

Supplementary Materials

The liver maximum function capacity test (LiMAx) is associated with short-term survival in patients with early stage HCC undergoing transarterial treatment

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Table S1: Changes in LiMAx, laboratory parameters and liver function scores according Child A and Child B group. All values presented as median (range).

Parameter	Child A (n=29)			Child B (n=5)			Child A vs. Child B (p value)	
	Before TACE/TARE	After TACE/TARE	p value	Before TACE/TARE	After TACE/TARE	p value	Before TACE/TARE	After TACE/TARE
LiMAx (µg/kg/h)	229 (87-686)	261 (53-604)	0.018	181 (35-282)	84 (60-228)	0.625	0.292	0.010
ALT (µkat/L)	0.58 (0.23-1.03)	0.46 (0.25-12.58)	0.081	0.63 (0.52-0.68)	0.59 (0.25-0.79)	1.000	0.370	0.227
AST (µkat/L)	0.74 (0.37-12.70)	0.71 (0.28-12.93)	0.250	1.12 (0.61-1.58)	1.26 (0.49-1.56)	0.625	0.026	0.092
GGT (µkat/L)	2.39 (0.42-6.95)	2.17 (0.58-7.45)	0.571	2.99 (1.43-10.53)	2.90 (0.90-6.09)	0.125	0.444	0.737
Bilirubin (µmol/L)	13.8 (4.8-34.1)	16.6 (5.5-44.6)	0.421	17.9 (7.1-87.8)	35.2 (6.9-70.8)	0.625	0.154	0.055
Platelets (x10 ⁹ /L)	133 (51-221)	120 (40-240)	0.741	109 (74-144)	123 (74-145)	1.000	0.611	0.780
Albumin (g/L)	40.9 (31.7-46.6)	40.4 (21.7-47.0)	0.003	36.1 (28.5-39.5)	31.2 (25.2-36.1)	0.063	0.011	0.004
INR	1.2 (0.9-1.9)	1.2 (0.9-1.9)	0.717	1.2 (1.0-1.5)	1.3 (1.0-1.4)	1.000	0.698	0.383
Creatinine (µmol/L)	77 (32-93)	70 (29-109)	0.577	86 (61-124)	73 (60-135)	1.000	0.167	0.300
ALBI score	-2.76 (-3.38--1.77)	-2.58 (-3.20--0.92)	0.0007	-1.95 (-2.53--1.44)	-1.87 (-1.99--1.25)	0.125	0.008	0.0008
CTP score	5 (5-6)	5 (5-7)	0.563	7 (7-7)	7 (7-7)	1.000	3.95x10 ⁻⁶	2.16x10 ⁻⁵
MELD score	8 (6-15)	8 (6-15)	0.243	10 (8-18)	13 (10-16)	0.813	0.027	0.003

The Mann–Whitney U-test and Wilcoxon signed-rank test were applied to compare the quantitative variables. ALT: alanine aminotransferase, AST: aspartate aminotransferase, CTP: Child-Turcotte-Pugh, GGT: gamma-glutamyl transpeptidase, LiMAx: liver maximum capacity test, INR: international normalized ratio, TACE: transarterial chemoembolization, TARE: transarterial radioembolization

Table S2: Changes in LiMAx, laboratory parameters and liver function scores according ALBI grade 1 and ALBI grade 2/3 group.

All values presented as median (range).

