

Supplementary Table SI. Patient characteristics and muscle mass variables stratified by sex and FFMI

Parameter	Males (n = 96)			Females (n = 61)		
	Low FFMI (n = 48)	High FFMI (n = 48)	P-value	Low FFMI (n = 30)	High FFMI (n = 31)	P-value
Clinical characteristics:						
Age [years]	58.69 ±9.06	53.42 ±10.58	0.021	56.33 ±9.39	55.65 ±9.23	0.525
Height [cm]	170.88 ±5.26	170.02 ±4.79	0.317	159.10 ±5.47	158.81 ±6.42	0.745
Weight [kg]	65.90 ±7.26	68.98 ±9.83	0.138	53.18 ±6.72	59.52 ±6.28	< 0.001
BMI [kg/m ²]	22.61 ±2.75	23.82 ±2.96	0.036	21.00 ±2.27	23.62 ±2.32	< 0.001
FFMA [cm ²]	35.13 ±5.09	49.11 ±6.52	< 0.001	23.43 ±2.41	32.79 ±4.31	< 0.001
FFMI [cm ² /m ²]	12.02 ±1.64	16.97 ±1.99	< 0.001	9.26 ±0.90	13.00 ±1.52	< 0.001
History of HBV infection	40 (83.3%)	41 (85.4%)	1.000	20 (66.7%)	24 (77.4%)	0.515
History of cholelithiasis	7 (14.6%)	11 (22.9%)	0.433	5 (16.7%)	5 (16.1%)	1.000
Cirrhosis	22 (45.8%)	23 (47.9%)	1.000	4 (13.3%)	7 (22.6%)	0.544
CA19-9 [U/ml]	895.86 ±1909.12	326.18 ± 811.80	0.401	1578.27 ± 2832.31	449.26 ±822.17	0.383
Albumin [g/l]	39.21 ±3.77	40.50 ±3.91	0.157	38.39 ±8.61	40.05 ±4.37	0.729
Serum total bilirubin [mg/dl]	19.39 ±23.94	19.82 ±29.46	0.739	15.53 ±20.40	19.68 ±28.31	0.498
Child-Pugh score:	1.000			0.963		
A	45 (93.8%)	46 (95.8%)		26 (86.7%)	28 (90.3%)	
B	3 (6.2%)	2 (4.2%)		4 (13.3%)	3 (9.7%)	
Tumour characteristics:						
Multifocal tumour	7 (14.6%)	15 (31.2%)	0.089	9 (30.0%)	3 (9.7%)	0.094
Tumour diameter [mm]	51.44 ±22.95	51.29 ±24.55	0.668	53.63 ±23.78	50.03 ±17.30	0.745
Macrovascular invasion	14 (29.2%)	11 (22.9%)	0.642	10 (33.3%)	9 (29.0%)	0.931
Microvascular invasion	18 (37.5%)	12 (25.0%)	0.271	11 (36.7%)	13 (41.9%)	0.874
Histologic subtype:	0.090			1.000		
Large duct	22 (45.8%)	13 (27.1%)		12 (40.0%)	12 (38.7%)	
Small duct	26 (54.2%)	35 (72.9%)		18 (60.0%)	19 (61.3%)	
Histologic differentiation:	1.000			0.712		
Good or moderate	20 (41.7%)	19 (39.6%)		14 (46.7%)	12 (38.7%)	
Poor	28 (58.3%)	29 (60.4%)		16 (53.3%)	19 (61.3%)	
Surgical margin status (R1)	2 (4.2%)	2 (4.2%)	1	2 (6.7%)	0	0.458
Lymph node metastasis	17 (35.4%)	12 (25.0%)	0.374	17 (56.7%)	9 (29.0%)	0.054
Metastases	0	0	NA	1 (3.3%)	2 (6.5%)	1.000
T stage:	0.414			0.685		
T1a	16 (33.3%)	20 (41.7%)		9 (30.0%)	11 (35.5%)	
T1b	12 (25.0%)	7 (14.6%)		4 (13.3%)	6 (19.4%)	
T2	19 (39.6%)	21 (43.8%)		16 (53.3%)	12 (38.7%)	
T3	1 (2.1%)	0		0	0	
T4	0	0		1 (3.3%)	2 (6.5%)	
Treatment:						
Extension of hepatectomy:	0.374			0.251		
Minor resection	31 (64.6%)	36 (75.0%)		13 (43.3%)	19 (61.3%)	
Major resection	17 (35.4%)	12 (25.0%)		17 (56.7%)	12 (38.7%)	
Lymphadenectomy	16 (33.3%)	15 (31.2%)	1.000	13 (43.3%)	16 (51.6%)	0.696
Adjuvant therapy	16 (33.3%)	13 (27.1%)	0.657	12 (40.0%)	12 (38.7%)	1.000
TACE	3 (6.2%)	8 (16.7%)	0.200	0	1 (3.2%)	1.000
Ablation therapy	5 (10.4%)	4 (8.3%)	1.000	1 (3.3%)	2 (6.5%)	1.000

