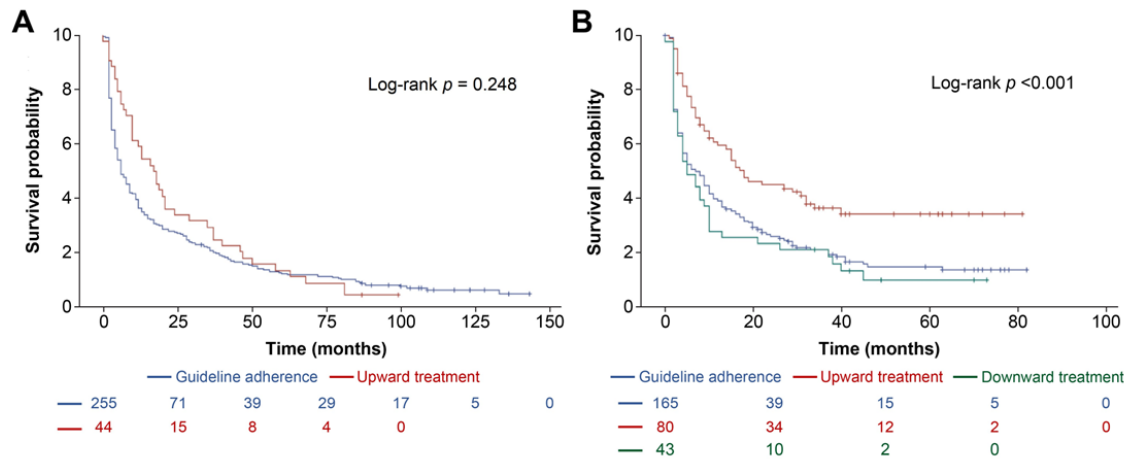


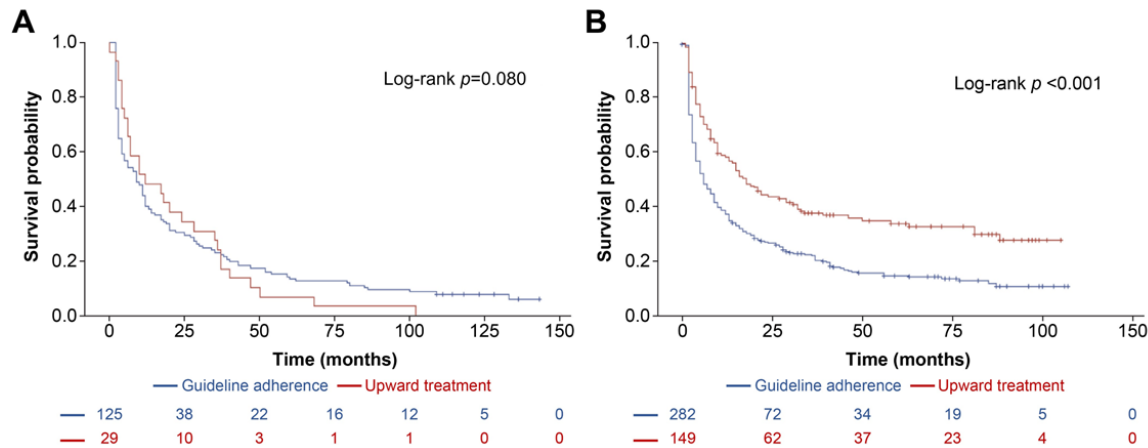
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Supplementary Figure 1 Kaplan-Meier survival curves of hepatocellular carcinoma-related deaths for hepatocellular carcinoma patients according to 2010 Asian Pacific Association for the Study of Liver guideline.



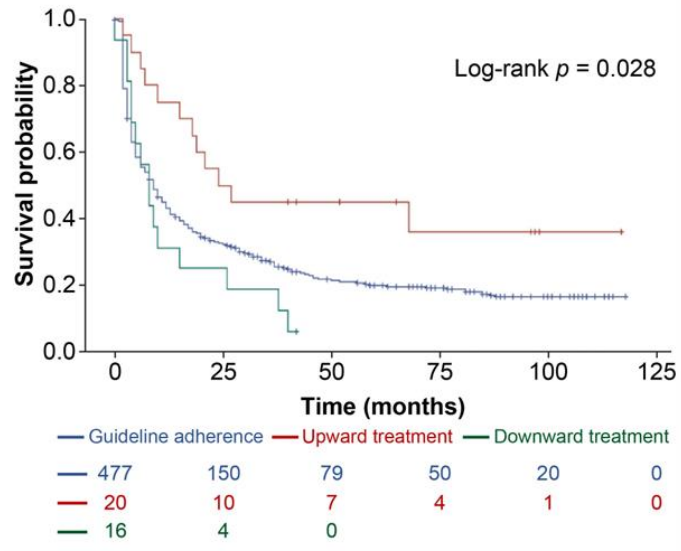
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Supplementary Figure 2 Kaplan-Meier survival curves of progression free survival for hepatocellular carcinoma patients according to European Association for the Study of Liver guideline A: Kaplan-Meier curve of 2008–2012 hepatocellular carcinoma (HCC) patients for progression free survival according to 2000 European Association for the Study of Liver (EASL) guideline; B: Kaplan-Meier curve of 2013–2016 HCC patients for progression free survival according to 2012 EASL guideline.



