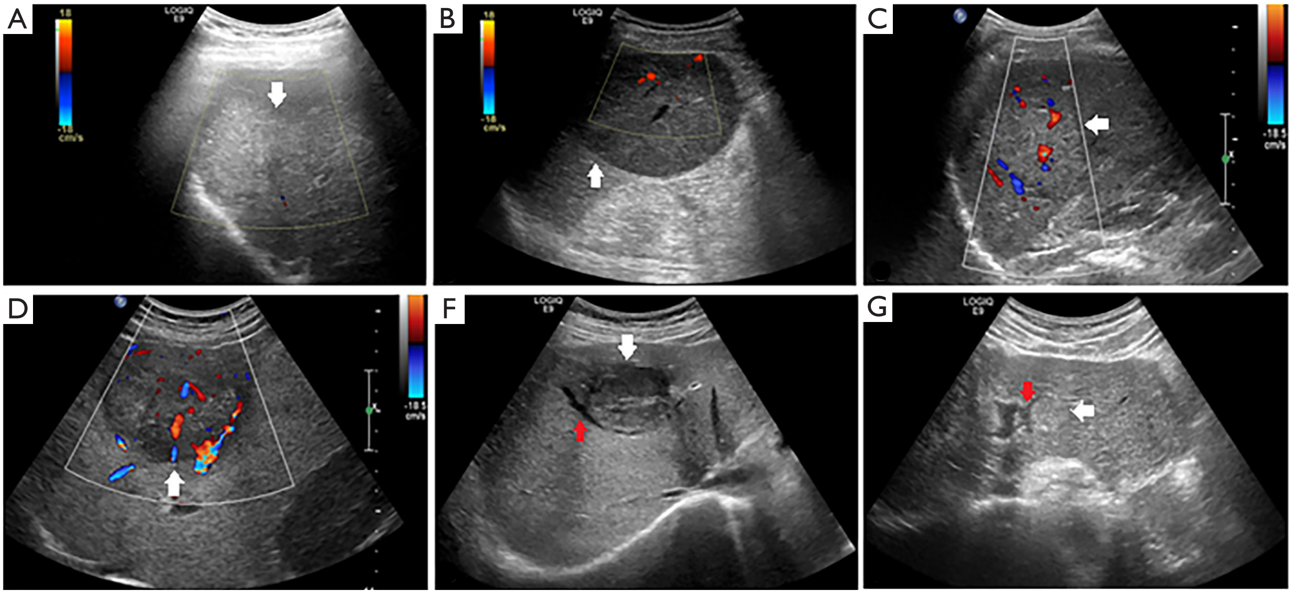

Figure S2 Image analysis of CDFI. (A) Grade 0 (absent): no blood flow visualized (arrow). (B) Grade I (minimal): one- or two-pixel containing flow (arrow). (C) Grade II (moderate): a main vessel and/or several small vessels (arrow). (D) Grade III (marked): four or more vessels (arrow). (E-F) Visualized macrovascular around the tumor on CUS, including prominent peripheral portal veins, hepatic vein, or their branches located near (<1 cm) the tumor. Tumors are indicated by white arrows and visualized macrovascularity by red arrows. CDFI, color Doppler flow imaging; CUS, conventional ultrasound.