Parameter	ALBI grade 1 (n=22)			ALBI grade 2/3 (n=14)			ALBI grade 1 vs. ALBI grade 2/3 (p value)	
	Before TACE/TARE	After TACE/TARE	p value	Before TACE/TARE	After TACE/TARE	p value	Before TACE/TAR E	After TACE/TAR E
LiMAx (µg/kg/h)	276 (156-686)	316 (53-604)	0.168	173 (35-282)	192 (60-283)	0.414	0.0001	0.0002
ALT (µkat/L)	0.55 (0.23-1.01)	0.42 (0.25-12.58)	0.468	0.63 (0.38-1.03)	0.54 (0.25-0.79)	0.185	0.090	0.178
AST (µkat/L)	0.62 (0.38-1.07)	0.55 (0.28-12.93)	0.962	0.96 (0.56-1.58)	0.79 (0.49-1.56)	0.223	0.0001	0.016
GGT (µkat/L)	2.14 (0.44-5.21)	1.93 (0.71-7.45)	0.732	2.95 (0.44-10.53)	3.05 (0.58-7.02)	0.122	0.299	0.243
Bilirubin (µmol/L)	19.7 (4.8-23.2)	14.4 (4.9-44.6)	0.156	21.6 (7.1-87.8)	21.5 (6.9-70.8)	0.867	0.0008	0.002
Platelets (x10 ⁹ /L)	149 (51-265)	138 (40-225)	0.168	102 (55-221)	108 (58-240)	0.021	0.130	0.555
Albumin (g/L)	43.4 (39.0-48.0)	42.7 (236.2-48.3)	0.109	36.0 (28.5-39.5)	34.5 (21.7-37.1)	0.003	6.06x10 ⁻⁹	6.85x10 ⁻⁹
INR	1.1 (0.9-1.4)	1.1 (0.9-1.9)	0.546	1.2 (1.0-1.9)	1.3 (1.0-1.6)	0.797	0.088	0.058
Creatinine (µmol/L)	79 (48-95)	72 (40-109)	0.231	78 (32-124)	71 (29-135)	0.841	0.892	0.917
ALBI score	-2.96 (-3.40-- 2.63)	-2.85 (-3.39--2.25)	0.033	-2.25 (-2.53-- 1.44)	-1.97 (-2.39-- 0.92)	0.004	5.27x10 ⁻¹⁰	2.11x10 ⁻⁹
CTP score	5 (5-6)	5 (5-7)	0.312	6 (5-7)	5 (5-7)	1.000	0.002	0.121
MELD score	8 (6-10)	8 (6-15)	0.073	10 (7-18)	11 (7-16)	0.920	0.002	0.014

The Mann–Whitney U-test and Wilcoxon signed-rank test were applied to compare the quantitative variables. ALT: alanine aminotransferase, AST: aspartate aminotransferase, CTP: Child-Turcotte-Pugh, GGT: gamma-glutamyl transpeptidase, LiMAx: liver maximum capacity test, INR: international normalized ratio, TACE: transarterial chemoembolization, TARE: transarterial radioembolization

Table S3: Changes in LiMAx, laboratory parameters and liver function scores according LiMAx ≤150 µg/kg/h and LiMAx >150 µg/kg/h levels. All values presented as median (range).

Parameter	LiMAx ≤150 µg/kg/h (n=5)			LiMAx >150 µg/kg/h (n=31)			LiMAx ≤150 vs. LiMAx >150 µg/kg/h (p value)	
	Before TACE/TARE	After TACE/TARE	p value	Before TACE/TARE	After TACE/TARE	p value	Before TACE/TARE	After TACE/TARE
LiMAx (µg/kg/h)	92 (35-115)	165 (60-261)	0.063	266 (156-686)	272 (53-604)	0.223	8.60x10 ⁻⁷	0.028
ALT (µkat/L)	0.65 (0.53-0.68)	0.51 (0.41-0.75)	0.438	0.56 (0.23-1.03)	0.46 (0.25-12.58)	0.301	0.143	0.449
AST (µkat/L)	1.09 (0.73-1.58)	0.78 (0.72-1.53)	0.613	0.81 (0.38-1.17)	0.64 (0.28-12.93)	0.758	0.021	0.122
GGT (µkat/L)	1.97 (0.42-3.54)	2.06 (0.58-6.95)	0.316	2.90 (0.38-10.53)	2.23 (0.71-7.44)	0.413	0.261	0.554
Bilirubin (µmol/L)	34.1 (31.4-87.8)	30.9 (15.5-70.8)	0.438	13.5 (4.8-26.0)	15.6 (4.9-44.6)	0.117	2.64x10 ⁻⁶	0.002
Platelets (x10 ⁹ /L)	89 (55-180)	92 (53-173)	1.000	140 (51-265)	136 (40-240)	0.637	0.162	0.229
Albumin (g/L)	35.7 (31.9-38.3)	34.7 (21.7-37.9)	0.063	41.0 (28.5-48.0)	40.6 (25.2-48.3)	0.007	0.006	0.010
INR	1.3 (1.1-1.8)	1.3 (1.1-1.6)	0.500	1.1 (0.9-1.9)	1.1 (0.9-1.9)	0.470	0.041	0.116
Creatinine (µmol/L)	81 (32-109)	80 (29-110)	0.500	79 (48-124)	71 (40-135)	0.335	0.976	0.849
ALBI score	-2.01 (-2.26--1.44)	-1.91 (-2.44--0.92)	0.063	-2.83 (-3.40--1.61)	-2.71 (-3.39--1.25)	0.003	4.40x10 ⁻⁴	0.001
CTP score	6 (5-7)	5 (5-7)	0.500	5 (5-7)	5 (5-7)	0.359	0.095	0.763
MELD score	13 (8-18)	13 (8-16)	0.312	8 (6-15)	9 (6-15)	0.059	0.001	0.021

