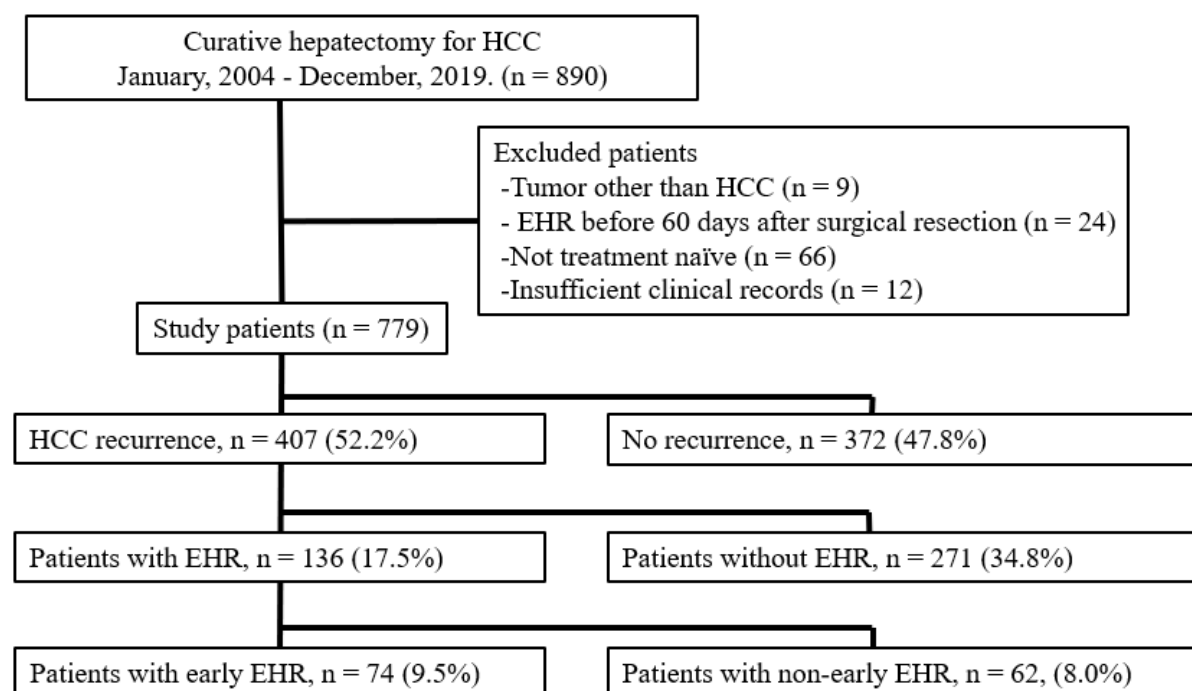


Supplementary Figure 1 Flow chart of the study



HCC: Hepatocellular carcinoma; HER: Extrahepatic recurrence.

Supplementary Table 1 Baseline characteristics of the enrolled patients categorized according to the presence of early extrahepatic recurrence among patients with extrahepatic recurrence

	Patients without EHR (n=643)		Patients with non-early EHR (n=62)		Patients with early EHR (n=74)		P-value	P-value ^a	P-value ^b	P-value ^c
Age (years)	59.66	± 10.12	57.72	± 9.61	56.51	± 10.37	0.019	0.352	0.785	0.040
Male sex (n, %)	547	(85.1)	56 (90.3)		64 (86.5)		0.518	0.262	0.499	0.745
BMI (kg/m ²)	23.95	± 3.06	24.10	± 2.98	23.91	± 3.03	0.268	0.312	0.341	0.922
ALP (U/L)	88.19	± 41.57	100.17	± 63.67	113.23	± 106.76	<0.001	0.239	0.362	0.001
Albumin (mg/dL)	4.38	± 0.45	4.22	± 0.46	4.19	± 0.48	<0.001	0.022	0.946	0.003
ALBI grade ≥ 2, n (%)	85 (13.3)		12 (19.4)		16 (21.9)		0.077	0.188	0.714	0.046
ICG R15	12.12	± 7.30	11.06	± 7.11	12.58	± 7.62	0.505	0.596	0.532	0.896
Preoperative serum AFP >1500 (IU/mL)	56	(9.0%)	5 (8.1%)		18	(24.7%)	<0.001	0.796	0.011	<0.001
Sum of tumor size	4.09	± 2.36	4.96	± 3.06	6.06	± 3.38	<0.001	0.037	0.048	<0.001
Tumor numbers ^d	1.14	± 0.41	1.26	± 0.56	1.32	± 0.63	0.002	0.177	0.762	0.006

BCLC stage, <i>n</i> (%)	15 (2.3)	1 (1.6)	8 (10.8)	<0.001	0.713	0.032	<0.001
Pathological mUICC stage ($\geq$ III), <i>n</i> (%)	139 (21.7)	21 (33.9)	40 (54.1)	<0.001	0.029	0.018	<0.001
Beyond Milan criteria, <i>n</i> (%)	153 (23.8%)	26 (41.9%)	40 (54.1%)	<0.001	0.002	0.159	<0.001
Macrovascular invasion, <i>n</i> (%)	31 (4.9)	1 (1.6)	11 (14.9)	0.001	0.243	0.007	0.001

^a*P*-value = Patients without EHR *vs* Patients with non-early EHR

^b*P*-value = Patients with non-early EHR *vs* Patients with early EHR

^c*P*-value = Patients without EHR *vs* Patients with early EHR

^dNumber of tumors counted during pathological examination.

