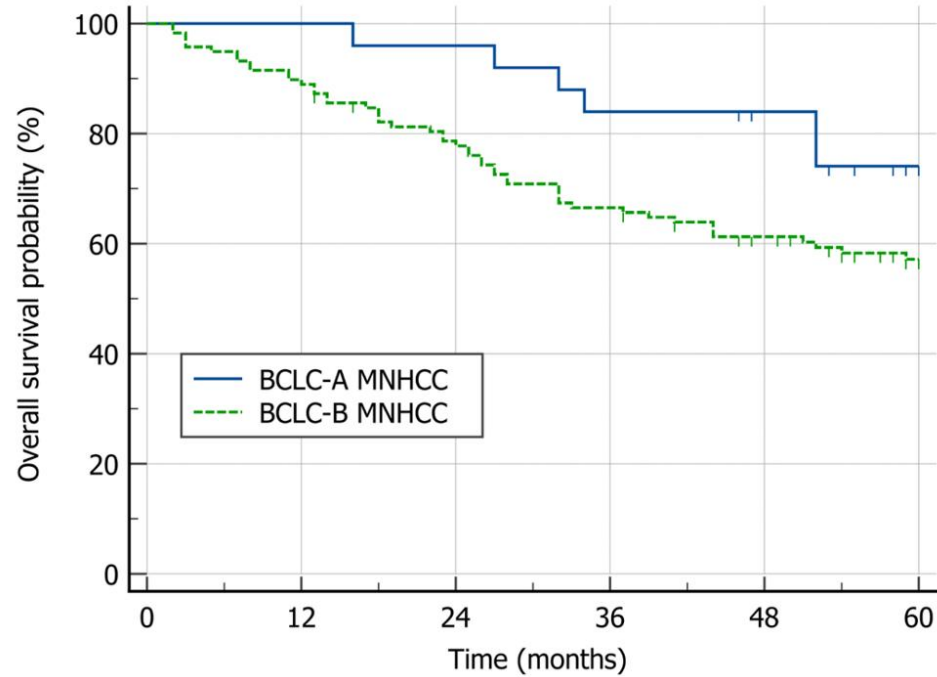
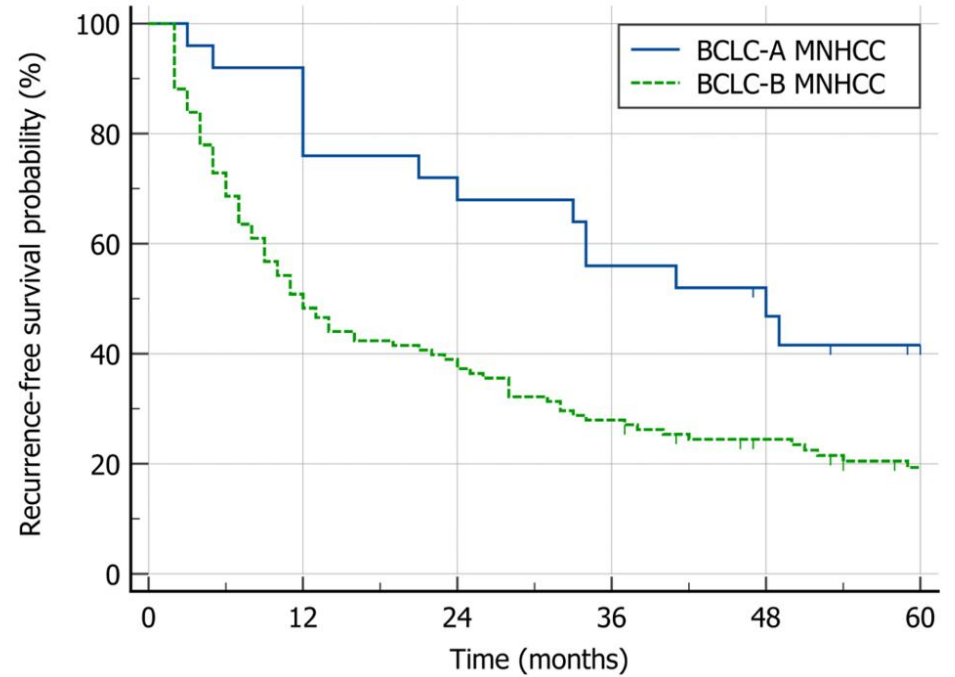