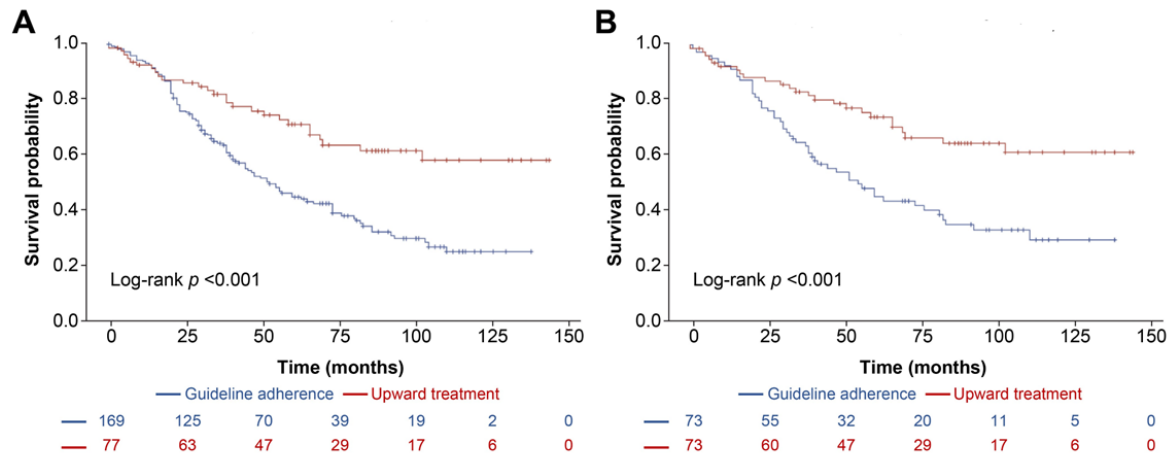
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Supplementary Figure 3 Kaplan-Meier survival curves of progression free survival for hepatocellular carcinoma patients according to American Association for the Study of Liver Diseases guideline. A: Kaplan-Meier curve of 2008–2010 hepatocellular carcinoma (HCC) patients for progression free survival according to 2005 American Association for the Study of Liver Diseases (AASLD) guideline; B: Kaplan-Meier curve of 2011–2016 HCC patients for progression free survival according to 2010 AASLD guideline.



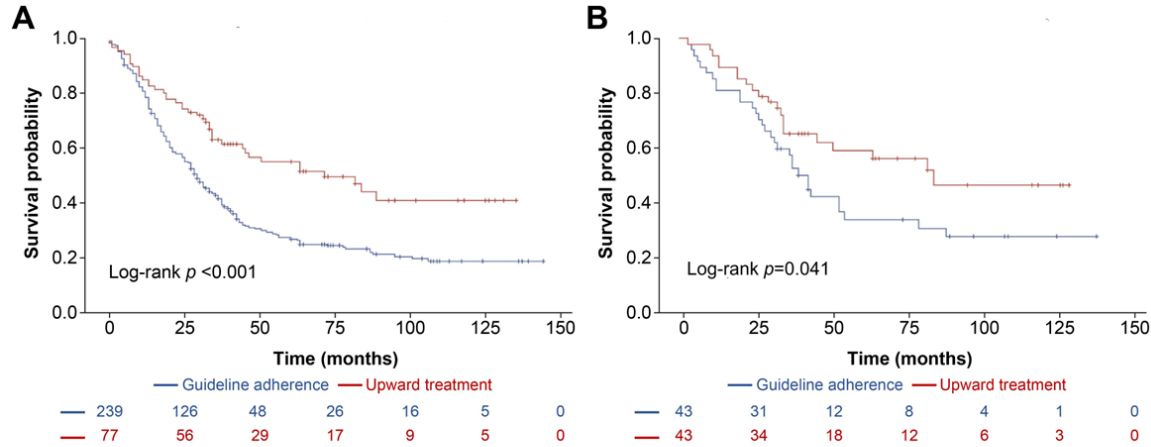
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Supplementary Figure 4 Kaplan-Meier survival curves of progression free survival for 2010-2016 hepatocellular carcinoma patients according to 2010 Asian Pacific Association for the Study of Liver guideline.



