

Supplementary methods

MRI hallmarks

The major features of LI-RADS (version 2018) (24,25) were as follows: (I) tumor size, the longest axis diameter measured on HBP images; (II) enhancing capsule, an uniform, thin, smooth, linear and enhanced border surrounded most or all of the tumor on PVP or TP images; (III) non-peripheral washout, defined as non-peripheral hypoenhancement on PVP images as the result of the reduction of tumor enhancement from earlier to later phase; (IV) non-rim arterial phase hyperenhancement (APHE), defined as nonrim-like enhancement in arterial phase unequivocally greater in whole or in part of tumor than liver. Furthermore, the algorithms of LI-RADS categories were calculated by the above major features.

Some ancillary features of LI-RADS (24) were as below: (I) intratumoral necrosis, (II) intratumoral hemorrhage, (III) intratumoral fat deposition; (IV) targetoid architecture is defined as rim APHE, peripheral washout, delayed central enhancement, targetoid restriction on DWI, or targetoid appearance on TP or HBP; (V) nodule in nodule architecture, defined as the presence of smaller inner nodule within and having architecture different imaging features than larger outer nodule; (VI) mosaic architecture is defined as the presence of randomly distributed internal nodules or compartments, usually with different imaging features; (VII) hypointensity of tumor on HBP images.

Non-LI-RADS morphologic hallmarks comprised the presence or absence of: (I) non-smooth tumor margin; (II) peritumoral enhancement is defined as an enhancement region adjacent to tumor boundary in arterial phase images, which became isointense with the background liver parenchyma on PVP or TP images (26); (III) peritumoral hypointensity presented as an irregular, wedge-shaped, or flame-like hypointense area of liver parenchyma located outside of the tumor margin on HBP images (26); (IV) ascites.

Sample size calculation

The sample size was estimated by the log-rank test (Lakatos: median survival time). The parameters of Lakatos were set as below: α (significance level), $1-\beta$ (power), the sample proportion of MVI-positive group, accrual time and follow-up time were 0.05, 0.90, 0.25, 96 and 103 months, respectively.

Based on the previous study (6), the median RFS of MVI was 9.2 months and that of non-MVI was 46.7 months. Hence, the sample size needs to be satisfied with ≥ 23 , ≥ 9 and ≥ 14 in the overall, MVI-positive, and MVI-negative datasets, respectively.

In terms of our study population, the median RFS of MVI-positive and MVI-negative cohorts before PSM were 43.0 and 85.4 months, respectively. The corresponding sample sizes were 212 in total, 82 in MVI and 130 in non-MVI cases.

Generally, our sample sizes basically meet the statistical requirements: 441 subjects in the total population (>212 and >23 calculated patients), 79 patients in the MVI-positive dataset (>9 but slight less than 82 calculated MVI HCCs), and 171 cases in the MVI-negative group (>14 and >130 calculated non-MVI HCCs).

Table S1 Parameters of MRI sequences

Parameters	TR (millisecond)	TE (millisecond)	Bandwidth (Hz/pixel)	FOV (mm)	Matrix	Section thickness (mm)	Acquisition time (second)
Respiratory-triggered T2-weighted imaging	4,918	106	195	285×380	384×273	5.5	Respiration-dependent
Free-breathing DWI [†]	5,100	55	1565	285×380	192×154	5.5	74
Breath-hold T1-weighted in-phase and opposed-phase imaging	6.88	2.39/4.77	435	356×380	320×240	3.5	18
Breath-hold T1-weighted VIBE imaging	3.47	1.36	400	308×380	320×240	3	15

[†], DWI was performed with b values of 0 and 500 sec/mm². TR, repetition time; TE, echo time; BW, bandwidth; FOV, field of view; DWI, diffusion-weighted Imaging; VIBE, volumetric interpolated breath-hold examination.

Table S2 Clinicopathologic and imaging characteristics of 455 eligible patients for MVI prediction in cohorts

