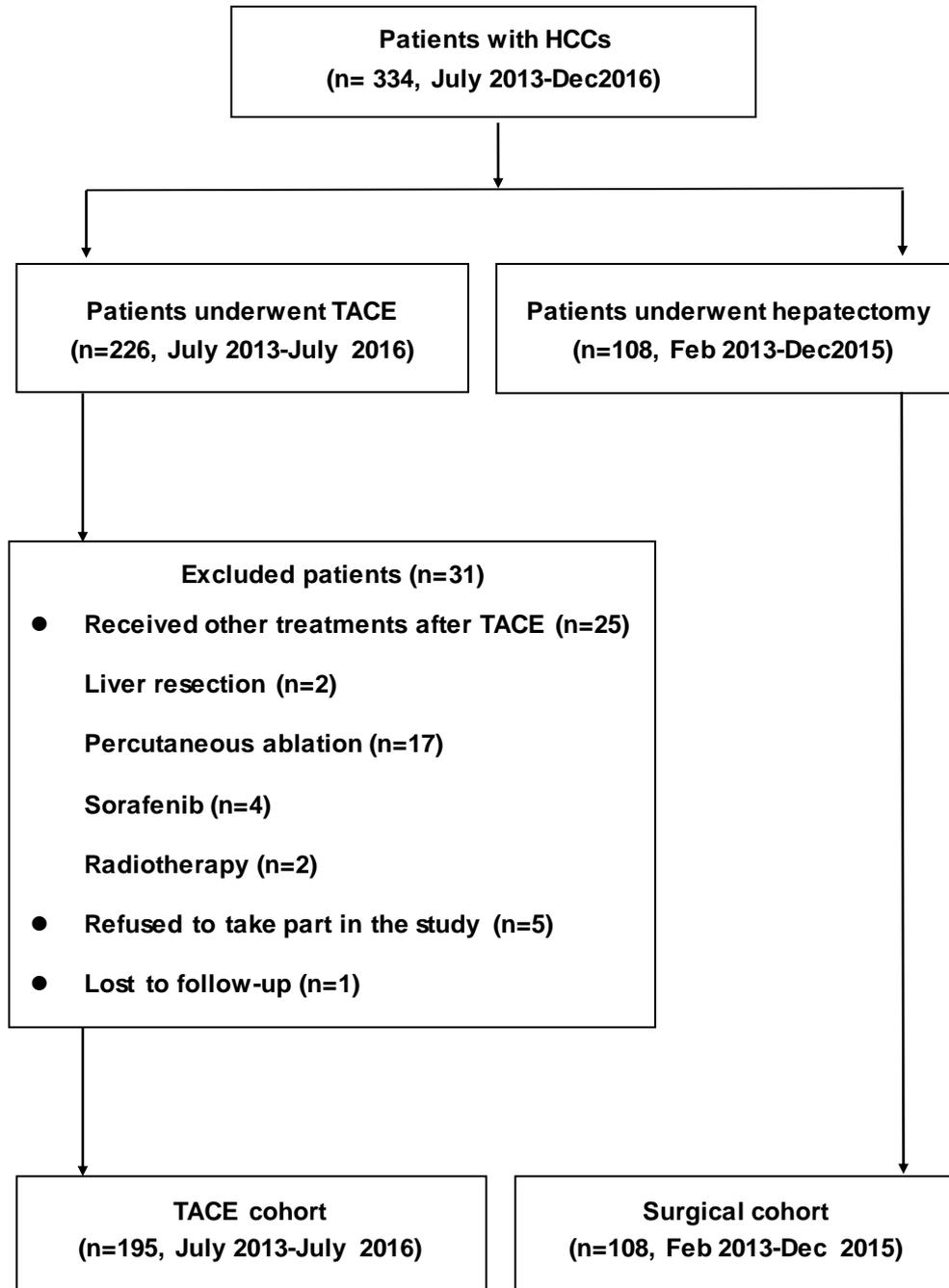