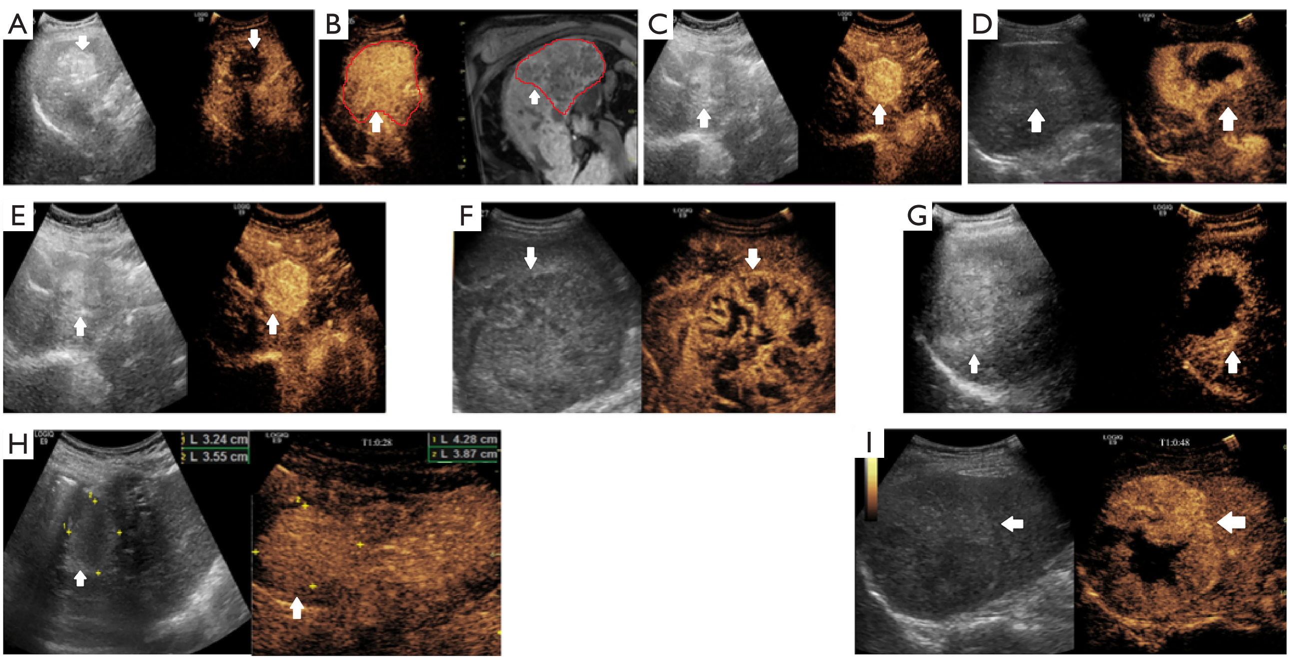

Figure S3 Major features in CEUS in arterial phases. (A-D) The degree of enhancement (arrows): (A) hypo-, (B) iso-, (C) hyper-, and (D) mixed enhancement. (E-G) Enhancement pattern (arrows): (E) homogeneous, (F) heterogeneous, (G) ring-like, (H) arterial peritumoral (arrows), and (I) capsular enhancement (arrows). CEUS, contrast-enhanced ultrasound.

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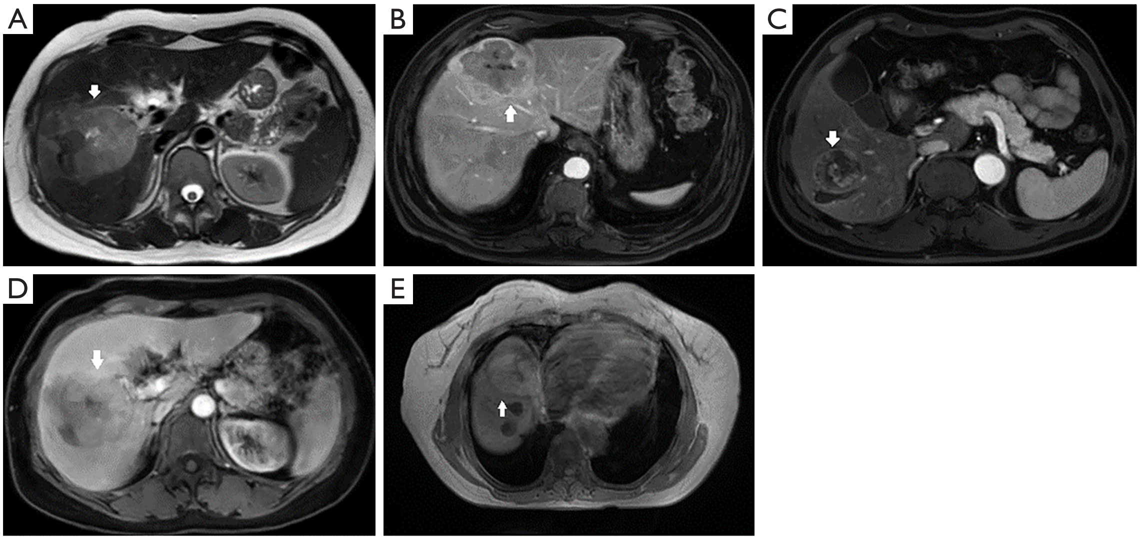