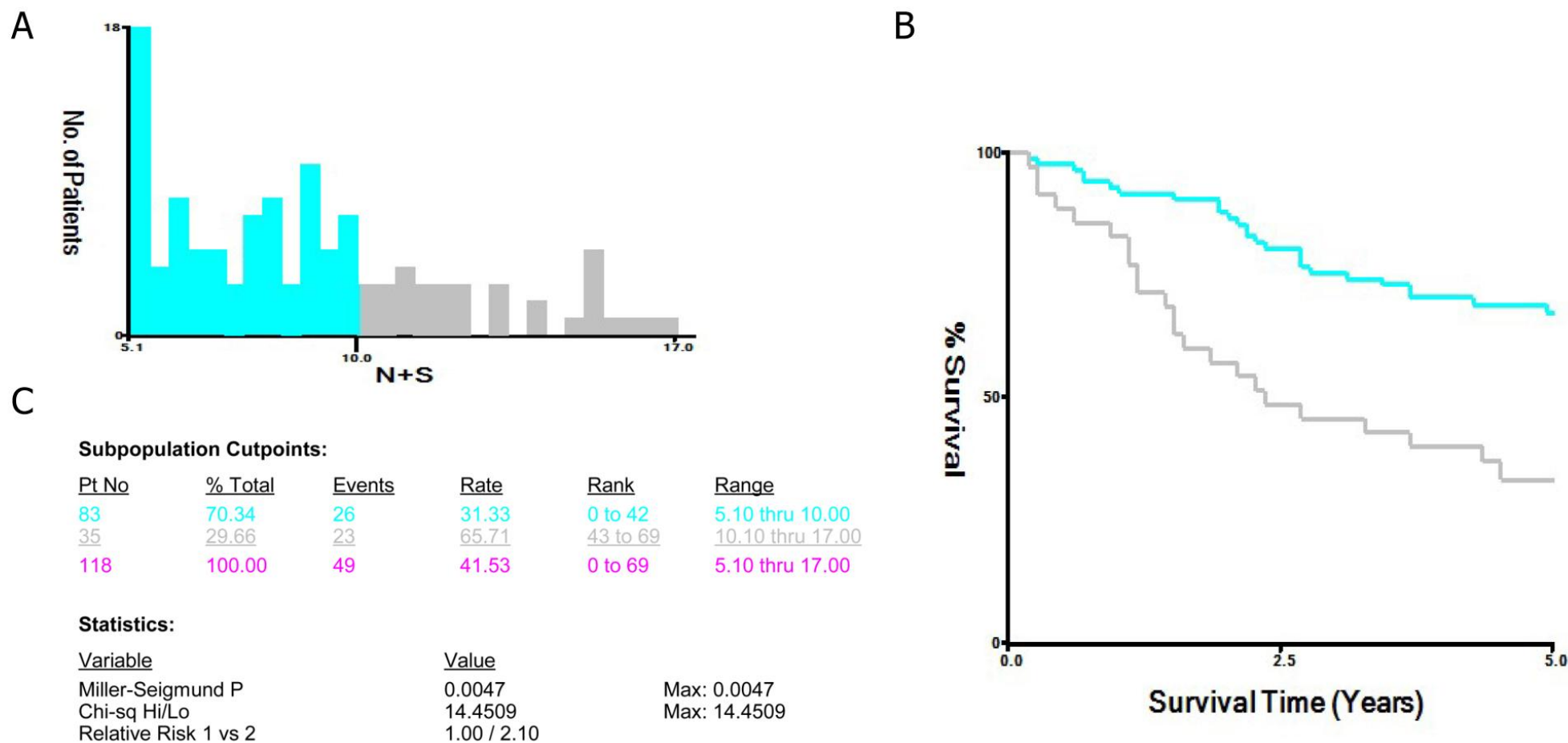