Categorical variables were presented as number (percentage), and continuous variables were presented as mean and standard deviation. BMI – body mass index, CA19-9 – carbohydrate antigen 19-9, FFMA – fat-free muscle area, FFMI – fat-free skeletal muscle index, HBV – hepatitis B virus, TACE – transhepatic arterial chemotherapy and embolization.

Supplementary Table SII. Univariable Cox regression analysis for overall survival in the entire patient cohort

Parameter	Univariate analysis		
	HR	95% CI	P-value
Clinical characteristics:			
Sex (female)	1.031	0.647–1.644	0.897
Age (> 65 years)	0.946	0.527–1.697	0.852
BMI [kg/m ²]	0.956	0.881–1.037	0.281
Low FFMI	1.891	1.185–3.019	0.008
History of HBV infection	0.913	0.509–1.636	0.759
History of cholelithiasis	0.706	0.351–1.421	0.330
Cirrhosis	0.884	0.546–1.430	0.615
CA19-9 (> 1000 U/ml)	1.872	1.058–3.313	0.031
Albumin [g/l]	0.971	0.940–1.003	0.072
Serum total bilirubin [mg/dl]	1.005	0.997–1.013	0.194
Child-Pugh score (B)	1.262	0.546–2.917	0.587
Tumour characteristics:			
Multifocal tumour	1.693	1.026–2.792	0.039
Tumour diameter [mm]	1.010	1.002–1.019	0.020
Large duct subtype	1.375	0.872–2.169	0.170
Macrovascular invasion	2.195	1.361–3.540	0.001
Microvascular invasion	1.421	0.889–2.271	0.143
Poor differentiation	1.595	0.985–2.581	0.058
Surgical margin status (R1)	2.882	1.037–8.005	0.042
TNM stage (3, 4 vs. 1, 2)	2.090	1.322–3.304	0.002
Treatment:			
Major resection	1.931	1.214–3.071	0.005
Radical lymphadenectomy	1.850	1.166–2.936	0.009
Adjuvant therapy	0.716	0.435–1.177	0.187
TACE	0.676	0.272–1.679	0.399
Ablation therapy	0.501	0.183–1.377	0.181

BMI – body mass index, CA19-9 – carbohydrate antigen 19-9, FFMI – fat-free muscle index, HBV – hepatitis B virus, HR – hazard ratio, TACE – transhepatic arterial chemotherapy and embolization, 95% CI – 95% confidence intervals.

Supplementary Table SIII. Univariable Cox regression analysis for overall survival in male and female patients

Characteristics	Univariate analysis (female)			Univariate analysis (male)		
	HR	95% CI	P-value	HR	95% CI	P-value
Clinical characteristics:						
Age (> 65 years)	1.161	0.440–3.067	0.763	0.790	0.367–1.697	0.546
BMI [kg/m ²]	0.863	0.731–1.018	0.080	0.999	0.908–1.099	0.987
FFMI [cm ² /m ²]	0.853	0.717–1.015	0.073	0.838	0.756–0.93	0.001
History of HBV infection	0.828	0.364–1.884	0.653	0.975	0.409–2.321	0.954
History of cholelithiasis	0.334	0.079–1.416	0.137	1.043	0.466–2.336	0.918
Cirrhosis	0.884	0.304–2.566	0.820	0.827	0.461–1.483	0.524
CA19-9 (> 1000 U/ml)	1.742	0.763–3.98	0.188	2.138	0.941–4.859	0.070
Albumin [g/l]	0.983	0.943–1.025	0.414	0.911	0.84–0.987	0.022
Serum total bilirubin [mg/dl]	1.010	0.996–1.024	0.172	1.004	0.994–1.014	0.473
Child-Pugh score (B)	1.413	0.487–4.099	0.524	1.065	0.257–4.413	0.931
Tumour characteristics:						
Multifocal tumour	1.349	0.568–3.202	0.498	1.839	0.992–3.411	0.053
Tumour diameter [mm]	1.005	0.991–1.021	0.475	1.013	1.002–1.025	0.019
Large duct subtype	0.800	0.372–1.719	0.567	1.980	1.109–3.533	0.021
Macrovascular invasion	2.655	1.195–5.897	0.016	1.993	1.083–3.667	0.027
Microvascular invasion	1.409	0.652–3.044	0.383	1.463	0.805–2.659	0.211
Poor differentiation	1.346	0.628–2.884	0.445	1.760	0.938–3.304	0.078
Surgical margin status (R1)	16.949	1.507–190.6	0.022	2.254	0.689–7.376	0.179
TNM stage (3, 4 vs. 1, 2)	1.407	0.670–2.952	0.367	2.832	1.568–5.117	0.001
Treatment:						
Major resection	1.970	0.914–4.247	0.084	1.992	1.090–3.640	0.025
Lymphadenectomy	2.556	1.152–5.669	0.021	1.583	0.859–2.919	0.141
Adjuvant therapy	0.531	0.239–1.178	0.120	0.811	0.420–1.568	0.534
TACE	NA	NA	NA	0.798	0.315–2.024	0.635
Ablation therapy	NA	NA	NA	0.829	0.296–2.320	0.721