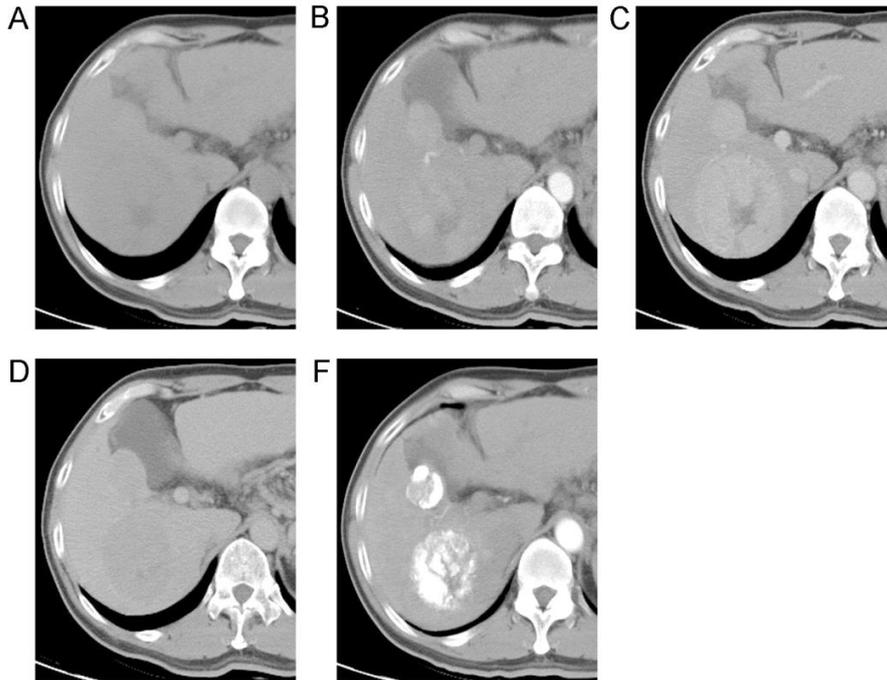