The Mann–Whitney U-test and Wilcoxon signed-rank test were applied to compare the quantitative variables. ALT: alanine aminotransferase, AST: aspartate aminotransferase, CTP: Child-Turcotte-Pugh, GGT: gamma-glutamyl transpeptidase, LiMAx: liver maximum capacity test, INR: international normalized ratio, TACE: transarterial chemoembolization, TARE: transarterial radioembolization.

Table S4. Adverse events within 4 weeks after transarterial treatment.

Adverse effect	Number (%)	
	TARE (n=12)	TACE (n=57)
Mental confusion	0	2 (3.5%)
Fatigue	0	8 (14.0%)
Epigastric pressure	2 (16.7%)	3 (5.3%)
Abdominal fullness	0	2 (3.5%)
Flatulence	0	3 (5.3%)
Diarrhea	0	3 (5.3%)
Pruritus	2 (16.7%)	2 (3.5%)
Ascites		
Mild to moderate	1 (8.3%)	2 (3.5%)
Severe	0	5 (8.8%)
Hepatic encephalopathy	0	2 (3.5%)
Kidney failure	0	2 (3.5%)
Liver failure	0	1 (1.8%)
Myocardial infarct		1 (1.8%)
Death		2 (3.5%)
Lost to follow up		1 (1.8%)

Table S5: Univariate and multivariate logistic regression analyses for the occurrence of adverse events.

Parameter	Univariate analysis				Multivariate analysis			
	RC	SE	OR (95% CI)	p value	RC	SE	OR (95% CI)	p value
LiMAx ≤ 150 $\mu\text{g/kg/h}$	1.197	0.702	3.31 (0.84-13.11)	0.088	1.240	1.210	3.46 (0.32-37.27)	0.307
Male sex	0.367	0.590	1.44 (0.45-4.59)	0.534			-	
Age (years)	0.020	0.028	1.02 (0.98-1.07)	0.474			-	
CTP score	0.776	0.357	2.15 (1.07-4.33)	0.032	0.452	0.460	1.57 (0.64-3.84)	0.320
MELD	0.121	0.082	1.13 (0.93-1.33)	0.143			-	
ALBI score	1.005	0.508	2.73 (1.01-7.40)	0.048	-1.539	5.040	0.22 (0-4165.97)	0.760
ALT ($\mu\text{kat/L}$)	1.043	0.912	2.84 (0.48-16.94)	0.252			-	
AST ($\mu\text{kat/L}$)	1.762	0.858	5.83 (1.08-31.98)	0.040	1.460	1.310	4.31 (0.33-55.97)	0.264
GGT ($\mu\text{kat/L}$)	-0.970	0.115	0.91 (0.72-1.14)	0.400			-	
Bilirubin ($\mu\text{mol/L}$)	0.041	0.021	1.04 (1.00-1.09)	0.050	0.002	0.070	1.00 (0.87-1.16)	0.973
Platelets ($\times 10^9/\text{L}$)	-0.002	0.004	1.00 (0.99-1.01)	0.641			-	
Albumin (g/L)	-0.092	0.054	0.91 (0.82-1.01)	0.085	-0.122	0.450	0.89 (0.37-2.14)	0.788
INR	1.239	1.216	3.45 (0.32-37.44)	0.308			-	
Creatinine ($\mu\text{mol/L}$)	-0.003	0.009	1.00 (0.98-1.01)	0.738			-	
BCLC Score								
A			REF				-	
B	-0.118	0.521	0.89 (0.32-2.47)	0.821			-	
C	1.620	1.129	5.06 (0.55-46.24)	0.151			-	
Treatment								
TACE	0.099	0.646	1.10 (0.31-3.92)	0.878			-	
TARE			REF				-	

ALBI: albumin-bilirubin, ALT: alanine aminotransferase, AST: aspartate aminotransferase, BCLC: Barcelona Clinic Liver Cancer score, CI: confidence interval, CTP: Child-Turcotte-Pugh, GGT: gamma-glutamyl transpeptidase, LiMAx: liver maximum capacity test, HR: hazard ratio, INR: international normalized ratio,

MELD: model for end-stage liver disease, RC: regression coefficient, REF: reference, SE: standard error, TACE: transarterial chemoembolization, TARE: transarterial radioembolization

Table S6: Univariate and multivariate Cox regression analyses for overall survival.

