

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Factors Associated With Posttransplant HCC Recurrence and Poor Overall Survival

Predictor	HCC Recurrence				Overall survival				
	Univariable		Multivariable		Univariable		Multivariable		
	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	
<i>Pretransplant factors</i>									
Beyond Milan criteria at time of transplant	3.45 (2.62 - 4.53)	< 0.001	1.82 (1.32 - 2.49)	< 0.001	1.68 (1.36 - 2.07)	< 0.001	1.22 (0.97 - 1.54)	0.092	
Downstaged to within Milan criteria	1.37 (1.02 - 1.83)	0.035	1.09 (0.79 - 1.51)	0.592	1.19 (0.99 - 1.45)	0.07	1.16 (0.95 - 1.42)	0.258	
Number of pretransplant locoregional therapies									
0	Reference	-	Reference	-	Reference	-	Reference	-	
1	0.70 (0.48 - 1.01)	0.059	1.12 (0.76 - 1.65)	0.571	0.83 (0.68 - 1.01)	0.056	1.08 (0.87 - 1.45)	0.472	
2	1.12 (0.79 - 1.59)	0.526	1.53 (1.06 - 2.21)	0.024	0.87 (0.71 - 1.07)	0.192	1.11 (0.88 - 1.41)	0.360	
3 or more	1.77 (1.26 - 2.50)	0.001	2.11 (1.46 - 3.04)	< 0.001	0.98 (0.79 - 1.21)	0.85	1.15 (0.90 - 1.46)	0.267	
Laboratory MELD score (per unit increase)	1.00 (0.99 - 1.02)	0.878			1.02 (1.01 - 1.03)	< 0.001	1.02 (1.01 - 1.03)	0.001	
Neutrophil-to-lymphocyte ratio at transplant (per log unit increase)	1.17 (1.01 - 1.36)	0.041	1.16 (0.99 - 1.35)	0.055	1.21 (1.10 - 1.33)	< 0.001	1.12 (1.01 - 1.25)	0.033	
Alpha-fetoprotein at time of transplant - ng/mL									
< 20	Reference	-	Reference	-	Reference	-	Reference	-	
20 - 199	2.30 (1.79 - 2.96)	< 0.001	1.72 (1.33 - 2.23)	< 0.001	1.42 (1.21 - 1.66)	< 0.001	1.28 (1.09 - 1.51)	0.003	
200 - 1000	3.43 (2.45 - 4.81)	< 0.001	2.29 (1.62 - 3.23)	< 0.001	1.60 (1.24 - 2.06)	< 0.001	1.37 (1.05 - 1.77)	0.019	
> 1000	5.06 (3.35 - 7.65)	< 0.001	2.20 (1.36 - 3.55)	0.001	1.81 (1.30 - 2.54)	< 0.001	1.18 (0.82 - 1.69)	0.387	
<i>Posttransplant factors</i>									
Size of largest viable tumor on explant (per cm increase)	1.23 (1.20 - 1.27)	< 0.001	1.12 (1.04 - 1.17)	< 0.001	1.13 (1.10 - 1.15)	< 0.001	1.07 (1.04 - 1.11)	< 0.001	
Tumor differentiation									

Necrotic/no viable tumor	Reference	-		Reference	-		Reference	-		Reference	-
Well	1.98 (1.24 - 3.16)	0.004		1.29 (0.79 - 2.11)	0.302		1.14 (0.92 - 1.42)	0.230		0.82 (0.64 - 1.05)	0.113
Moderate	3.49 (2.34 - 5.19)	< 0.001		1.62 (1.04 - 2.51)	< 0.001		1.42 (1.19 - 1.72)	< 0.001		0.90 (0.72 - 1.12)	0.345
Poor	8.41 (5.51 - 12.85)	< 0.001		2.74 (1.69 - 4.45)	< 0.001		2.17 (1.72 - 2.73)	< 0.001		1.12 (0.85 - 1.48)	0.427
Vascular invasion											
None	Reference	-		Reference	-		Reference	-		Reference	-
Microvascular	3.12 (2.47 - 3.92)	< 0.001		1.78 (1.38 - 2.29)	< 0.001		1.77 (1.52 - 2.07)	< 0.001		1.45 (1.23 - 1.73)	< 0.001
Macrovascular	7.01 (4.76 - 10.32)	< 0.001		2.69 (1.75 - 4.15)	< 0.001		3.49 (2.62 - 4.65)	< 0.001		2.45 (1.79 - 3.37)	< 0.001

eTable 2. Clinicopathologic Characteristics of Liver Transplant Recipients by Tumor Recurrence