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Supplementary Figure 5 Kaplan-Meier curves of hepatocellular carcinoma-related death with propensity score matching according to European Association for the Study of Liver. A: Kaplan-Meier curve of 2008–2016 B1 hepatocellular carcinoma (HCC) patients for HCC-related death according to Barcelona clinic liver cancer subclassification European Association for the Study of Liver (EASL) guideline before propensity score (PS) matching; B: Kaplan-Meier curve of 2008–2016 B1 HCC patients HCC-related death according to EASL guideline after PS matching.



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Supplementary Figure 6 Kaplan–Meier curves of hepatocellular carcinoma-related death with propensity score matching according to Barcelona clinic liver cancer subclassification. A: Kaplan–Meier curve of 2008–2016 B2 hepatocellular carcinoma (HCC) patients for HCC-related death before propensity score (PS) matching; B: Kaplan–Meier curve of 2008–2016 B2 HCC patients HCC-related death after PS matching.

Supplementary Table 1 Hepatocellular carcinoma guideline recommendations for intermediate hepatocellular carcinoma

Curative treatment		Non-curative treatment		
Liver resection	Radiofrequency ablation	Liver transplantation	TACE	Systemic therapy

EASL 2000			Within Milan criteria	One of best evaluated options	
EASL 2012			Beyond Milan and Up to seven	First-line	Under clinical trials combined with TACE
AASLD 2005			Within Milan criteria	First-line	
AASLD 2010			Within Milan criteria	First-line	
APASL 2010	¹ First-line	For small HCC with 3 or fewer nodules	Within Milan criteria and Child-Pugh C	First-line	

AASLD: American Association for the Study of Liver Diseases; APASL: Asian Pacific Association for the Study of Liver; BCLC: Barcelona Clinic Liver Cancer; EASL: European Association for the Study of Liver; TACE: Transarterial chemoembolization.

¹In case of multifocal HCCs confined to the liver: anatomically respectable: And with satisfactory liver function reserve.

Supplementary Table 2 Baseline characteristics of 2010–2016 hepatocellular carcinoma patients according to 2010 Asian Pacific Association for the Study of Liver guideline

Variables	Guideline adherence	Upward treatment	Downward treatment
No. of patients	486	22	22
Age (yr)	61.5 ± 10.5	58.5 ± 6.9	60.7 ± 12.3
Male sex (<i>n</i> , %)	418 (86.0)	21 (95.5)	19 (86.4)
BMI (kg/m ²)	24 ± 3.5	25.3 ± 3.9	21.9 ± 2.4
DM (<i>n</i> , %)	133 (27.4)	5 (22.7)	5 (22.7)
Hypertensive (<i>n</i> , %)	186 (38.3)	8 (36.4)	6 (27.3)
Etiology			
Hepatitis B (<i>n</i> , %)	280 (57.6)	16 (72.7)	16 (72.7)
Hepatitis C (<i>n</i> , %)	66 (13.6)	1 (4.5)	2 (9.1)
Alcohol (<i>n</i> , %)	205 (42.2)	8 (36.4)	8 (36.4)
Ascites (<i>n</i> , %)	48 (9.9)	2 (9.1)	2 (9.1)
Creatinine (mg/dL)	0.9 ± 0.5	0.9 ± 0.2	0.9 ± 0.2
Sodium (mmol/L)	139.0 ± 3.2	139.3 ± 2.7	136.9 ± 3.1
Alanine aminotransferase (IU/L)	46.7 ± 35.9	41.5 ± 24.7	63.3 ± 47.6
Platelet count (10 ⁹ /L)	154.8 ± 72.4	125.4 ± 49.4	208.0 ± 117.9
Serum albumin (g/dL)	3.9 ± 0.6	3.8 ± 0.7	3.8 ± 0.5
Total bilirubin (mg/dL)	1.0 ± 1.0	1.5 ± 1.6	1.0 ± 0.4

INR	1.1 ± 0.1	1.2 ± 0.2	1.1 ± 0.1
Child-Pugh score	5.4 ± 0.8	5.6 ± 1.0	5.6 ± 0.9
MELD score	8.4 ± 2.6	9.5 ± 2.9	8.0 ± 1.6
Alpha-fetoprotein (ng/mL)	2790.6 ± 15389.2	117.7 ± 204.6	5334.9 ± 14179.9
Numbers of tumor	5.2 ± 3.1	3.5 ± 2.3	4.2 ± 1.4
Maximum tumor diameter (cm)	5.1 ± 3.0	5.5 ± 3.5	8.9 ± 4.8

Data are presented as mean ± SD or number (%)

BMI: Body mass index; DM: Diabetes mellitus; INR: International normalized ratio; MELD: Mayo End-Stage Liver Disease.