Variables	Training cohort			Validation cohort			Test cohort		
	MVI- (n=230)	MVI+ (n=58)	P	MVI- (n=102)	MVI+ (n=21)	P	MVI- (n=37)	MVI+ (n=7)	P
Age, mean ± SD, year	54.5±11.15	55.4±9.64	0.608 [†]	54.8±12.24	52.4±9.86	0.398	55.6±11.46	53.3±13.93	0.639
Female/Male	27/203	10/48	0.263	22/80	2/19	0.334 [§]	9/28	1/6	0.929 [§]
Size (cm, mean ± SD)	1.6±0.62	2.0±0.56	<0.001 [†]	1.6±0.65	2.1±0.60	0.005 [†]	1.0±0.76	1.0±0.82	0.706 [†]
≤1/1–2/>2 cm	62/128/40	4/28/26	<0.001	26/50/26	2/7/12	0.014	10/16/11	2/3/2	0.996
ES (I–II/III–IV)	150/80	25/33	0.002	68/34	13/8	0.675	31/6	3/4	0.060 [§]
Cirrhosis [†]	77/153	16/42	0.391	41/61	8/13	0.858	12/25	2/5	0.100 [§]
Ki-67 (%)	23.4±16.85	31.2±21.12	0.012 [†]	24.3±20.60	35.3±23.81	0.035 [†]	31.1±24.15	55.7±31.55	0.089 [†]
HBV or HCV [†]	29/201	6/52	0.637	42/60	8/13	0.793	10/27	1/6	0.812 [§]
HBV-DNA (≤10 ⁴ / ^{>} 10 ⁴)	168/62	36/22	0.100	74/28	15/6	0.917	27/10	3/4	0.260 [§]
Multifocality [†]	202/28	45/13	0.046	84/18	17/4	1.000 [§]	31/6	7/0	0.585 [§]
Anatomical resection [†]	207/23	50/8	0.405	92/10	18/3	0.827 [¶]	34/3	6/1	0.513 [§]
AFP (≤20/20–400/>400 ng/mL)	140/68/22	22/26/10	0.006	60/35/7	12/6/3	0.506	24/12/1	4/1/2	0.039
TBIL (≤20.4/>20.4 μmol/L)	203/27	49/9	0.437	82/20	14/7	0.274 [§]	29/8	7/0	0.409 [§]
DBIL (≤20.4/>20.4 μmol/L)	183/47	43/15	0.369	85/17	14/7	0.146 [§]	35/2	7/0	1.000 [¶]
ALB (>35/≤35 g/L)	224/6	58/0	0.466 [§]	99/3	21/0	1.000 [¶]	36/1	6/1	0.296 [§]
ALT (≤50/>50 U/L)	189/41	50/8	0.465	86/16	18/3	1.000 [§]	30/7	6/1	1.000 [§]
AST (≤40/>40 U/L)	179/51	52/6	0.043	82/20	18/3	0.793 [§]	31/6	5/2	0.808 [§]
AKP (≤125/>125 U/L)	212/18	55/3	0.487	97/5	21/0	0.587 [¶]	35/2	6/1	0.413 [¶]
GGT (≤60/>60 U/L)	160/70	47/11	0.083	78/24	13/8	0.166	29/8	6/1	1.000 [§]
PALB (>180/≤180 mg/L)	56/174	12/46	0.558	23/79	2/19	0.177	19/18	5/2	0.572 [§]
PT (≤13/>13 s)	197/33	50/8	0.914	86/16	19/2	0.698 [§]	28/9	5/2	1.000 [§]
Child-Pugh (A/B)	219/11	54/4	0.517	97/5	21/0	0.587	35/2	6/1	0.413 [¶]
Nodule in nodule [†]	217/13	56/2	0.500	96/6	20/1	1.000 [§]	33/4	7/0	1.000 [¶]

Table S2 (continued)

Table S2 (continued)

Variables	Training cohort			Validation cohort			Test cohort		
	MVI- (n=230)	MVI+ (n=58)	P	MVI- (n=102)	MVI+ (n=21)	P	MVI- (n=37)	MVI+ (n=7)	P
Fat deposition [†]	161/69	37/21	0.362	71/31	17/4	0.294	28/9	5/2	1.000 [§]
Necrosis [†]	199/31	41/17	0.004	84/18	16/5	0.725 [§]	29/8	6/1	1.000 [§]
Hemorrhage [†]	200/30	51/7	0.843	86/16	18/3	1.000 [§]	31/6	7/0	0.568 [¶]
Ascites [†]	217/13	54/4	0.962 [§]	99/3	21/0	1.000 [¶]	36/1	7/0	1.000 [¶]
Nonim APHE [†]	50/180	19/39	0.079	21/81	7/14	0.326 [§]	23/14	5/2	0.969 [§]
Mosaic architecture [†]	227/3	57/1	1.000 [¶]	10/2	20/1	0.433 [¶]	35/2	7/0	1.000 [¶]
Targetoid [†]	209/21	56/2	0.248 [§]	95/7	18/3	0.487 [§]	30/7	5/2	0.944 [§]
HBP hypointensity [†]	6/224	2/56	1.000 [§]	3/99	1/20	0.532 [¶]	4/33	0/7	1.000 [¶]
Non-smooth margin [†]	154/76	10/48	<0.001	72/30	5/16	<0.001	28/9	0/7	0.001 [§]
Non-peripheral washout [†]	28/202	5/53	0.448	14/88	2/19	0.869	6/31	0/7	0.568 [¶]
LI-RADS (3/4/5)	17/67/146	5/19/34	0.790	7/27/68	2/6/13	0.879	6/15/16	0/2/5	0.311
Enhancing capsule (intact/incomplete/absent)	163/26/41	10/28/20	<0.001	73/14/15	5/5/11	<0.001	22/4/11	0/4/3	0.003
Peritumoral enhancement [†]	183/47	22/36	<0.001	86/16	9/12	<0.001	32/5	4/3	0.190 [§]
Peritumoral hypointensity [†]	200/30	35/23	<0.001	95/7	15/6	0.011	2/2	5/1	0.118 [§]

