

Supplemental Table 1. NASH CRN feature scoring system definitions.

Item	Definition	Score/Code
Steatosis, grade		
	<5%	0
	5-33%	1
	33-66%	2
	>66%	3
Inflammation, grade		
Lobular inflammation	No foci	0
	<2 foci per 200x field	1
	2-4 foci per 200x field	2
	>4 foci per 200x field	3
Portal inflammation	None	0
	Mild	1
	More than Mild	2
Ballooning degeneration, grade		
	None	0
	Few balloon cells	1
	Many cells/prominent ballooning	2
Fibrosis, stage		
	None	0
	Mild, zone 3, perisinusoidal	1A
	Moderate, zone 3, perisinusoidal	1B
	Portal/periportal	1C
	Perisinusoidal and portal/periportal	2
	Bridging fibrosis	3
	Cirrhosis	4
NASH category		
	Not Steatohepatitis	0
	Borderline, Zone 3 pattern	1A
	Borderline, Zone 1 pattern	1B
	Definite Steatohepatitis	2

Supplemental Table 2. Univariate unadjusted hazard ratios and 95% CI's of outcome mortality/liver transplantation

	Hazard Ratio	95% CI of HR	P value
Steatosis, grade			
1	1 (reference)		
2	0.84	0.60, 1.8	0.324
3	0.91	0.64, 1.3	0.616
Lobular inflammation, grade			
0	1 (reference)		
1	0.71	0.39, 1.33	0.288
2	0.93	0.47, 1.83	0.837
3	0.85	0.40, 1.82	0.681
Portal inflammation, grade			
0	1 (reference)		
1	1.16	0.80, 1.66	0.434
2	2.65	1.72, 4.09	<0.001
Ballooning, grade			
0	1 (reference)		
1	1.42	1.01, 2.00	0.043
2	2.40	1.62, 3.55	<0.001
NAS category			
1-2	1 (reference)		
3-4	1.18	0.84, 1.66	0.338
5-8	1.40	0.98, 2.01	0.070
NASH category			
Non-NASH	1 (reference)		
Borderline/suspicious	1.92	1.32, 2.79	0.001
Definitive NASH	2.29	1.65, 3.19	<0.001
Fibrosis stage			
0	1 (reference)		
1	1.88	1.28, 2.76	0.001
2	2.89	1.93, 4.33	<0.001
3	3.76	2.40, 5.89	<0.001
4	10.90	6.06, 19.62	<0.001

Supplemental Table 3. Univariate unadjusted hazard ratios and 95% CI's of outcome liver-related events

	Hazard Ratio	95% CI of HR	P value
Steatosis, grade			
1	1 (reference)		
2	0.68	0.26, 1.82	0.447
3	1.27	0.52, 3.11	0.600
Lobular inflammation, grade			
0	1 (reference)		
1	0.71	0.39, 1.33	0.288
2	0.93	0.47, 1.83	0.837
3	0.85	0.40, 1.82	0.681
Portal inflammation, grade			
0	1 (reference)		
1	1.78	0.51, 6.25	0.368
2	8.24	2.26, 30.00	0.001
Ballooning, grade			
0	1 (reference)		
1	2.36	0.93, 5.98	0.072
2	5.77	2.25, 14.76	<0.001
NAS category			
1-2	1 (reference)		
3-4	1.44	0.51, 4.06	0.486
5-8	2.70	0.99, 7.31	0.051
NASH category			
Non-NASH	1 (reference)		
Borderline/suspicious	6.37	1.86, 21.78	0.003
Definitive NASH	10.16	3.34, 30.93	<0.001
Fibrosis stage			
0	1 (reference)		
1	2.31	0.62, 8.66	0.213
2	6.68	2.02, 22.06	0.002
3	13.42	4.23, 42.55	<0.001
4	52.89	13.31, 210.15	<0.001