Supplementary Table 3 Univariate and multivariate cox regression analysis for overall survival in 2010–2016 hepatocellular carcinoma patients according to 2010 Asian Pacific Association for the Study of Liver guideline

Variables	Overall survival			
	Univariate analysis		Multivariate analysis	
	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value
Age (≥ 70 yr)	1.590 (1.260–2.006)	< 0.001	1.648 (1.289–2.106)	< 0.001
Male sex	0.864 (0.644–1.161)	0.333		
BMI (≥ 25 kg/m ²)	0.780 (0.626–0.972)	0.027		
DM	1.049 (0.828–1.329)	0.691		
Hypertension	1.037 (0.835–1.287)	0.744		

Etiology					
Hepatitis B	0.898 (0.724–1.115)	0.330			
Hepatitis C	1.136 (0.843–1.530)	0.404			
Alcohol	1.039 (0.840–1.284)	0.726			
Ascites					
Mild	1.899 (1.324–2.723)	0.001			
Moderate to severe	1.354 (0.698–2.629)	0.370			
Creatinine (> 1 mg/dL)	1.179 (0.919–1.513)	0.196			
Sodium (> 135 mmol/L)	0.592 (0.437–0.804)	0.001			
Alanine					
aminotransferase (> 80 IU/L)	1.013 (0.729–1.409)	0.937			
Platelet count (> 10 ⁵ /μL)	0.754 (0.598–0.951)	0.017	0.726 (0.550–0.958)	0.024	
Serum albumin (≥ 3.5 g/dL)	0.596 (0.467–0.760)	< 0.001			
Total bilirubin (> 1.2 mg/dL)	1.455 (1.148–1.844)	0.002	1.351 (1.034–1.764)	0.027	

INR (> 1.2)	1.514 (1.163–1.971)	0.002	1.438 (1.061–1.949)	0.019
Child-Pugh score (\geq 7)	1.868 (1.347–2.590)	< 0.001		
MELD score (> 9)	1.567 (1.233–1.991)	< 0.001		
Alpha-fetoprotein (\geq 200 ng/mL)	1.458 (1.168–1.820)	0.001		
Numbers of tumor (> 3)	1.778 (1.436–2.202)	< 0.001	2.035 (1.613–2.569)	< 0.001
Maximum tumor diameter				
< 2	Ref			
2–5	0.989 (0.656–1.490)	0.958	1.300 (0.841–2.011)	0.238
5–10	1.547 (1.020–2.344)	0.040	2.275 (1.449–3.572)	< 0.001
>10	3.194 (1.979–5.154)	< 0.001	3.304 (1.925–5.673)	< 0.001
Treatment Guideline adherence				
	Ref			
Upward	0.685 (0.376–1.250)	0.218	0.704 (0.372–1.333)	0.281
Downward	4.181 (2.669–6.549)	< 0.001	3.492 (2.056–5.931)	< 0.001

95%CI: 95%confidence interval; BMI: Body mass index; DM: Diabetes mellitus; HR: Hazard ratio; INR: International normalized

ratio; MELD: Mayo End-Stage Liver Disease.

Supplementary Table 4 Univariate and multivariate cox regression analysis for progression free survival in 2013–2016 hepatocellular carcinoma patients according to 2012 European Association for the Study of Liver guideline

Variables	Progression free survival			
	Univariate analysis		Multivariate analysis	
	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value
Age (≥ 70 yr)	1.241 (0.931–1.655)	0.141	1.019 (1.005–1.033)	0.007
Male sex	0.821 (0.575–1.174)	0.280		
BMI (≥ 25 kg/m ²)	0.856 (0.651–1.125)	0.264		
DM	1.005 (0.751–1.344)	0.976		
Hypertensive	1.04 (0.839–1.289)			
Etiology				
Hepatitis B	0.821 (0.623–1.083)	0.163		
Hepatitis C	1.073 (0.759–1.517)	0.690		
Alcohol	1.032 (0.812–1.312)	0.796		
Ascites				
Mild	1.007 (0.642–1.580)	0.975		
Moderate to severe	1.047 (0.643–3.271)	0.370		

Creatinine (> 1 mg/dL)	1.162 (0.839–1.607)	0.366		
Sodium (> 135 mmol/L)	1.045 (0.694–1.572)	0.834	1.046 (0.996–1.097)	0.071
Alanine aminotransferase (> 80 IU/L)	1.106 (0.739–1.654)	0.624		
Platelet count (> 10 ⁵ /μL)	0.800 (0.596–1.073)	0.137		
Serum albumin (≥ 3.5 g/dL)	0.846 (0.616–1.162)	0.301	0.74 (0.568–0.964)	0.026
Total bilirubin (> 1.2 mg/dL)	1.068 (0.796–1.434)	0.659		
INR (> 1.2)	1.113 (0.772–1.605)	0.565		
Child–Pugh score (≥ 7)	1.170 (0.766–1.787)	0.4685		
MELD score (> 9)	0.943 (0.694–1.281)	0.7084		
Alpha-fetoprotein (≥ 200 ng/mL)	1.114 (0.845–1.470)	0.4428		
Numbers of tumor (> 3)	1.459 (1.120–1.902)	0.0052		
Maximum tumor diameter				
< 2	Ref			
2–5	1.045 (0.646–1.690)	0.859		