[†], absent/present; [‡], Mann-Whitney U test; [§], Fisher's test; [¶], continuity correction. The other categorical variables, Chi-square test; the other numeric variables, independent samples *t*-test. MVI, microvascular invasion; PSM, propensity score matching; ES, Edmondson-Steiner grade; HBV, hepatitis B virus; HCV, hepatitis C virus; HBV-DNA, deoxyribonucleic acid of hepatitis B virus; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; AKP, alkaline phosphatase; GGT, γ -glutamyl transpeptidase; ALB, albumin; PALB, prealbumin; PT, prothrombin time; APHE, arterial phase hyperenhancement; HBP, hepatobiliary phase; LI-RADS, Liver Imaging Reporting and Data System.

Table S3 Baseline characteristics for predicting postoperative recurrence and mortality

Variables	Pre-PSM cohort (n=411)						After-PSM cohort (n=241)		
	Non-relapse (n=273)	Relapse (n=138)	P value	Non-mortality (n=375)	Mortality (n=36)	P value	Non-relapse (n=148)	Relapse (n=93)	P value
MVI [†]	40/233	39/99	0.001	68/307	11/25	0.071	36/112	34/59	0.042
Age (year; mean ± SD)	53.7±11.38	56.30±10.51	0.021 [‡]	54.09±11.10	59.61±10.51	0.002 [‡]	54.57±11.21	56.85±10.03	0.921
Male/ Female	234/39	116/22	0.656	321/54	29/7	0.416	133/15	78/15	0.170
Size (cm; mean ± SD)	1.59±0.62	1.79±0.67	0.003 [‡]	1.64±0.62	1.91±0.77	0.049 [‡]	1.82±0.58	1.94±0.61	0.113 [‡]
ES (III–IV/I–II)	92/181	63/75	0.018	136/239	19/17	0.051	49/99	44/49	0.027
Cirrhosis [†]	181/92	88/50	0.610	245/130	24/12	0.872	93/55	60/33	0.792
Ki-67 (%)	24.51±18.38	26.94±20.43	0.366 [‡]	24.93±18.84	29.50±21.50	0.201 [‡]	26.98±19.27	27.35±19.91	0.882 [‡]
ERASL-pre risk (intermediate/low risk)	3/270	4/134	0.353 [§]	5/370	2/34	0.118 [¶]	2/146	2/91	1.000 [§]
ERASL-post risk (intermediate/low risk)	8/265	7/131	0.274	12/363	3/33	0.270 [§]	7/141	5/88	1.000 [§]
TNM (T1a/T1b/T2 stage)	191/32/50	78/17/43	0.010	251/43/81	18/6/12	0.124	88/26/34	47/15/31	0.207
BCLC (0/A/B stage)	188/83/2	75/61/2	0.014	246/126/3	7/18/1	0.062	88/59/1	46/46/1	0.310
HBV or HCV [†]	211/62	115/23	0.153	299/76	27/9	0.503	129/19	74/19	0.115
HBV-DNA (>10 ⁴ /≤10 ⁴)	75/198	43/95	0.438	103/272	15/21	0.072	44/104	33/60	0.351
Multifocality [†]	35/238	28/110	0.047	56/319	7/29	0.473	21/127	20/73	0.141
Anatomical hepatectomy [†]	29/244	15/123	0.939	37/338	7/29	0.135 [§]	14/134	8/85	0.822
AFP (≤20/20–400/>400 ng/mL)	157/89/27	77/46/15	0.929	215/123/37	19/12/5	0.725	88/45/15	54/29/10	0.975
TBIL (>20.4/≤20.4 μmol/L)	43/230	20/118	0.738	60/315	3/33	0.223	20/128	14/79	0.738
DBIL (>20.4/≤20.4 μmol/L)	54/219	32/106	0.422	77/298	9/27	0.529	28/120	22/71	0.377
ALB (>35/≤35 g/L)	5/268	4/134	0.485	8/367	1/35	1.000 [§]	2/146	2/91	0.636
ALT (>50/≤50 U/L)	43/230	25/113	0.542	60/315	8/28	0.337	24/124	17/76	0.678
AST (>40/≤40 U/L)	52/221	28/110	0.764	71/304	9/27	0.380	29/119	20/73	0.720
AKP (>125/≤125 U/L)	17/256	9/129	0.908	21/354	5/31	0.111 [§]	8/140	8/85	0.332
GGT (>60/≤60 U/L)	69/204	44/94	0.156	101/274	12/24	0.411	39/109	34/59	0.093
PALB (≤250/>250 mg/L)	203/70	115/23	0.040	287/88	31/5	0.190	110/38	81/12	0.017
PT (>13/≤13 s)	40/233	19/119	0.809	55/320	4/32	0.561	23/125	17/76	0.578
ALBI grade (2/1)	46/227	24/114	0.890	40/233	6/23	0.556 [§]	28/120	16/77	0.737
Child-Pugh (B/A)	11/262	9/129	0.267	18/357	2/34	1.000 [§]	8/140	6/87	0.735
Nodule in nodule [†]	15/258	7/131	0.858	22/353	0/36	0.269 [§]	9/139	5/88	0.820
Fat deposition [†]	81/192	44/94	0.645	115/260	10/26	0.719	50/98	31/62	0.943
Necrosis [†]	48/225	23/115	0.817	63/312	8/28	0.411	34/114	14/79	0.134
Hemorrhage [†]	31/242	25/113	0.059	47/328	9/27	0.067 [§]	17/131	17/76	0.140
Ascites [†]	11/262	9/129	0.267	16/359	4/32	0.156 [§]	7/141	6/87	0.565