Variable	Recurrent HCC (n=330)	No recurrent HCC (n=2315)	P Value
Milan criteria at time of transplant - no. (%)			<0.001
Within	266 (80.6)	2197 (94.9)	
Beyond	64 (19.4)	118 (5.1)	
Number of pretransplant LRT - no. (%)			<0.001
0	46 (14.1)	341 (14.8)	
1	70 (21.4)	801 (34.8)	
2	96 (29.4)	664 (28.8)	
3 or more	115 (35.2)	497 (21.6)	
Downstaged to within Milan - no. (%)	54 (16.4)	287 (12.4)	0.044
Maximum AFP - no. (%)			<0.001
< 20	120 (37.0)	1372 (61.0)	
20 - 199	113 (34.9)	600 (26.7)	
200 - 1000	54 (16.7)	192 (8.5)	
> 1000	37 (11.4)	84 (3.7)	
Pretransplant AFP - no. (%)			<0.001
< 20	143 (44.1)	1568 (70.7)	
20 - 199	107 (33.0)	493 (22.2)	
200 - 1000	46 (14.2)	118 (5.3)	
> 1000	28 (8.6)	39 (1.8)	
Pretransplant NLR - median (IQR)	3.1 (1.9-4.7)	2.7 (1.8-4.3)	0.043
Size of largest viable tumor on explant pathology - median (IQR), cm	3.0 (2.0-5.0)	1.8 (0-3.0)	<0.001
Tumor differentiation - no. (%)			<0.001
Necrotic/no viable tumor	28 (8.6)	598 (26.3)	
Well	46 (14.2)	470 (20.7)	
Moderate	165 (50.9)	996 (43.9)	
Poor	85 (26.2)	206 (9.1)	

Vascular invasion - no. (%)			<0.001
None	179 (54.2)	1869 (80.8)	
Microvascular invasion	121 (36.7)	398 (17.2)	
Macrovascular invasion	30 (9.1)	47 (2.0)	