5-10	1.071 (0.654-1.752)	0.7855		
>10	1.603 (0.905-2.838)	0.1056		
Treatment				
Guideline adherence	Ref			
Upward	0.691 (0.499-0.956)	0.026	0.648 (0.461-0.909)	0.012
Downward	1.454 (1.014-2.085)	0.042	0.953 (0.657-1.38)	0.797

95%CI: 95%confidence interval; BMI: Body mass index; DM: Diabetes mellitus; HR: Hazard ratio; INR: International normalized ratio; MELD: Mayo End-Stage Liver Disease.

Supplementary Table 5 Univariate and multivariate cox regression analysis for progression free survival in 2011-2016 hepatocellular carcinoma patients according to 2010 American Association for the Study of Liver Diseases guideline

Variables	Progression free survival			
	Univariate analysis		Multivariate analysis	
	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value
Age (≥ 70 yr)	1.585 (1.245-2.018)	< 0.001		
Male sex	0.936 (0.693-1.264)	0.667		
BMI (≥ 25 kg/m ²)	0.769 (0.616-0.960)	0.020		
DM	1.154 (0.908-1.468)	0.241		
Hypertension	0.949 (0.761-1.183)	0.641		

Etiology					
Hepatitis B	0.925 (0.742–1.154)	0.492			
Hepatitis C	1.297 (0.956–1.758)	0.095			
Alcohol	1.098 (0.885–1.363)	0.394			
Ascites					
Mild	1.262 (0.875–1.818)	0.213			
Moderate to severe	1.367 (0.728–2.569)	0.331			
Creatinine (> 1 mg/dL)	1.075 (0.832–1.390)	0.581			
Sodium (> 135 mmol/L)	0.911 (0.647–1.282)	0.593			
Alanine aminotransferase (> 80 IU/L)					
	1.066 (0.766–1.483)	0.706			
Platelet count (> 10 ⁵ /μL)	0.745 (0.588–0.943)	0.015	0.867 (0.664–1.131)		0.294
Serum albumin (≥ 3.5 g/dL)	0.695 (0.540–0.895)	0.005	0.689 (0.511–0.928)		0.014
Total bilirubin (> 1.2 mg/dL)	1.181 (0.923–1.510)	0.185			

INR (> 1.2)	1.309 (0.986–1.737)	0.062			
Child-Pugh score (≥ 7)	1.315 (0.951–1.817)	0.098			
MELD score (> 9)	1.108 (0.859–1.428)	0.431			
Alpha-fetoprotein (≥ 200 ng/mL)	1.088 (0.865–1.369)	0.469			
Numbers of tumor (> 3)	1.615 (1.302–2.004)	<0.001	1.306 (1.033–1.862)		0.002
Maximum tumor diameter					
< 2					
2–5	0.945 (0.642–1.389)	0.773			
5–10	1.043 (0.702–1.550)	0.834			
> 10	1.396 (0.858–2.273)	0.180			
Treatment					
Guideline adherence	Ref				
Upward	0.674 (0.533–0.853)	0.001	0.556 (0.426–0.726)		< 0.001

95%CI: 95%confidence interval; BMI: Body mass index; DM: Diabetes mellitus; HR: Hazard ratio; INR: International normalized ratio; MELD: Mayo End-Stage Liver Disease.

Supplementary Table 6 Univariate and multivariate cox regression analysis for progression free survival in 2010–2016 hepatocellular carcinoma patients according to 2010 Asian Pacific Association for the Study of Liver guideline

Variables	Progression free survival			
	Univariate analysis		Multivariate analysis	
	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value
Age (≥ 70 yr)	1.499 (1.201–1.871)	< 0.001	1.423 (1.129–1.795)	0.003
Male sex	0.992 (0.746–1.318)			
BMI (≥ 25 kg/m ²)	0.794 (0.648–0.973)	0.026		
DM	1.046 (0.838–1.306)	0.691		
Hypertension	0.927 (0.757–1.135)	0.461		
Etiology				
Hepatitis B	0.891 (0.728–1.090)	0.261		
Hepatitis C	1.222 (0.922–1.619)	0.163		
Alcohol	1.141 (0.937–1.389)	0.191		
Ascites				
Mild	1.269 (0.896–1.797)	0.179		
Moderate to severe	1.377 (0.734–2.582)	0.3187		
Creatinine (> 1 mg/dL)	1.053 (0.830–1.336)	0.671		
Sodium (> 135 mmol/L)	0.890 (0.655–1.211)	0.459		