Figure S4 Major features in MRI. (A) Heterogeneous signal intensity of the tumor on transverse T2-WI (arrow). (B) Tumor with peritumoral enhancement (arrow). (C) Tumor with rim enhancement (arrow). (D) Tumor with asynchronous enhancement (arrow). (E) Presence of tumor pseudocapsule (arrow). MRI, magnetic resonance imaging; T2-WI, T2-weighted imaging.

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Table S1 Baseline characteristics of the included patients

Characteristic	Total (n=259)	Modeling cohort			Validation cohort		
		MVI− (n=132)	MVI+ (n=47)	P	MVI− (n=43)	MVI+ (n=37)	P
Demographics							
Sex				0.09			0.16
Female	38 (14.67)	26 (19.70)	4 (8.51)		4 (9.30)	4 (10.81)	
Male	221 (85.33)	106 (80.30)	43 (91.49)		39 (90.70)	33 (89.19)	
Age	60 [52,66]	60 [53,65]	57 [49,66]	0.10	61.23±11.61	58.46±10.84	0.25
Histological characteristics							
Pathological type				0.04			0.53
HCC	249 (96.14)	130 (98.49)	43 (91.49)		40 (93.02)	36 (97.30)	
cHCC-CC	10 (3.86)	2 (1.51)	4 (8.51)		3 (6.98)	1 (2.70)	
Cirrhosis	129 (49.81)	59 (44.70)	19 (40.43)	0.61	28 (65.12)	23 (62.16)	<0.05
Biochemical profile							
ALR	59.43 [38.95, 96.55]	54.44 [35.87, 74.30]	60.54 [41.65, 87.31]	0.15	71.25 [38.95, 112.86]	85.00 [59.00, 117.78]	0.72
PLR	104.55 [76.32, 142.00]	93.13 [73.87, 119.09]	103.89 [72.27, 147.50]	0.07	127.78 [90.38, 155.71]	129.47 [89.33, 185.00]	<0.05
NLR	2.35 [1.73, 3.69]	1.95 [1.58, 2.75]	2.22 [1.81, 2.94]	0.20	3.71 [2.50, 5.38]	3.60 [2.22, 5.77]	0.07
ALT, U/L				<0.05			<0.05
≤40	155 (59.85)	103 (78.03)	25 (53.19)		17 (39.54)	10 (27.03)	
>40	104 (40.15)	29 (21.97)	22 (46.81)		26 (60.46)	27 (72.97)	
AST, U/L				<0.05			<0.05
≤40	182 (70.27)	107 (81.06)	30 (63.83)		26 (60.46)	19 (51.35)	
>40	77 (29.73)	25 (18.94)	17 (36.17)		17 (39.54)	18 (48.65)	
GGT, U/L				0.09			0.27
≤50	110 (42.47)	58 (43.94)	14 (29.79)		24 (55.81)	14 (37.84)	
>50	149 (57.53)	74 (56.06)	33 (70.21)		19 (44.19)	23 (62.16)	
TB, μmol/L				0.13			<0.05
≤19	226 (87.26)	128 (96.97)	43 (91.49)		29 (67.44)	26 (70.27)	
>19	33 (12.74)	4 (3.03)	4 (8.51)		14 (32.56)	11 (29.73)	
ALB, g/L				0.24			<0.05
≤40	174 (67.18)	75 (56.82)	22 (46.81)		42 (97.68)	35 (94.60)	
>40	85 (32.89)	57 (43.18)	25 (53.19)		1 (2.32)	2 (5.40)	
Scr, μmol/L				0.99			0.95
≤133	249 (96.14)	125 (94.70)	47 (100.00)		42 (97.67)	35 (94.60)	
>133	10 (3.86)	7 (5.30)	0 (0.00)		1 (2.33)	2 (5.40)	
PLT count, 10^9/L				0.80			0.23
>100	163 (62.93)	87 (65.91)	30 (63.83)		27 (62.79)	19 (51.35)	