Values are presented as mean $\pm$ SD.

SD, standard deviation; EHR, extrahepatic recurrence; BMI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase; AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; mUICC, modified Union for International Cancer Control

Supplementary Table 2 Comparison of surgical findings and clinical outcomes in patients with and without extrahepatic recurrence

	Patients without EHR (<i>n</i> =643)	Patients with non- early EHR (<i>n</i> =62)	Patients with early EHR (<i>n</i> =74)	<i>P</i> - value	<i>P</i> - value ^a	<i>P</i> - value ^b	<i>P</i> - value ^c
Margin involvement, <i>n</i> (%)	13 (2.0)	3 (5.0)	4 (5.5)	0.103	0.143	0.902	0.069
Microvascular invasion, <i>n</i> (%)	100 (15.6)	14 (22.6)	33 (44.6)	<0.001	0.158	0.007	<0.001
Serosal invasion, <i>n</i> (%)	10 (1.6)	3 (5.0)	4 (5.4)	0.035	0.064	0.916	0.026
Bile duct invasion, <i>n</i> (%)	6 (1.0)	3 (5.0)	1 (1.4)	0.031	0.008	0.217	0.746
Capsule formation, <i>n</i> (%)	413 (66.2)	43 (71.7)	53 (71.6)	0.475	0.390	0.995	0.348
Multicentricity, <i>n</i> (%)	48 (7.6)	6 (10.0)	8 (10.8)	0.545	0.512	0.879	0.337
Satellite nodule, <i>n</i> (%)	65 (10.3)	19 (31.7)	17 (23.0)	<0.001	<0.001	0.259	0.001
Intrahepatic metastasis, <i>n</i> (%)	6 (1.0)	2 (3.3)	2 (2.7)	0.163	0.100	0.831	0.180
Necrosis, <i>n</i> (%)	253 (40.2)	33 (55.0)	61 (82.4)	<0.001	0.026	<0.001	<0.001
Hemorrhage, <i>n</i> (%)	265 (42.1)	31 (51.7)	46 (62.2)	0.003	0.154	0.222	0.001

Fatty change, <i>n</i>	223	23 (39.0)	15 (20.5)	0.027	0.613	0.020	0.010
(%)	(35.7)						
Major	271	27 (45.0)	41 (56.2)	0.129	0.847	0.200	0.043
Edmondson-	(43.7)						
Steiner grade							
≥3, <i>n</i> (%)							
Worst	508	43 (71.7)	68 (91.9)	0.010	0.093	0.002	0.019
Edmondson-	(80.8)						
Steiner grade							
≥3, <i>n</i> (%)							

^a*P*-value = Patients without EHR *vs* Patients with non-early EHR

^b*P*-value = Patients with non-early EHR *vs* Patients with early EHR

^c*P*-value = Patients without EHR *vs* Patients with early EHR

Supplementary Table 3 Clinical characteristics and outcomes on first recurrence and extrahepatic recurrence categorized by extrahepatic recurrence interval

	Patients non-early (<i>n</i> =62)	with EHR	Patients early EHR (<i>n</i> =74)	<i>P</i> - value
Serum AFP >1,500 (IU/mL) on first recurrence	3 (4.8)		13 (18.3)	0.017
Recurrence-free survival (months, median, range)	21.6 (2.70-100.34)		5.2 (2.04-20.28)	<0.001
mUICC stage ≥ 3 on first recurrence, <i>n</i> (%)	24 (38.7)		56 (75.7)	<0.001
Time to EHR (months, median, range)	58.57 (24.13-146.56)		8.81 (4.07-23.57)	<0.001
EHR on first recurrence	14 (22.6%)		39 (52.7%)	<0.001
mUICC T stage at EHR, <i>n</i> (%)				0.199
0/1	18 (29.0)/4 (6.5)		32 (43.2)/4 (5.4)	
2/3	7 (11.3)/24 (38.7)		7 (9.5)/16 (21.6)	
4	9 (14.5)		15 (20.3)	
Location of extrahepatic recurrence, <i>n</i> (%)				0.145
Lung	41 (66.1)		26 (34.7)	
Solitary/multiple	9 (14.5)/32 (51.6)		4 (5.4)/22 (29.7)	
Bone	12 (19.4)		17 (23.0)	
Lymph nodes	7 (11.3)		22 (29.7)	
Hollow viscus	3 (4.8)		-	
Adrenal gland	3 (4.8)		9 (12.2)	
Peritoneum	11 (17.7)		11 (14.9)	
Brain	1 (1.6)		1 (1.4)	
Brain	-		-	
Gall bladder	1 (1.6)		-	
Heart	1 (1.6)		1 (1.4)-	
Muscle	2 (3.2)		-	

Spleen	2 (3.2)	-	
Diaphragm	1 (1.6)	-	
Inferior vena cava			
Cause of death			0.483
Liver related	45 (72.6)	55 (74.3)	
Non-liver related	3 (4.8) ^a	1 (1.4)	

EHR, Extrahepatic recurrence; AFP, alpha-fetoprotein; mUICC, modified Union for International Cancer Control

^aTwo patients died due to malignancy (gastric and colon cancer, respectively) and one patient died from pneumonia.