Alanine aminotransferase (> 80 IU/L)	1.107 (0.819-1.496)	0.509		
Platelet count (>10 ⁵ /μL)	0.789 (0.636-0.979)	0.032	0.740 (0.587-0.932)	0.011
Serum albumin (≥ 3.5 g/dL)	0.722 (0.572-0.910)	0.006		
Total bilirubin (> 1.2 mg/dL)	1.146 (0.915-1.437)	0.236		
INR (> 1.2)	1.370 (1.060-1.771)	0.016		
Child-Pugh score (≥ 7)	1.353 (0.995-1.840)	0.054		
MELD score (> 9)	1.098 (0.872-1.382)	0.426		
Alpha-fetoprotein (≥ 200 ng/mL)	1.174 (0.954-1.445)	0.129		
Numbers of tumor (> 3)	1.507 (1.238-1.836)	<0.001	1.638 (1.320-2.031)	< 0.001
Maximum tumor diameter				
< 2	Ref			
2-5	0.989 (0.689-1.418)	0.950	1.285 (0.857-1.926)	0.225
5-10	0.822 (0.803-1.724)	0.357	1.638 (1.078-2.491)	0.021
> 10	1.569 (1.005-2.449)	0.047	1.854 (1.118-3.074)	0.017

Treatment					
Guideline adherence	Ref				
Upward	0.598 (0.336–1.064)	0.080	0.561 (0.313–1.004)	0.052	
Downward	2.923 (1.733–4.931)	< 0.001	1.162 (0.691–1.954)	0.572	

95%CI: 95%confidence interval; BMI: Body mass index; DM: Diabetes mellitus; HR: Hazard ratio; INR: International normalized ratio; MELD: Mayo End-Stage Liver Disease.

Supplementary Table 7 Treatment modalities in B1 hepatocellular carcinoma patients according to European Association for the Study of Liver guideline

	LR	LT	RFA	cTACE	TACE with beads	TARE	Chemotherapy	Radiation therapy	Total
Guideline adherence, <i>n</i> (%)	0	0	0	173 (100)	0	0	0	0	173
Upward treatment, <i>n</i> (%)	55 (70.5)	5 (6.4)	12 (15.4)	0	5 (6.4)	1 (1.3)	0	0	78

Downward									
treatment, <i>n</i> (%)	0	0	0	9 (90)	0	0	1 (10)	0	10

LR: Liver resection; LT: Liver transplantation; RFA: Radiofrequency ablation; cTACE: Conventional transarterial chemoembolization; TARE: Transarterial radioembolization.

Supplementary Table 8 Baseline characteristics of patients with B1 hepatocellular carcinoma between 2008 and 2016 according to European Association for the Study of Liver guideline

Variables	Before PS matching			After PS matching		
	Guideline-adherent	Upward treatment	<i>P</i> value	Guideline-adherent	Upward treatment	<i>P</i> value
No. of patients	169	77		73	73	
Age (yr)	62.1 ± 9.4	58.1 ± 10.6	0.6	62.5 ± 10.2	57.7 ± 10.4	0.006
Male sex (<i>n</i> , %)	130 (80.7)	62 (84.9)	0.47	63(86.3)	62 (84.9)	1
BMI (kg/m ²)	24.2 ± 4.3	24.7 ± 2.9	0.063	24.4 ± 4.9	24.5 ± 2.8	0.889
Etiology						
Hepatitis B (<i>n</i> , %)	104 (64.6)	52 (71.2)	0.37	46 (63.0)	52 (71.2)	0.291
Hepatitis C (<i>n</i> , %)	28 (17.4)	6 (8.2)	0.073	13 (17.8)	6 (8.2)	0.085
Alcohol (<i>n</i> , %)	52 (32.3)	32 (43.8)	0.106	29 (67.4)	32 (43.8)	0.615
Creatinine (mg/dL)	0.9 ± 0.7	0.9 ± 0.2	0.124	0.9 ± 0.2	0.9 ± 0.2	0.688