Supplementary Data

Supplementary Figure 1. Flow diagram of patients' inclusion

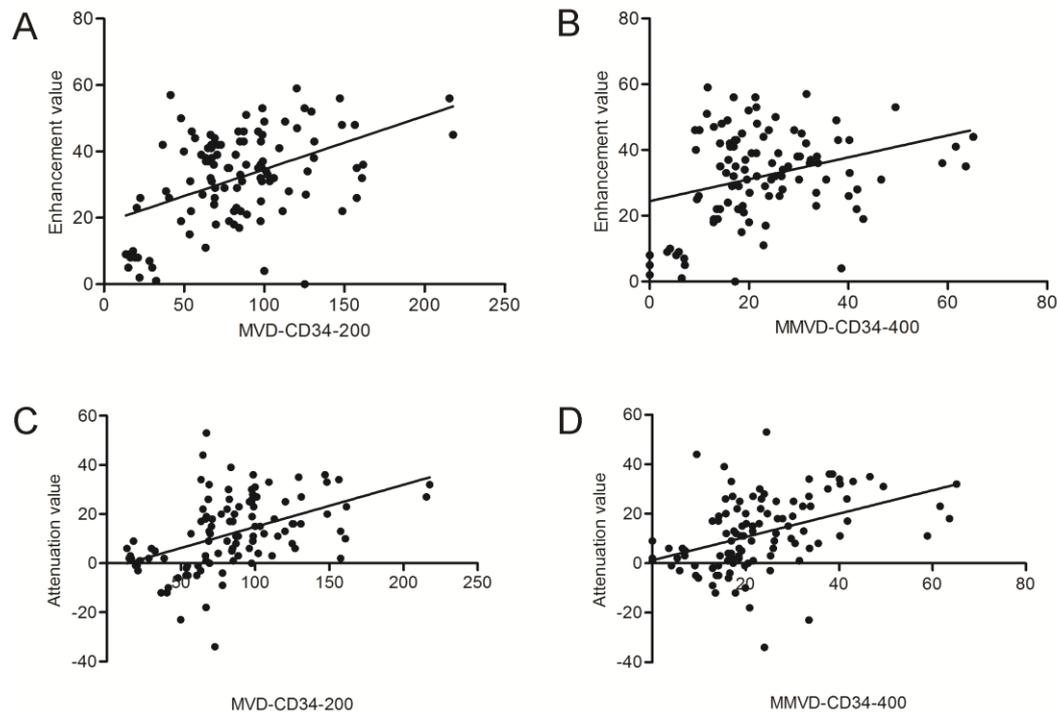




Supplementary Figure 2. The pattern of tumor enhancement and attenuation on CT scan and the filling of lipiodol in nodules of the patient with multiple HCCs

Shown are the CT scan images of a 42-year-old male patient with type I HCC who received one session of TACE. Except for the central necrosis region of the tumor, similar patterns of tumor enhancement and attenuation were found in the two tumor nodules. The pattern of lipiodol retained in the tumor was similar to that of tumor enhancement.

A, B, C, D showed the images of the four sequential phases of CT scan, indicating a marked contrast enhancement on the arterial and portal venous phases and washout of contrast medium on the delay phase. F indicated lipiodol retention in tumors one month after TACE.

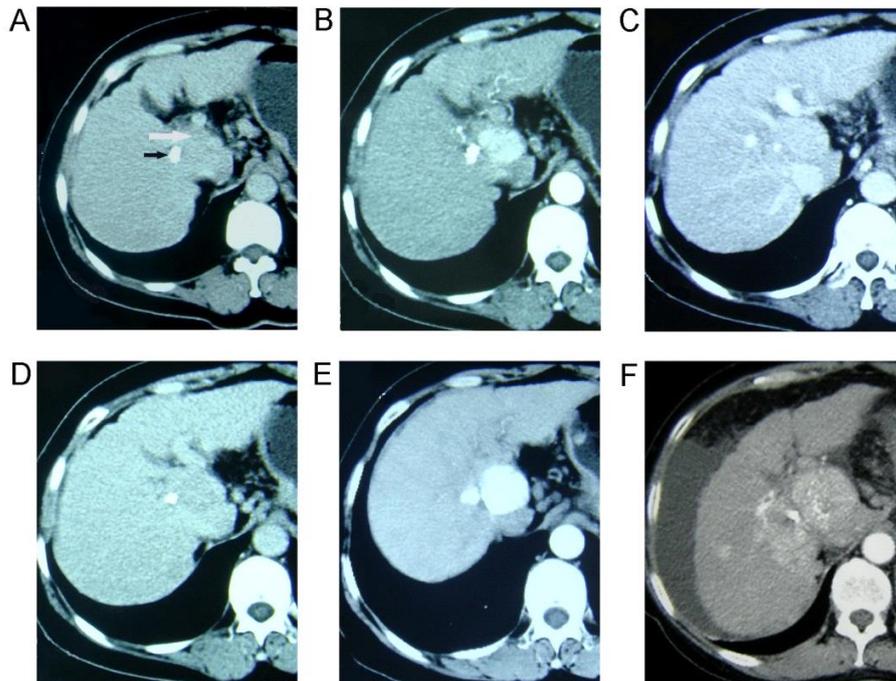


Supplementary Figure 3. Association of MVD and MMVD with the characteristics of HCC on CT scan

MVD (A) and MMVD (B) are correlated with tumor enhancement on CT scan, showing Pearson $r=0.463$ and 0.313 as well as $p<0.0001$ and $p=0.001$, respectively.