BMI – body mass index, CA19-9 – carbohydrate antigen 19-9, FFMI – fat-free muscle index, HBV – hepatitis B virus, HR – hazard ratio, TACE – transhepatic arterial chemotherapy and embolization, 95% CI – 95% confidence intervals.

Supplementary Table SIV. Association between dichotomous fat-free muscle index and overall survival in female and male patients

Characteristics	Univariate analysis (females)			Univariate analysis (males)			Multivariate analysis (males)		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Clinical characteristics:									
Age (> 65 years)	1.161	0.44–3.067	0.763	0.790	0.367–1.697	0.546	0.571	0.256–1.274	0.171
BMI [kg/m ²]	0.863	0.731–1.018	0.08	0.999	0.908–1.099	0.987			
Low FFMI	0.802	0.378–1.702	0.565	0.349	0.187–0.652	0.001	2.145	1.113–4.133	0.023
History of HBV infection	0.828	0.364–1.884	0.653	0.975	0.409–2.321	0.954			
History of cholelithiasis	0.334	0.079–1.416	0.137	1.043	0.466–2.336	0.918			
Cirrhosis	0.884	0.304–2.566	0.820	0.827	0.461–1.483	0.524			
CA19-9 (> 1000 U/ml)	1.742	0.763–3.98	0.188	2.138	0.941–4.859	0.07			
Albumin [g/l]	0.983	0.943–1.025	0.414	0.911	0.84–0.987	0.022	0.962	0.886–1.044	0.351
Serum total bilirubin [mg/dl]	1.010	0.996–1.024	0.172	1.004	0.994–1.014	0.473			
Child-Pugh score (B)	1.413	0.487–4.099	0.524	1.065	0.257–4.413	0.931			
Tumour characteristics:									
Multifocal tumour	1.349	0.568–3.202	0.498	1.839	0.992–3.411	0.053			
Tumour diameter (mm)	1.005	0.991–1.021	0.475	1.013	1.002–1.025	0.019	1.015	1.001–1.029	0.042
Large duct subtype	0.800	0.372–1.719	0.567	1.980	1.109–3.533	0.021	2.083	1.043–4.161	0.038
Macrovascular invasion	2.655	1.195–5.897	0.016	1.993	1.083–3.667	0.027	1.508	0.74–3.072	0.258
Microvascular invasion	1.409	0.652–3.044	0.383	1.463	0.805–2.659	0.211			
Poor differentiation	1.346	0.628–2.884	0.445	1.760	0.938–3.304	0.078			
Surgical margin status (R1)	16.949	1.507–190.6	0.022	2.254	0.689–7.376	0.179			
TNM stage (3, 4 vs. 1, 2)	1.407	0.67–2.952	0.367	2.832	1.568–5.117	0.001	1.675	0.858–3.272	0.131
Treatment:									
Major resection	1.970	0.914–4.247	0.084	1.992	1.09–3.64	0.025	1.024	0.515–2.038	0.946
Lymphadenectomy	2.556	1.152–5.669	0.021	1.583	0.859–2.919	0.141			
Adjuvant therapy	0.531	0.239–1.178	0.120	0.811	0.42–1.568	0.534			
TACE	NA	NA	NA	0.798	0.315–2.024	0.635			
Ablation therapy	NA	NA	NA	0.829	0.296–2.32	0.721			

Age and variables with a p-value < 0.05 identified on univariable analysis were selected for the multivariable analysis. BMI – body mass index, CA19-9 – carbohydrate antigen 19-9, FFMI – fat-free muscle index, HBV – hepatitis B virus, HR – hazard ratio, TACE – transhepatic arterial chemotherapy and embolization, 95% CI – 95% confidence intervals.