Sodium (mmol/L)	139.5 ± 3.5	140.5 ± 2.4	0.772	139.9 ± 3.2	140.6 ± 2.3	0.121
Alanine aminotransferase (IU/L)	47.9 ± 36.9	43.3 ± 25.2	0.16	42.6 ± 31.1	43.3 ± 25.1	0.879
Platelet count (10 ⁵ /μL)	131.6 ± 64.2	185.8 ± 74.6	0.009	157.7.5 ± 67.1	169.2 ± 66.4	0.299
Serum albumin (g/ dL)	3.8 ± 0.5	4.1 ± 0.4	0.002	4.0 ± 0.5	4.2 ± 0.5	0.032
Total bilirubin (mg/ dL)	1.0 ± 0.4	0.8 ± 0.8	0.46	0.8 ± 0.4	0.9 ± 0.5	0.724
MELD score	8.7 ± 2.2	7.9 ± 1.9	0.021	8.0 ± 1.6	7.8 ± 1.8	0.439
Alpha-fetoprotein (ng/mL)	630.6 ± 2433.8	650.0 ± 2865.9	0.459	541.3 ± 1501.7	682.8.8 ± 2940.8	0.715
Numbers of tumor	3.1 ± 1.3	2.5 ± 1.0	<0.001	2.6 ± 1.0	2.5 ± 1.0	0.247
Maximum tumor diameter (cm)	3.1 ± 1.2	3.6 ± 1.1	0.021	3.4 ± 1.0	3.6 ± 1.0	0.261

Data are presented as mean ± SD or number (%).

PS: Propensity score; BMI: Body mass index; DM, diabetes mellitus; MELD, Mayo End-Stage Liver Disease.

Supplementary Table 9 Univariate and multivariate Cox regression analysis for hepatocellular carcinoma-related death in B1 hepatocellular carcinoma patients between 2008 and 2016 according to European Association for the Study of Liver guideline

Before PS matching

After PS matching

Variables	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value
Age (< 70 yr)	0.432(0.301–0.621)	< 0.001	0.438 (0.299–0.642)	< 0.001	0.432(0.301–0.621)	< 0.001	0.446 (0.273–0.729)	0.001
Male sex	0.902(0.591–1.376)	0.6321			0.902(0.591–1.376)	0.6321		
BMI (≥ 25 kg/m ²)	1.042 (0.747–1.453)	0.8084			1.042 (0.747–1.453)	0.8084		
Etiology								
Hepatitis B	0.804(0.564–1.147)	0.2295			0.804(0.564–1.147)	0.2295		
Hepatitis C	1.101(0.691–1.755)	0.6858			1.101(0.691–1.755)	0.6858		
Alcohol	1.245(0.878–1.764)	0.2182			1.245(0.878–1.764)	0.2182		
Creatinine (> 1 mg/dL)	1.190(0.803–1.765)	0.3854			1.190(0.803–1.765)	0.3854		

Sodium (> 135 mmol/L)	0.588(0.344-1.004)	0.0518			0.588(0.344-1.004)	0.0518		
Alanine aminotransferase (> 80 IU/L)	1.214(0.740-1.990)	0.4429			1.214(0.740-1.990)	0.4429		
Platelet count (> 10 ⁵ /μL)	0.489(0.350-0.685)	< 0.001	0.505 (0.351-0.726)	< 0.001	0.489(0.350-0.685)	< 0.001	0.472 (0.262-0.848)	0.012
Serum albumin (≥ 3.5 g/dL)	0.556(0.383-0.809)	0.0022			0.556(0.383-0.809)	0.0022		
Total bilirubin (> 1.2 mg/dL)	2.030(1.392-2.962)	0.0002			2.030(1.392-2.962)	0.0002		
MELD score (> 9)	0.578(0.396-0.842)	0.0043			0.578(0.396-0.842)	0.0043		
Alpha-fetoprotein (≥ 200 ng/mL)	0.969(0.657-1.431)	0.8757			0.969(0.657-1.431)	0.8757		
Numbers of tumor (> 3)	1.154(0.815-1.633)	0.42			1.154(0.815-1.633)	0.42		
Maximum tumor diameter (> 3)	0.867(0.612-1.227)	0.42	0.591(0.277-1.261)	0.174	0.867(0.612-1.227)	0.42		

Treatment

Guideline adherence

			0.511					
Upward	0.435 (0.285– 0.664)	< 0.001	(0.323– 0.809)	0.004	0.435 (0.285– 0.664)	< 0.001	0.470(0.288– 0.766)	0.002

PS: Propensity score; BMI: Body mass index; 95%CI: 95% confidence interval; HR: Hazard ratio; MELD: Mayo End-Stage Liver Disease.

Supplementary Table 10 Treatment modalities in B2 hepatocellular carcinoma patients according to European Association for the Study of Liver guideline

	LR	LT	RFA	cTACE	TACE with beads	TARE	Chemotherapy	Radiation therapy	Total
Guideline adherence, <i>n</i> (%)	0	0	0	236 (96.7)	0	0	8 (1.23)	0	244
Upward treatment, <i>n</i> (%)	57 (74.0)	7 (9.1)	1 (1.3)	0	9 (11.7)	3 (3.9)	0	0	77

Downward treatment, <i>n</i> (%)	0	0	0	20 (60.6)	0	0	11 (33.3)	2 (6.7)	33
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LR: Liver resection; LT: Liver transplantation; RFA: Radiofrequency ablation; cTACE: Conventional transarterial chemoembolization; TARE: Transarterial radioembolization.