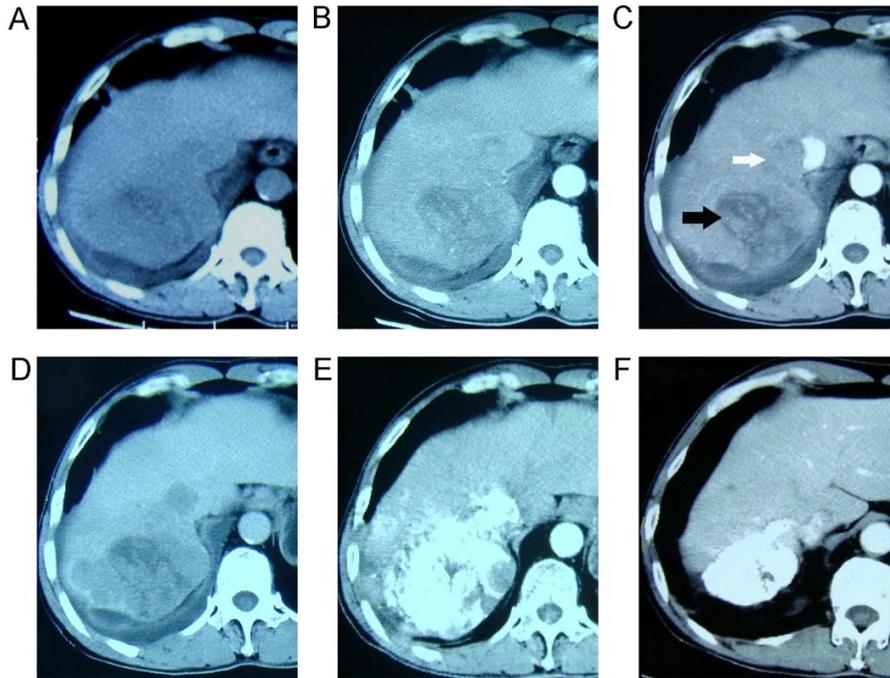
MVD (C) and MMVD (D) are correlated with tumor attenuation on CT scan, showing Pearson $r=0.467$ and 0.416 , respectively, as well as $p<0.0001$.

X: The values of MVD-CD34-200 (A, C) and MMVD-CD34-400 (B, D); Y: Differences in CT values between the pre-contrast phase and the point of peak enhancement (A, B) and between the point of peak enhancement and the delay phase (C, D).



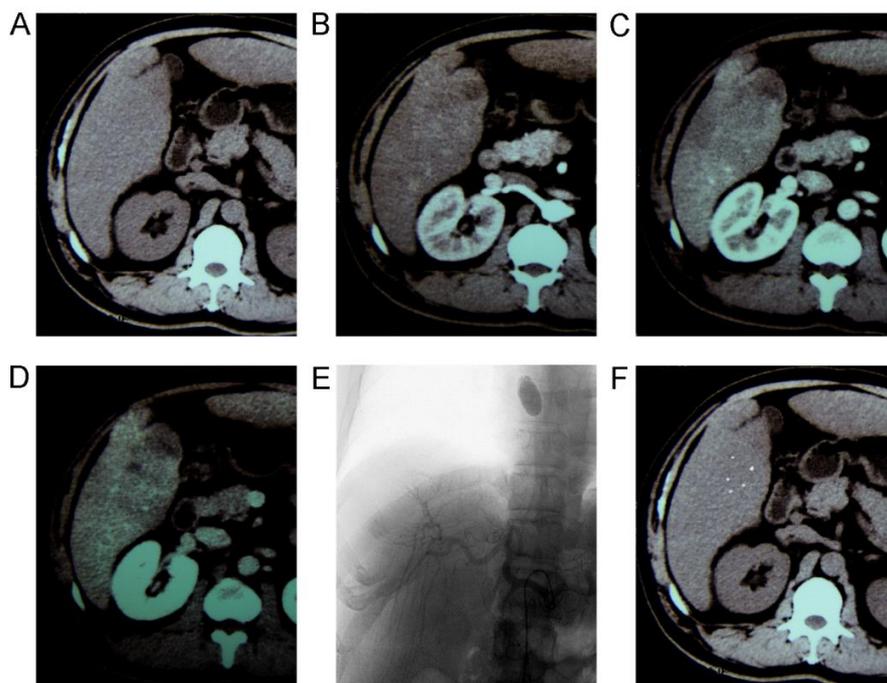
Supplementary Figure 4. Characteristics of type I HCC on CT scan before and after TACE