A**B**

Supplementary Figure 1 Kaplan-Meier survival curves for multinodular hepatocellular carcinoma patients by Barcelona Clinic Liver Cancer staging system. A: Overall survival by Barcelona Clinic Liver Cancer (BCLC) stage; B: Recurrence-free survival by BCLC stage. MNHCC: Multinodular hepatocellular carcinoma.



Supplementary Figure 2 Determining the optimal cutoff value of the sum of tumor size and number for predicting overall survival in Barcelona Clinic Liver Cancer stage B patients using X-tile software. A: Bar graph representing population distribution; B: Kaplan-Meier survival curves divided by the sum of tumor size and number (N + S) cutoff; C: Relative risk analysis among subgroups divided by cutoff value of N + S.

Supplementary Table 1 Comparison of the clinical characteristics in multinodular hepatocellular carcinoma patients with Barcelona Clinic Liver Cancer stage A, B1 and B2

Variables	BCLC-A (n = 25)	BCLC-B1 (n = 83)	BCLC-B2 (n = 35)	<i>P</i> value BCLC-B1 versus BCLC-A	<i>P</i> value BCLC-B2 versus BCLC-A	<i>P</i> value BCLC-B1 versus BCLC-B2
Male gender, n (%)	25 (100)	76 (91.6)	33 (94.3)	0.299	0.506	0.898
Age [years, mean (SD)]	50.5 (14.5)	54.2 (12)	48.2 (12.3)	0.197	0.509	0.015
BMI (mean ± SD)	23.05 (3.35)	23.01 (3.29)	22.84 (2.72)	0.952	0.791	0.777
HBs-Ag positive, n (%)	24 (96)	75 (90.4)	32 (91.4)	0.630	0.861	1.000
Albumin [g/L, mean (SD)]	39.95 (5.15)	38.72 (4.42)	38.51 (4.2)	0.246	0.244	0.816
Bilirubin [μmol/L, median (IQR)]	12.9 (10.2, 20.9)	13.4 (9.98, 18.05)	14.9 (8.5, 17.2)	0.590	0.621	0.786
ALBI grade, n (%)				0.585	0.965	0.575
1	13 (52)	38 (45.8)	18 (51.4)			
2/3	12/0 (48/0)	45/0 (54.2/0)	17/0 (48.6/0)			
AFP [μg/L, median (IQR)]	74 (6, 390)	114 (10, 1562)	2092 (161, 13469)	0.114	< 0.001	< 0.001
Maximum tumor size [cm, median (IQR)]	2.5 (2.1, 2.9)	5 (3.8, 6.4)	10.1 (8.8, 12.9)	< 0.001	< 0.001	< 0.001
Tumor number, n (%)				1.000	0.221	0.224
≤ 3	25 (100)	80 (96.4)	31 (88.6)			
> 3	0	3 (3.6)	4 (11.4)			
Tumor distribution, n (%)				0.834	0.023	0.001

Unilateral	16 (64)	55 (66.3)	12 (34.3)			
Bilateral	9 (36)	28 (33.7)	23 (65.7)			
Presence of microvascular invasion, n (%)	1 (4)	8 (9.6)	6 (17.1)	0.630	0.248	0.401
Edmondson-Steiner grade, n (%)				0.420	0.285	0.633
I-II	17 (68)	49 (59)	19 (54.3)			
III-IV	8 (32)	34 (41)	16 (45.7)			
Major resection, n (%)	4 (16)	34 (41)	26 (74.3)	0.022	< 0.001	0.001
Anatomical hepatectomy, n (%)	4 (16)	14 (16.9)	4 (11.4)	1.000	0.898	0.453
Preoperative TACE, n (%)				0.838	0.582	0.550
No	20 (80)	70 (84.3)	31 (88.6)			
Yes	5 (20)	13 (15.7)	4 (11.4)			

BMI: Body mass index; HBs-Ag: Hepatitis B surface antigen; ALBI: Albumin-bilirubin; AFP: Alpha-fetoprotein; TACE: Transarterial chemoembolization.

Supplementary Table 2 Comparison of the recurrence patterns and treatment after recurrence in Barcelona Clinic Liver Cancer stage A, B1 and B2 multinodular hepatocellular carcinoma patients with recurrence

Variables	BCLC-A (n = 14)	BCLC-B1 (n = 57)	BCLC-B2 (n = 30)	<i>P</i> value BCLC-B1 versus BCLC-A	<i>P</i> value BCLC-B2 versus BCLC-A	<i>P</i> value BCLC-B1 versus BCLC-B2
Recurrence time [months, median (IQR)]	22.5 (12, 35.8)	11 (5, 26.5)	6 (2.8, 10.3)	0.108	0.001	0.007
Recurrence within 2-year, n (%)	7 (50)	40 (70.2)	27 (90)	0.265	0.010	0.037
Tumor characteristics at recurrence						
Tumor number >3, n (%)	0	13 (22.8)	8 (26.7)	0.112	0.086	0.689
Maximum tumor size >5 cm, n (%)	1 (7.1)	8 (14)	6 (20)	0.806	0.520	0.680
With macrovascular invasion and/or extrahepatic spread, n (%)				0.686	0.040	0.005
Yes	1 (7.1)	9 (15.8)	13 (43.3)			
No	13 (92.9)	48 (84.2)	17 (56.7)			
Treatment after recurrence, n (%)				0.061	0.010	0.206
Curative treatments	11 (78.6)	29 (50.9)	11 (36.7)			
Noncurative treatments	3 (21.4)	28 (49.1)	19 (63.3)			

BCLC: Barcelona Clinic Liver Cancer

Supplementary Table 3 Univariate and multivariate analysis of recurrence-to-death survival in multinodular hepatocellular carcinoma patients with recurrence

Variables	Univariate analysis		Multivariate analysis	
	HR (95%CI)	P value	HR (95%CI)	P value
Initial tumor with BCLC-A/BCLC-B1	1 (reference)		1 (reference)	
Initial tumor with BCLC-B2	3.144 (1.814-5.449)	< 0.001	2.696 (1.468-4.953)	0.001
Recurrence within 2-year	9.896 (2.407-40.686)	0.001	4.353 (1.024-18.503)	0.046
Recurrent tumor number > 3	4.297 (2.354-7.843)	< 0.001	3.247 (1.629-6.474)	0.001
Maximum recurrent tumor size > 5 cm	2.979 (1.549-5.729)	0.001		
Recurrence with macrovascular invasion and/or extrahepatic spread	6.370 (3.457-11.735)	< 0.001	2.894 (1.458-5.746)	0.002
Noncurative treatments after recurrence	5.040 (2.747-9.248)	< 0.001	2.423 (1.209-4.854)	0.013

BCLC: Barcelona Clinic Liver Cancer.