Table S3 (continued)

Table S3 (continued)

Variables	Pre-PSM cohort (n=411)						After-PSM cohort (n=241)		
	Non-relapse (n=273)	Relapse (n=138)	P value	Non-mortality (n=375)	Mortality (n=36)	P value	Non-relapse (n=148)	Relapse (n=93)	P value
Non-rim APHE [†]	215/58	99/39	0.114	289/86	25/11	0.304	111/37	70/23	0.963
Mosaic architecture [†]	7/266	0/138	0.135 [§]	7/368	0/36	1.000 [¶]	4/144	0/93	0.280 [§]
Targetoid [†]	20/253	13/125	0.461	27/348	6/30	0.094 [§]	13/135	9/84	0.815
HBP hypointensity [†]	264/9	135/3	0.743 [§]	363/12	36/0	0.568 [§]	143/5	92/1	0.264
Non-smooth margin [†]	100/173	70/68	0.006	146/229	24/12	0.001	63/85	49/44	0.125
Non-peripheral washout [†]	242/31	120/18	0.618	328/47	34/2	0.335 [§]	133/15	83/10	0.878
LI-RADS (LR-3/4/5)	19/78/176	12/41/85	0.769	28/108/239	3/11/22	0.950	9/47/92	6/26/61	0.823
Capsule enhancement (absent/incomplete/intact)	50/41/182	37/32/69	0.005	77/60/238	10/13/13	0.002	29/28/91	28/25/40	0.019
Peritumoral enhancement [†]	61/212	50/88	0.003	91/284	20/16	<0.001	43/105	40/53	0.026
Peritumoral hypointensity [†]	34/239	32/106	0.005	53/322	13/23	0.001	25/123	25/68	0.063

[†], present/absent; [‡], Mann-Whitney U test; [§], Continuity correction; [¶], Fisher's test; the other numeric variables, independent samples *t*'-test; the other categorical variables, Chi-square test. MVI, microvascular invasion; PSM, propensity score matching; ES, Edmondson-Steiner grade; HBV, hepatitis B virus; HCV, hepatitis C virus; HBV-DNA, deoxyribonucleic acid of hepatitis B virus; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; AKP, alkaline phosphatase; GGT, γ -glutamyl transpeptidase; ALB, albumin; PALB, prealbumin; PT, prothrombin time; APHE, arterial phase hyperenhancement; HBP, hepatobiliary phase; LI-RADS, Liver Imaging Reporting and Data System.