Shown are the CT scan images of a 65-year-old female patient with type I HCC who received one session of TACE. A: Precontrast phase, the white arrow indicates a 2.9 cm × 2.7 cm tumor in the caudate lobe; the black arrow indicates a 0.9 cm × 0.8 cm calcification. B: Arterial phase, the tumor was enhanced locally and markedly. C and D: Portal venous and delay phase, the local enhancement were decreased significantly. E: One month after TACE, the tumor was completely filled with lipiodol, suggesting CN of the tumor. F: 6 months after TACE, lipiodol was completely washed out, accompanied with tumor progression and ascites occurrence.



Supplementary Figure 5. Characteristics of type II HCC on CT scan before and after TACE

Shown are the CT scan images of a 63-year-old male patient with type II HCC who received one session of TACE. A: Precontrast phase, a 9 cm × 8.2 cm tumor located in the right liver. B and C: Arterial and the portal venous phase, the tumor were enhanced locally. D: Delay phase, the tumor was enhanced continually. E: One month after TACE, lipiodol completely retained in the tumor. F: 12 months after TACE, lipiodol retained in the tumor without signs of tumor progression, and the tumor became obviously smaller.



Supplementary Figure 6. Characteristics of type III HCC on CT scan before and after TACE

Shown are the CT scan images of a 40-year-old male patient with type III HCC who received one session of TACE. A: Precontrast phase, a 7.2 cm ×5.3 cm tumor was found in the right posterior section without capsulation; B: Arterial phase, the tumor had almost no enhancement. C and D: The tumor had slight changes of CT values in the portal venous and delayed phases. E and F: The tumor had almost no lipiodol retention in the tumor on DSA and 1 month after TACE. The patient died 3 months after the initial TACE due to tumor progression and liver function decompensation.

Supplementary Table 1. The baseline characteristics of HCC patients who underwent TACE or liver resection

Variable	TACE cohort (n=195) No. of patients (%)	Surgical cohort (n=108) No. of patients (%)
Age, years		
<50	87(44.6)	51(47.2)
≥50	108(55.4)	57(52.8)
Gender		
male	178(91.3)	91(84.3)
female	17(8.7)	17(15.7)
Child-Pugh grade		
A	191(97.9)	108(100.0)
B	4(2.1)	0(0.0)
BCLC stage		
0	0(0.0)	5(4.6)
A	30(15.4)	31(28.7)
B	165(84.6)	72(66.7)
HBsAg		
positive	156(80.0)	51(47.2)
negative	39(20.0)	57(52.8)
HBeAg		
positive	63(32.3)	86(79.6)
negative	132(67.7)	22(20.4)
HBV-DNA load		
<1x10 ³	169(86.7)	90(83.3)
≥1x10 ³	26(13.3)	16(16.7)
TBIL, μmol/L		
<17.1	117(60.0)	59(54.6)
≥17.1	78(40.0)	49(45.4)
Albumin, g/L		
<35	36(18.5)	12(11.1)
≥35	159(81.5)	96(88.9)
ALT, U/L		
<40	92(47.2)	57(52.8)
≥40	103(52.8)	51(47.2)
AST, U/L		
<40	68(34.9)	55(50.9)
≥40	127(65.1)	53(49.1)
AFP, ng/ml		
<400	103(52.8)	60(55.6)
≥400	92(47.2)	48(44.4)
Maximum tumor, cm		
<5	44(22.6)	36(33.3)
≥5	151(77.4)	72(66.7)
Tumor number		
single	119(61.0)	77(71.3)
multiple	76(39.0)	31(28.7)

Categorical variables are presented as numbers and percentages of patients in parentheses.