Parameter	Univariate analysis				Multivariate analysis			
	RC	SE	HR (95% CI)	p value	RC	SE	HR (95% CI)	p value
LiMAx ≤150 µg/kg/h	0.502	0.430	1.65 (0.71-3.84)	0.243			-	
Male sex	0.147	0.500	1.16 (0.44-3.09)	0.769			-	
Age (years)	-0.047	0.026	0.95 (0.91-1.01)	0.074	-0.015	0.030	0.99 (0.93-1.04)	0.605
CTP Child A			REF				REF	
Child B	1.070	0.424	2.93 (1.27-6.76)	0.012	0.317	0.582	1.37 (0.44-4.30)	0.586
MELD	0.161	0.058	1.17 (1.05-1.31)	0.005	0.142	0.072	1.15 (1.00-1.33)	0.048
ALBI score	1.120	0.368	3.10 (1.51-6.37)	0.002				
Grade 1			REF				REF	
Grade 2	0.950	0.458	2.58 (1.05-6.34)	0.038	0.133	0.557	1.14 (0.38-3.41)	0.812
Grade 3	3.921	0.932	50.43 (8.12-313.06)	2.57x10⁻⁵	2.881	1.110	17.83 (2.02-157.11)	0.009
BCLC Score								
A			REF				-	
B	0.160	0.428	1.17 (0.51-2.71)	0.708			-	
C	0.219	0.652	1.25 (0.35-4.47)	0.737			-	
Treatment								
TACE	-0.547	0.512	0.58 (0.21-1.58)	0.264			-	
TARE			REF				-	

ALBI: albumin-bilirubin, BCLC: Barcelona Clinic Liver Cancer score, CI: confidence interval, CTP: Child-Turcotte-Pugh, LiMAx: liver maximum capacity test, HR: hazard ratio, ratio, MELD: model for end-stage liver disease, RC: regression coefficient, REF: reference, SE: standard error, TACE: transarterial chemoembolization, TARE: transarterial radioembolization

Table S7: Univariate and multivariate Cox regression analyses for 180-day survival in patients with BCLC stage A.

Parameter	Univariate analysis				Multivariate analysis			
	RC	SE	HR (95% CI)	p value	RC	SE	HR (95% CI)	p value
LiMAx ≤150 µg/kg/h	2.710	1.120	15.03 (1.67-134.94)	0.016	0.608	1.786	1.84 (0.01-60.85)	0.733
Male sex	3.652	3.969	38.57 (0.02-92240)	0.357			-	
Age (years)	-0.094	0.063	0.91(0.80-1.03)	0.136			-	
CTP Child A			REF				-REF	
Child B	2.667	1.120	14.39 (1.60-129.21)	0.017	2.425	1.657	11.30 (0.44-290.58)	0.143
MELD	0.405	0.134	1.50 (1.15-1.95)	0.003	0.489	0.219	1.63 (1.06-2.51)	0.026
ALBI score	2.767	0.998	15.91 (2.25-112.45)	0.006	1.899	1.911	6.68 (0.16-282.63)	0.320
Grade 1			REF					
Grade 2	11.330	171.011	0	0.947			-	
Grade 3	13.881	171.012	0	0.935			-	
Treatment								
TACE	3.161	6.540	23.61 (0-870987)	0.629			-	
TARE			REF				-	

ALBI: albumin-bilirubin, BCLC: Barcelona Clinic Liver Cancer score, CI: confidence interval, CTP: Child-Turcotte-Pugh, LiMAx: liver maximum capacity test, HR: hazard ratio, MELD: model for end-stage liver disease, RC: regression coefficient, REF: reference, SE: standard error, TACE: transarterial chemoembolization, TARE: transarterial radioembolization