eTable 3. Comparison of Recurrent Tumor Characteristics of by Treatment Modality

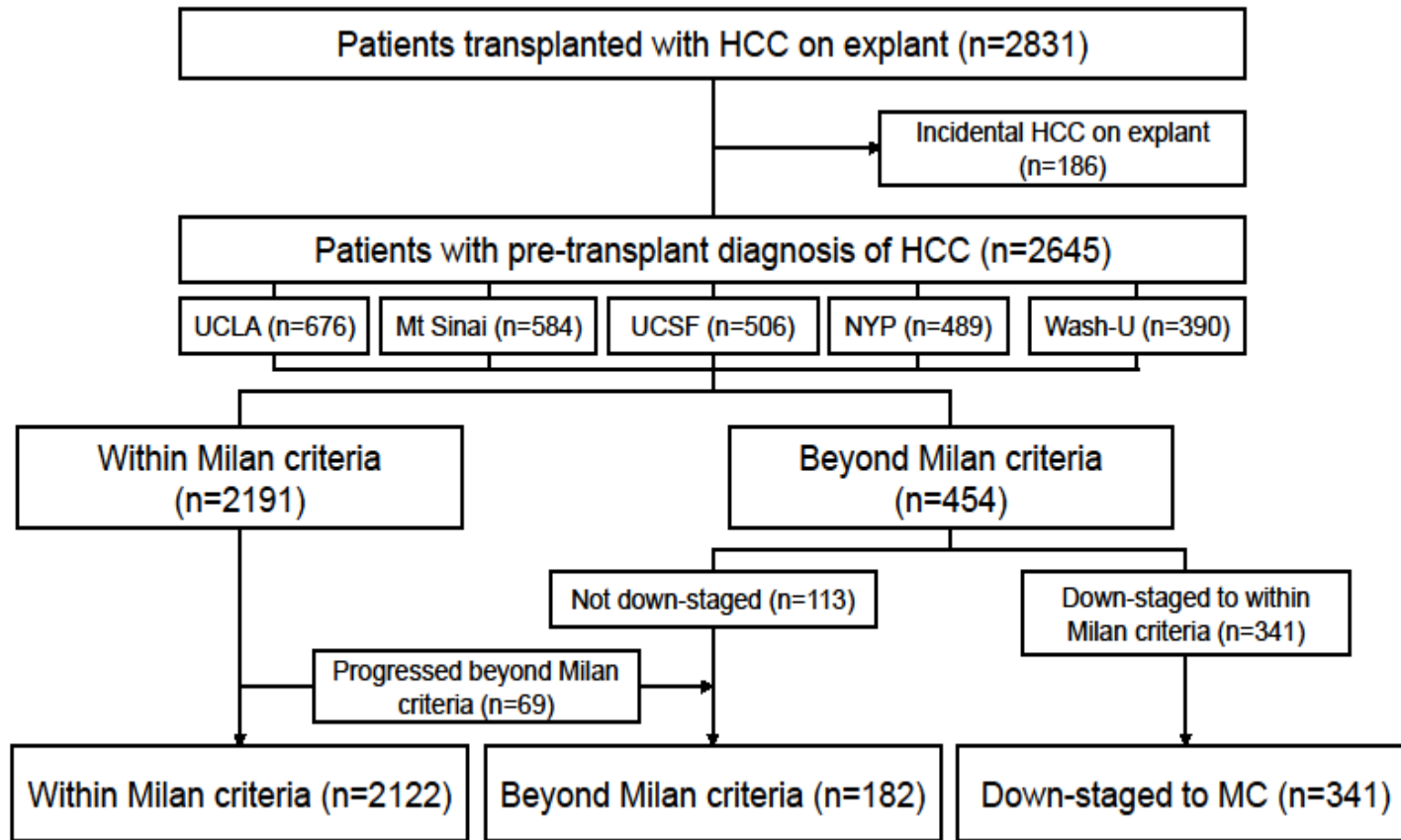
Comparison of Recurrent Tumor Characteristics of by Treatment Modality			
Variable	Resection (n=101)	Other treatment (n=215)	P
Milan criteria at transplant			0.077
Within	87 (86.1)	167 (77.7)	
Outside	14 (13.9)	48 (22.3)	
AFP at transplant - no. (%)			0.232
< 200	82 (83.7)	159 (75.0)	
200 - 1000	10 (10.2)	34 (16.0)	
> 1000	6 (6.1)	19 (9.0)	
Downstaged to Milan - no. (%)	19 (18.9)	32 (14.9)	0.376
Size of largest viable tumor on explant pathology - median (IQR), cm	3.0 (2.0-4.6)	3.0 (1.9-5.0)	0.460
Tumor differentiation - no. (%)			0.537
Complete necrosis/no viable tumor	9 (9.1)	18 (8.5)	
Well differentiated	15 (15.2)	30 (14.2)	
Moderately differentiated	55 (55.6)	104 (49.3)	
Poorly differentiated	20 (20.2)	59 (30.0)	
Vascular invasion on explant pathology - no. (%)			0.148
None	58 (57.4)	109 (50.7)	
Microvascular invasion	38 (37.6)	81 (37.7)	
Macrovascular invasion	5 (5.0)	25 (11.6)	
Time to recurrence - median (IQR), months	25 (12.6-40.8)	14.2 (6.8-28.5)	<0.001
Time to recurrence - no. (%)			0.001
< 1 year	25 (24.8)	94 (43.7)	
> 1 year	76 (75.3)	121 (56.3)	
Number of recurrent tumors - no. (%)			<0.001
Solitary	70 (69.3)	53 (23.9)	
Multiple	31 (30.7)	160 (75.1)	
Size of recurrence - median (IQR), cm	2.5 (1.4-3.8)	2.8 (1.7-4.7)	0.148

Site of recurrence - no. (%)			<0.001
Intrahepatic	4 (4.0)	40 (18.6)	
Extrahepatic	90 (89.1)	122 (56.7)	
Both intra and extrahepatic	7 (6.9)	53 (24.7)	
AFP at recurrence - no. (%)			0.033
< 200	71 (73.2)	119 (60.7)	
200-1000	15 (15.5)	30 (15.3)	
> 1000	11 (11.3)	47 (24.0)	

eTable 4. Factors Associated With Survival After Liver Transplantation

Multivariate Predictors of Post-Recurrence Mortality (n=330)		
Variable	HR (95% CI)	P-Value
Time to recurrence		
> 1 year	Reference	-
< 1 year	2.06 (1.51-2.80)	<0.001
Multiple recurrent tumors		
	1.62 (1.17-2.25)	0.003
AFP at recurrence		
< 200	Reference	-
200 - 1000	1.28 (0.86-1.90)	0.231
> 1000	1.98 (1.34-2.93)	<0.001
Site of recurrence		
Extrahepatic	Reference	-
Intrahepatic	1.42 (0.90-2.23)	0.128
Both intra- and extrahepatic	1.45 (1.01-2.09)	0.045
Treatment of recurrence		
Systemic therapy alone	Reference	-
Resection	0.60 (0.41-0.89)	0.011
LRT	0.77 (0.53-1.14)	0.194
Supportive care	5.78 (3.54-9.42)	<0.001

eFigure 1. Cohort Diagram



eFigure 2. Overall Survival and Recurrence of the Whole Cohort of 2645 Patients With HCC After Transplantation

A, Actuarial probability of overall survival. B, Actuarial probability of recurrence