Supplementary Table 2. Values measured in the four phases of CT scan in the

TACE cohort (n=195)

No.	A	B	C	D	Type	No.	A	B	C	D	Type	No.	A	B	C	D	Type
1	54	60	102	81	I	64	43	54	80	51	I	52	45	65	78		
2	46	61	68	64	I	65	39	36	74	61	I	130	22	43	46	46	II
	58	67	92	69			33	42	68	52		131	35	47	51	62	II
3	44	78	99	87	I	66	33	71	77	59	I	132	42	55	42	65	II
	49	66	86	75		67	31	44	48	42	I	133	24	20	40	45	II
4	46	123	96	67	I	68	50	64	80	77	I		35	36	56	66	
5	43	58	73	66	I	69	48	72	77	75	I	134	41	50	70	70	II
6	53	83	88	75	I	70	57	91	92	25	I	135	54	72	67	84	II
7	41	60	93	85	I		52	82	76	36		136	72	81	92	102	II
8	42	40	69	51	I	71	47	45	87	67	I	137	34	40	50	54	II
9	51	79	106	79			48	66	69	55		138	40	40	45	51	II
	42	55	87	63	I		52	69	75	48		139	36	18	32	62	II
10	51	61	71	67	I	72	51	46	68	47	I	140	36	37	45	47	II
11	40	52	107	64	I	73	21	38	29	33	I	141	58	65	64	71	II
	46	54	96	68		74	15	18	28	23	I	142	36	55	57	76	II
	54	58	88	63			19	22	32	18		143	45	56	58	76	II
12	60	60	78	72	I		20	21	33	24			44	58	79	45	
	49	62	85	68	I	75	60	61	95	83	I	144	43	47	51	54	II
13	50	72	83	75	I		56	65	94	72			42	55	78	45	
	55	74	89	71		76	47	88	86	69	I		40	56	54	65	
14	101	142	123	113	I	77	40	69	80	58	I	145	46	79	86	105	II
15	56	75	89	75	I	78	49	52	80	71	I		42	65	82	88	
	49	68	85	69		79	44	53	76	70	I	146	37	35	68	83	II
16	55	59	90	80	I	80	16	11	26	18	I	147	44	58	67	93	II
	52	62	85	75			22	28	36	22			42	54	69	88	
17	59	38	60	44	I		28	32	42	36		148	60	74	79	84	II
	54	55	68	52		81	40	67	75	64	I	149	47	65	58	86	II
18	48	69	94	79	I		42	75	84	65			45	62	66	78	
19	45	53	83	75	I	82	81	89	100	69	I		42	68	72	95	
20	42	81	82	63	I		82	82	102	75		150	35	43	56	68	II
	41	82	86	60			78	79	98	72		151	41	48	50	64	II
21	32	59	58	58	I	83	43	53	71	64	I	152	49	65	59	66	II
	35	62	59	54		84	51	78	92	80	I	153	42	51	52	75	II
	42	58	72	61		85	57	94	98	88	I	154	49	76	69	85	II
22	46	45	54	49	I	86	47	63	72	70	I		56	68	75	92	
23	34	69	70	62	I		49	62	76	62		155	40	52	67	74	II
	38	52	69	46			39	56	88	54			45	56	72	88	
24	34	59	74	64	I	87	50	59	80	74	I		52	62	66	78	
25	39	65	63	55	I		48	52	78	70		156	47	86	93	95	II
	45	68	72	56			53	54	74	56			49	78	77	98	
	52	76	78	62		88	58	81	94	83	I		45	75	75	88	
26	53	67	71	54	I	89	40	43	73	66	I	157	39	46	68	68	II
	63	69	78	56		90	38	57	68	42	I	158	44	59	77	92	II
27	48	57	98	75	I	91	49	66	97	71	I	159	48	49	62	79	II
	55	65	87	66		92	42	55	106	74	I	160	22	41	37	43	II
28	60	62	88	60	I	93	57	75	84	73	I	161	38	64	78	78	II
	62	68	65	75		94	35	29	63	57	I	162	38	45	55	60	II
	56	69	82	72		95	46	60	82	75	I	163	48	55	60	67	II
29	45	52	63	47	I		42	58	88	65			42	52	62	72	
30	54	83	93	80	I	96	55	38	71	31	I	164	40	46	51	53	II
31	45	67	85	71	I	97	30	43	59	52	I	165	36	40	41	67	II
32	35	35	55	33	I		32	48	75	49		166	51	52	78	84	II
	36	42	58	36			45	56	69	56			45	56	75	82	
	38	44	62	42		98	35	39	57	54	I	167	42	59	72	73	II