Supplementary Table 11 Baseline characteristics of patients with B2 hepatocellular carcinoma between 2008 and 2016 according to European Association for the Study of Liver guideline

Variables	Before PS matching			After PS matching		
	Guideline-adherent	Upward treatment	<i>P</i> value	Guideline-adherent	Upward treatment	<i>P</i> value
No. of patients	244	77		43	43	
Age (yr)	61.3 ± 11.1	60.6 ± 9.5	0.095	58.4 ± 11.5	62.1 ± 9.7	0.106
Male sex (<i>n</i> , %)	215 (88.1)	68 (88.3)	0.856	38 (88.4)	40 (93.0)	0.713
BMI (kg/m ²)	24.3 ± 3.9	23.3 ± 4.1	0.03	25.0 ± 3.8	23.7 ± 3.1	0.1
Etiology						
Hepatitis B (<i>n</i> , %)	144 (59)	47 (61)	0.045	28 (65.3)	26 (60.5)	0.824
Hepatitis C (<i>n</i> , %)	31 (12.7)	5 (6.5)	0.001	1(2.3)	2(4.7)	1
Alcohol (<i>n</i> , %)	104 (42.6)	33 (42.9)	0.584	19 (44.2)	20 (46.5)	1
Creatinine (mg/dL)	1.0 ± 0.6	0.9 ± 0.2	0.199	0.9 ± 0.2	0.9 ± 0.2	0.39

Sodium (mmol/L)	139.0 ± 2.7	139.0 ± 4.1	0.046	139.7 ± 2.2	138.9 ± 4.8	0.369
Alanine aminotransferase (IU/L)	51.4 ± 40.9	43.8 ± 34.0	0.328	46 ± 31.8	43.2 ± 36.5	0.701
Platelet count (10 ⁹ /L)	158.6 ± 71.5	185.8 ± 74.6	0.01	182.5 ± 74.5	185.2 ± 72.6	0.863
Serum albumin (g/dL)	3.9 ± 0.5	4.1 ± 0.4	0	4.1 ± 0.4	4.1 ± 0.5	0.886
Total bilirubin (mg/dL)	1.0 ± 1.1	0.8 ± 0.8	0.621	0.7 ± 0.3	0.8 ± 0.3	0.086
MELD score	8.4 ± 2.4	7.5 ± 1.5	0.007	7.6 ± 1.6	7.5 ± 1.3	0.756
Alpha-fetoprotein (ng/mL)	3156.0 ± 11836.6	4547.3 ± 21730.8	0.765	5020.8 ± 19981.4	6002.8 ± 28020.2	0.852
Numbers of tumor	4.1 ± 1.2	3.2 ± 1.3	< 0.001	2.9 ± 2.4	2.5 ± 1.1	0.328
Maximum tumor diameter (cm)	6.2 ± 3.1	7.2 ± 3.1	0.021	7.2 ± 2.4	7.3 ± 2.9	0.971

Data are presented as mean ± SD or number (%).

PS: Propensity score; BMI: Body mass index; MELD: Mayo End-Stage Liver Disease.

Supplementary Table 12 Univariate and multivariate Cox regression analysis for hepatocellular carcinoma-related death in B2 hepatocellular carcinoma patients between 2008 and 2016 according to European Association for the Study of Liver guideline

	Before matching	PS		After matching	PS
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Variables	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value	HR (95%CI)	<i>P</i> value
Age (< 70 yr)	0.903 1.215)	(0.671- 0.500			1.277(0.654- 2.493)	0.473		
Male sex	0.780 1.144)	(0.532- 0.203			0.298(0.133- 0.670)	0.003		
BMI (≥ 25 kg/m ²)	0.866 1.052)	(0.713- 0.147			1.057 (0.600- 1.864)	0.847		
Etiology								
Hepatitis B	0.878 1.068)	(0.722- 0.193			0.992(0.565- 1.739)	0.976		
Hepatitis C	1.136(0.864- 1.493)	0.361			2.097 (0.650- 6.763)	0.215		
Alcohol	1.029(0.847- 1.251)	0.773			0.576 (0.329- 1.006)	0.053		
Creatinine (> 1 mg/dL)	1.226(0.982- 1.531)	0.072			1.160 (0.628- 2.141)	0.636		

Guideline adherence

Upward treatment	0.538	(0.340-	0.008	0.566	(0.325-	0.0448	0.553	(0.317-	0.037
	0.851)			0.987)			0.965)		

PS: Propensity score; BMI: Body mass index; 95%CI: 95%confidence interval; HR: Hazard ratio; MELD: Mayo End-Stage Liver Disease.