≤100	96 (37.07)	45 (34.09)	17 (36.17)		16 (37.21)	18 (48.65)	
Pt, s				0.94			0.69
<14	242 (93.44)	124 (93.94)	44 (93.62)		39 (90.70)	35 (94.60)	
>14	17 (6.56)	8 (6.06)	3 (6.38)		4 (9.30)	2 (5.40)	
Hepatitis B virus infection				0.17			<0.05
Negative	34 (13.13)	26 (19.70)	5 (10.64)		0 (0.00)	3 (8.11)	
Positive	225 (86.87)	106 (80.30)	42 (89.362)		43 (100.00)	34 (91.89)	
HBsAg				0.98			<0.05
Negative	50 (19.31)	34 (25.76)	12 (25.53)		0 (0.00)	4 (10.81)	
Positive	209 (80.69)	98 (74.24)	35 (74.47)		43 (100.00)	33 (89.19)	
AFP, ng/mL				0.64			<0.05
≤20	109 (42.09)	50 (37.88)	16 (34.04)		28 (65.12)	15 (40.54)	
>20	150 (57.91)	82 (62.12)	31 (65.96)		15 (34.88)	22 (59.46)	
CEA, ng/mL				0.46			0.08
≤10	253 (97.68)	131 (99.24)	46 (97.87)		40 (93.02)	36 (97.30)	
>10	6 (2.32)	1 (0.76)	1 (2.13)		3 (6.98)	1 (2.70)	
CA199, U/mL				0.62			0.06
≤39	208 (80.31)	103 (78.03)	35 (74.47)		34 (79.07)	36 (97.30)	
>39	51 (19.69)	29 (21.97)	12 (25.53)		9 (20.93)	1 (2.70)	
CA125, U/mL				0.94			0.97
≤30.2	243 (93.82)	124 (93.94)	44 (93.62)		41 (95.35)	34 (91.89)	
>30.2	16 (6.18)	8 (6.06)	3 (6.38)		2 (4.65)	3 (8.11)	
Radiological characteristics							
CUS							
Tumor location				0.51			0.38
Right lobe	196 (75.68)	106 (80.30)	33 (70.21)		29 (67.44)	28 (75.68)	
Left lobe	47 (18.15)	18 (13.64)	12 (25.53)		11 (25.58)	6 (16.22)	
Across the left and right lobes	14 (5.40)	6 (4.55)	2 (4.26)		3 (6.98)	3 (8.10)	
Caudate lobe	2 (0.77)	2 (1.51)	0 (0.00)		0 (0.00)	0 (0.00)	
Tumor number				0.05			<0.05
Single	235 (90.73)	128 (96.97)	42 (89.36)		34 (79.07)	31 (83.78)	
Multiple	24 (9.27)	4 (3.03)	5 (10.64)		9 (20.93)	6 (16.22)	
Diameter (cm)	3.60 [2.20, 6.20]	3.40 [2.30, 5.20]	5.20 [2.60, 7.20]	<0.05	2.60 [1.80, 3.80]	4.30 [2.60, 6.70]	0.56
Shape				0.38			<0.05
Regular	162 (62.55)	96 (72.73)	31 (65.96)		21 (48.84)	14 (37.84)	
Irregular	97 (37.45)	36 (27.27)	16 (34.04)		22 (51.16)	23 (62.16)	
Boundary				0.87			<0.05
Clear	151 (58.30)	86 (65.15)	30 (63.83)		18 (41.86)	17 (45.95)	
Unclear	108 (41.70)	46 (34.85)	17 (36.17)		25 (58.14)	20 (54.05)	
Echogenicity				0.23			<0.05
Hypoechoic	154 (59.46)	73 (55.30)	20 (42.55)		34 (79.07)	27 (72.97)	
Hyperechoic	62 (23.94)	36 (27.27)	13 (27.66)		8 (18.60)	5 (13.51)	
Isoechoic	13 (5.02)	7 (5.30)	6 (12.77)		0 (0.00)	0 (0.00)	
Mixed	30 (11.58)	16 (12.13)	8 (17.02)		1 (2.33)	5 (13.52)	

Table S1 (*continued*)

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Table S1 (*continued*)