33	48	84	92	78	I	99	30	43	108	65	I	41	52	75	75		
34	46	77	89	80	I	100	37	49	32	34	I	38	48	78	89		
	42	72	86	75			38	56	45	32		168	43	51	59	70	II
	41	68	78	68			36	52	38	31		169	46	71	59	75	II
35	57	72	74	48	I	101	44	69	73	66	I	170	56	75	76	83	II
36	49	56	94	81	I	102	48	79	93	59	I	171	40	49	62	68	II
37	64	50	76	66	I	103	55	50	64	37	I		45	62	78	88	
	58	50	78	55		104	54	86	100	67	I		46	56	72	92	
	52	59	82	59		105	48	67	74	54	I	172	49	68	63	69	II
38	49	60	70	69	I	106	47	84	91	71	I		45	75	75	88	
	44	58	76	66		107	51	64	87	64	I	173	52	68	64	73	II
	45	59	78	58			58	62	92	65		174	54	87	89	90	II
39	28	36	26	19	I	108	50	58	49	28	I	175	56	51	77	81	II
	26	38	46	25		109	41	46	65	55	I	176	27	41	40	63	II
40	45	69	69	62	I		46	52	72	59		177	48	69	70	77	II
41	53	64	79	71	I		49	58	78	68			45	75	78	86	
42	42	57	65	60	I	110	45	81	109	83	I		43	66	72	82	
43	39	64	75	65	I		49	68	98	78		178	54	55	90	93	II
	41	62	76	56			52	66	89	56			52	59	88	89	
	44	56	85	64		111	44	55	72	69	I		42	56	82	98	
44	46	65	84	69	I	112	28	44	114	87	I	179	41	49	73	86	II
	42	62	78	52		113	54	75	117	79	I	180	42	39	73	89	II
45	41	33	60	49	I		52	72	108	75			41	46	68	88	
	46	52	48	47		114	37	35	56	49	I	181	42	41	44	47	III
	38	42	44	39			35	39	52	44		182	31	29	25	27	III
46	53	53	85	71	I	115	49	71	81	65	I	183	31	36	35	26	III
47	43	56	73	64	I	116	44	55	83	72	I	184	32	32	26	35	III
48	44	34	58	55	I		41	59	89	70		185	39	34	48	37	III
49	27	61	95	82	I	117	46	88	96	77	I		42	44	46	58	
50	41	61	71	70	I		44	82	92	66			40	48	46	40	
51	45	39	67	59	I	118	47	56	73	74	II	186	60	70	63	64	III
52	30	31	70	69	I	119	36	42	68	70	II	187	33	28	25	33	III
53	51	59	66	56	I	120	41	61	54	71	II		36	32	36	40	
54	51	62	82	68	I	121	40	42	43	58	II		31	33	36	39	
55	52	88	94	65	I		38	44	69	52		188	49	59	58	55	III
56	41	46	65	57	I		44	45	65	55			52	58	60	56	
	46	52	72	62		122	27	33	31	45	II	189	54	61	66	60	III
	52	55	86	72		123	84	103	98	108	II		56	58	62	60	
57	51	79	86	67	I	124	63	82	94	124	II		52	60	56	57	
	45	71	88	62			55	78	85	98		190	26	29	34	34	III
	48	65	78	59			65	82	88	103		191	24	25	27	25	III
58	48	58	86	85	I	125	134	144	162	266	II		29	32	35	36	
59	54	74	83	72	I	126	31	46	70	74	II	192	28	32	33	31	III
60	41	49	87	60	I		35	52	68	79			29	33	35	33	
61	59	76	85	78	I	127	22	37	34	46	II	193	52	48	51	50	III
62	65	71	89	75	I		25	39	42	66		194	27	21	27	25	III
	62	78	92	71		128	47	59	69	74	II		28	28	29	26	
63	31	18	79	76	I	129	46	40	46	65	II	195	41	39	41	43	III