Characteristic	Total (n=259)	Modeling cohort			Validation cohort		
		MVI− (n=132)	MVI+ (n=47)	P	MVI− (n=43)	MVI+ (n=37)	P
Uniformity				0.87			<0.05
Homogeneous	92 (35.52)	41 (31.06)	14 (29.79)		27 (62.79)	10 (27.03)	
Heterogeneous	167 (64.48)	91 (68.94)	33 (70.21)		16 (37.21)	27 (72.97)	
Capsule				<0.05			<0.05
Present	189 (72.97)	115 (87.12)	34 (72.34)		28 (65.12)	12 (32.43)	
Absent	70 (27.03)	17 (12.88)	13 (27.66)		15 (34.88)	25 (67.57)	
Hypoechoic halo				0.28			0.22
Absent	212 (81.85)	108 (81.82)	35 (74.47)		38 (88.37)	31 (83.78)	
Present	47 (18.15)	24 (18.18)	12 (25.53)		5 (11.63)	6 (16.22)	
Adler blood flow grading				<0.05			0.21
0	143 (55.21)	89 (67.42)	17 (36.17)		28 (65.12)	9 (24.32)	
I	27 (10.43)	16 (12.12)	1 (2.13)		7 (16.28)	3 (8.11)	
II	62 (23.94)	10 (7.58)	25 (53.19)		7 (16.28)	20 (54.05)	
III	27 (10.42)	17 (12.88)	4 (8.51)		1 (2.32)	5 (13.51)	
Visualized macrovascularity around the tumor				<0.05			<0.05
Present	211 (81.47)	129 (97.73)	31 (65.96)		36 (83.72)	15 (40.54)	
Absent	48 (18.53)	3 (2.27)	16 (34.04)		7 (16.28)	22 (59.46)	
CEUS							
Enhancement pattern in arterial phase				0.67			<0.05
Homogeneous	137 (52.90)	66 (50.00)	20 (42.55)		34 (79.07)	17 (45.95)	
Heterogeneous	119 (45.95)	64 (48.49)	26 (55.32)		9 (20.93)	20 (54.05)	
Ring-like enhancement	3 (1.15)	2 (1.51)	1 (2.13)		0 (0.00)	0 (0.00)	
Arterial peritumoral enhancement				<0.05			0.88
Absent	231 (89.19)	124 (93.94)	36 (76.60)		41 (95.35)	30 (81.08)	
Present	28 (10.81)	8 (6.06)	11 (23.40)		2 (4.65)	7 (18.92)	
Capsular enhancement				0.78			0.80
Absent	255 (98.46)	130 (98.49)	46 (97.87)		42 (97.67)	37 (100.00)	
Present	4 (1.54)	2 (1.51)	1 (2.13)		1 (2.33)	0 (0.00)	
Nonenhancing area				<0.05			0.49
Absent	195 (75.29)	107 (81.06)	30 (63.83)		37 (86.05)	21 (56.76)	
Present	64 (24.71)	25 (18.94)	17 (36.17)		6 (13.95)	16 (43.24)	
Enhancement level in arterial phase				0.51			<0.05
Hyperenhancement	230 (88.80)	116 (87.88)	38 (80.85)		42 (97.67)	34 (91.89)	
Hypoenhancement	5 (1.93)	2 (1.52)	1 (2.13)		1 (2.33)	1 (2.70)	
Isoenhancement	7 (2.70)	4 (3.03)	1 (2.13)		0 (0.00)	2 (5.41)	
Mixed enhancement	17 (6.57)	10 (7.57)	7 (14.89)		0 (0.00)	0 (0.00)	
Start of enhancement time	16.00 [13.00, 21.000]	16.00 [14.00, 20.00]	15.00 [13.00, 19.00]	0.36	18.00 [14.00, 22.00]	18.00 [14.00, 23.00]	<0.05
Peak time	26.00 [22.00, 32.00]	27.00 [22.00, 32.00]	26.00 [21.00, 33.00]	0.48	25.00 [22.00, 29.00]	28.00 [24.00, 35.00]	0.44
Isoenhancement time	40.00 [34.00, 50.00]	40.00 [33.00, 55.00]	40.00 [34.00, 50.00]	0.70	40.00 [35.00, 48.00]	42.00 [35.00, 50.00]	0.75
Hypoenhancement time	70.00 [50.00, 120.00]	70.00 [53.00, 120.00]	70.00 [50.00, 110.00]	0.43	72.00 [50.00, 150.00]	62.00 [50.00, 90.00]	0.99
Enhancement level in portal venous phase				0.29			0.99
Hyperenhancement	178 (68.72)	88 (66.67)	36 (76.60)		27 (62.79)	27 (72.97)	
Hypoenhancement	79 (30.50)	43 (32.58)	10 (21.28)		16 (37.21)	10 (27.03)	
Isoenhancement	1 (0.39)	0 (0.00)	1 (2.12)		0 (0.00)	0 (0.00)	
Mixed enhancement	1 (0.39)	1 (0.75)	0 (0.00)		0 (0.00)	0 (0.00)	
Enhancement level in delayed phase				0.12			0.97
Hyperenhancement	230 (88.80)	114 (86.36)	46 (97.87)		34 (79.07)	36 (97.30)	
Hypoenhancement	27 (10.42)	17 (12.88)	0 (0.00)		9 (20.93)	1 (2.70)	
Isoenhancement	1 (0.39)	0 (0.00)	1 (2.13)		0 (0.00)	0 (0.00)	
Mixed	1 (0.39)	1 (0.76)	0 (0.00)		0 (0.00)	0 (0.00)	
Early washout				0.27			0.62
Absent	158 (61.00)	85 (64.39)	26 (55.32)		28 (65.12)	19 (51.35)	
Present	101 (39.00)	47 (35.61)	21 (44.68)		15 (34.88)	18 (48.65)	
Marked washout				<0.05			<0.05
Absent	96 (37.07)	42 (31.82)	4 (8.51)		32 (74.42)	18 (48.65)	
Present	163 (62.93)	90 (68.18)	43 (91.49)		11 (25.58)	19 (51.35)	
MR							
Non-nodular type tumor				<0.05			0.32
Present	151 (58.30)	101 (76.52)	7 (14.89)		34 (79.07)	9 (24.32)	
Absent	108 (41.70)	31 (23.48)	40 (85.11)		9 (20.93)	28 (75.68)	
Signal intensity				<0.05			0.84
Homogeneous	140 (54.05)	81 (61.36)	15 (31.92)		29 (67.44)	15 (40.54)	
Heterogeneous	119 (45.95)	51 (38.64)	32 (68.08)		14 (32.56)	22 (59.46)	
Enhancement pattern				0.60			<0.05
Early arterial enhancement with early washout	165 (63.71)	87 (65.91)	21 (44.68)		34 (79.07)	23 (62.16)	
Peritumoral enhancement	63 (24.32)	21 (15.91)	21 (44.68)		8 (18.61)	13 (35.14)	
Rim enhancement	13 (5.02)	9 (6.82)	2 (4.26)		1 (2.32)	1 (2.70)	
Asynchronous enhancement	18 (6.95)	15 (11.36)	3 (6.38)		0 (0.00)	0 (0.00)	
The presence of tumor pseudocapsule				0.18			<0.05
Absent	198 (76.45)	110 (83.33)	43 (91.49)		21 (48.84)	24 (64.87)	
Present	61 (23.55)	22 (16.67)	4 (8.51)		22 (51.16)	13 (35.13)	

Data are presented as n (%), mean ± SD, or median [IQR], as appropriate. AFP, alpha-fetoprotein; ALB, albumin; ALP, alkaline phosphatase; ALR, alkaline phosphatase-to-lymphocyte ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA125, cancer antigen 125; CA199, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CEUS, contrast-enhanced ultrasound; cHCC-CC, combined hepatocellular-cholangiocarcinoma; CUS, conventional ultrasound; GGT, gamma-glutamyl transferase; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma; IQR, interquartile range; MR, magnetic resonance (imaging); MVI, microvascular invasion; MVI−/MVI+, MVI negative/positive; N, neutrophil count; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PLT, platelet count; Pt, prothrombin time; Scr, serum creatinine; SD, standard deviation; TB, total bilirubin.