Notes: In the two cohorts, 107 patients with multifocal tumors (total 269 nodules), had great similarity pattern of enhancement and attenuation, with homogeneity of 91.6% (98 of 107 patients , Supplementary Figure 2). Thus, the CT-based prognostic model was mainly determined by the characteristics of the largest nodule in a patient with multiple HCCs.

A, B, C, D showed the four sequential phases of CT scan

A, B, C, D showed the four sequential phases of CT scan

Supplementary Patients and Methods

1. MVD and MVDD assessed by CD34

In the surgical cohort, microvessel density (MVD) and the maximum diameter of the lumen microvessels (MMVD) were evaluated by immunohistochemical (IHC) staining of CD34 using the methods of Weidner et al and Poon et al^{38,39} on the surgical specimens.

Immediately after resection, the central area of the tumor, the areas adjacent to the margin of the tumor, and the adjacent nontumorous liver tissues were collected, sliced to 4 mm thick sections, fixed with formalin, and embedded with paraffin wax. After antigen retrieval using microwave treatment with citrate buffer at a pH of 6.0 for 2 minutes, the section was stained with a monoclonal anti-CD34 antibody (Immunotech, DAKO) at 1/200 dilution to identify the vessels and to evaluate the MVD and the maximum diameter of the lumen microvessels (MMVD).

MVD was assessed independently by two pathologists using the counting method as recommended by Weidner et al and Poon et al. Briefly, the tumorous and non- tumorous tissue sections were scanned at low magnification (40× and 100×) to find the areas that showed the most intense vascularization (hot spots). 5 to 10 fields at 400×magnification (depending on the size of the section) of each section were chosen and captured by an HV-C20A CCD camera (Hitachi, Japan) coupled to a Leica DM-RXA2 microscope (Leica). The mean value of the counted 5-10 fields of the two observers was considered as the MVD of an individual tumor.

MMVD in HCC was defined as the maximum diameter of the microvessel in which the diameter of a lumen could be measured at 400×magnification by CD34

IHC staining. The mean value of the counted 5 -10 fields of the two observers was considered as the MMVD of an individual tumor.

2. Follow-up

The patients who received TACE treatment were followed-up one month after TACE, and then once every 2 months within the first year and once every 3 months thereafter. The follow-up program at each visit included a detailed history and physical examination, serum AFP and liver function tests, HBV immunological indexes and an abdominal ultrasound. A contrast-enhanced CT was performed 1 month after each TACE and then once every 3 or 4 months. Tumor with lipiodol diffusion or with new enhancement areas on CT scan during the follow-up was defined as tumor progression according to the criteria of mRECIST and recorded in detail. Extrahepatic metastasis was diagnosed with CT, MRI, positron emission tomography (PET) or bone scintigraphy.

The endpoints of this study were time to progression (TTP) and overall survival (OS) after TACE. TTP was defined as the interval between the first session of TACE and tumor progression assessed with mRECIST criteria, with lipiodol diffusion or appearance of new enhancement areas in the tumor on CT scan. OS was defined as the interval between the first session of TACE and patient's death or last follow-up.

Patients who received hepatectomy were followed-up one month after discharge

from the hospital, and then once every 2 months within the first 2 years and once every 3 months thereafter. They underwent similar examinations to patients who were treated with TACE as mentioned above. A contrast-enhanced CT/MRI was performed once every 3-6 months or earlier when tumor recurrence was clinically suspected. The diagnostic criterion for tumor recurrence was the appearance of new lesions with the typical radiological features of HCC on two imaging studies, regardless elevation of serum AFP level.