Supplemental Table 4. Cumulative probability (unadjusted) of outcomes by liver biopsy category in patients with early (fibrosis stage 0-2) disease

Liver Biopsy Features	Mortality/liver transplantation (n = 548)			Liver-related events (n = 547)		
	Events (n)	Unadjusted cumulative (%) ^a	P value	Events (n)	Unadjusted cumulative (%) ^a	P value
Steatosis, grade			0.722			0.093
1	71/236	30.1		5/236	2.1	
2	42/178	23.6		3/177	1.7	
3	39/134	29.1		7/134	5.2	
Lobular inflammation, grade			0.522			0.526
0	10/30	33.3		0/30	0	
1	109/392	27.8		11/391	2.8	
2	27/92	29.3		4/92	4.3	
3	6/34	17.6		0/34	0	
Portal inflammation, grade			0.367			0.590
0	40/157	25.5		3/156	1.9	
1	95/343	27.7		10/343	2.9	
2	17/48	35.4		2/48	4.2	
Ballooning, grade			0.050			0.162
0	102/378	28.3		8/377	2.1	
1	36/129	32.7		5/129	3.9	
2	14/41	42.5		2/41	4.9	
NAS category			0.730			0.461
1-2	58/201	28.9		5/201	2.5	
3-4	59/223	26.5		5/222	2.2	
5-8	35/124	28.2		5/124	4.0	
NASH category			0.009			0.004
Non-NASH	84/333	25.2		4/332	1.2	
Borderline/suspicious	33/93	35.5		5/93	5.4	
Definitive NASH	35/122	28.7		6/122	4.9	
Fibrosis stage			<0.001			0.001
0	74/322	23.0		5/321	1.6	
1	42/141	29.8		4/141	2.8	
2	36/85	42.3		6/85	7.1	

FOOTNOTE: ^a Estimated using Kaplan–Meier analysis

Supplemental Table 5. Multivariate-adjusted hazard ratios and 95% CI's of outcome mortality/liver transplantation in patients with early (stage 0-2) disease

	Hazard Ratio	95% CI of HR	P value
Model 1			
Fibrosis, stage 0	1 (reference)		
Fibrosis, stage 1	2.04	1.38, 3.02	<0.001
Fibrosis, stage 2	3.10	2.05, 4.68	<0.001
Model 2			
Fibrosis, stage 0	1 (reference)		
Fibrosis, stage 1	1.85	1.19, 2.89	0.007
Fibrosis, stage 2	2.17	1.34, 3.51	0.002
Age (years)	1.07	1.05, 1.08	<0.001
Diabetes (yes)	1.95	1.25, 3.03	0.003
Smoking, Never	1 (reference)		
Former	1.42	0.83, 2.44	0.203
Current	2.20	1.32, 3.67	0.002
Statins use (yes)	0.28	0.11, 0.72	0.008

FOOTNOTE

Model 1 includes the liver biopsy features statistically significant by univariate analysis (supplemental table 4) plus calendar year of liver biopsy and liver biopsy size.

Model 2 includes variables from model 1 plus age, gender, race, BMI, diabetes, hypertension, statins use, site, smoking.

Supplemental Table 6. Cumulative probability (unadjusted) of outcomes by NASH category and fibrosis stage

NASH category	Mortality/liver transplantation (n = 619)			Liver-related events (n = 615)		
	Events (n)	Unadjusted cumulative (%) ^a	P value	Events (n)	Unadjusted cumulative (%) ^a	P value
Non-NASH			<0.001			0.438
Fibrosis (-)	62/279	22.2		4/278	1.4	
Fibrosis (+)	23/56	41.1		0/56	0	
NASH (borderline, definitive)			0.018			0.070
Fibrosis (-)	12/43	27.9		1/43	2.3	
Fibrosis (+)	96/241	39.8		21/238	8.8	

FOOTNOTE: ^a Estimated using Kaplan–Meier analysis

SUPPLEMENTAL FIGURES LEGEND

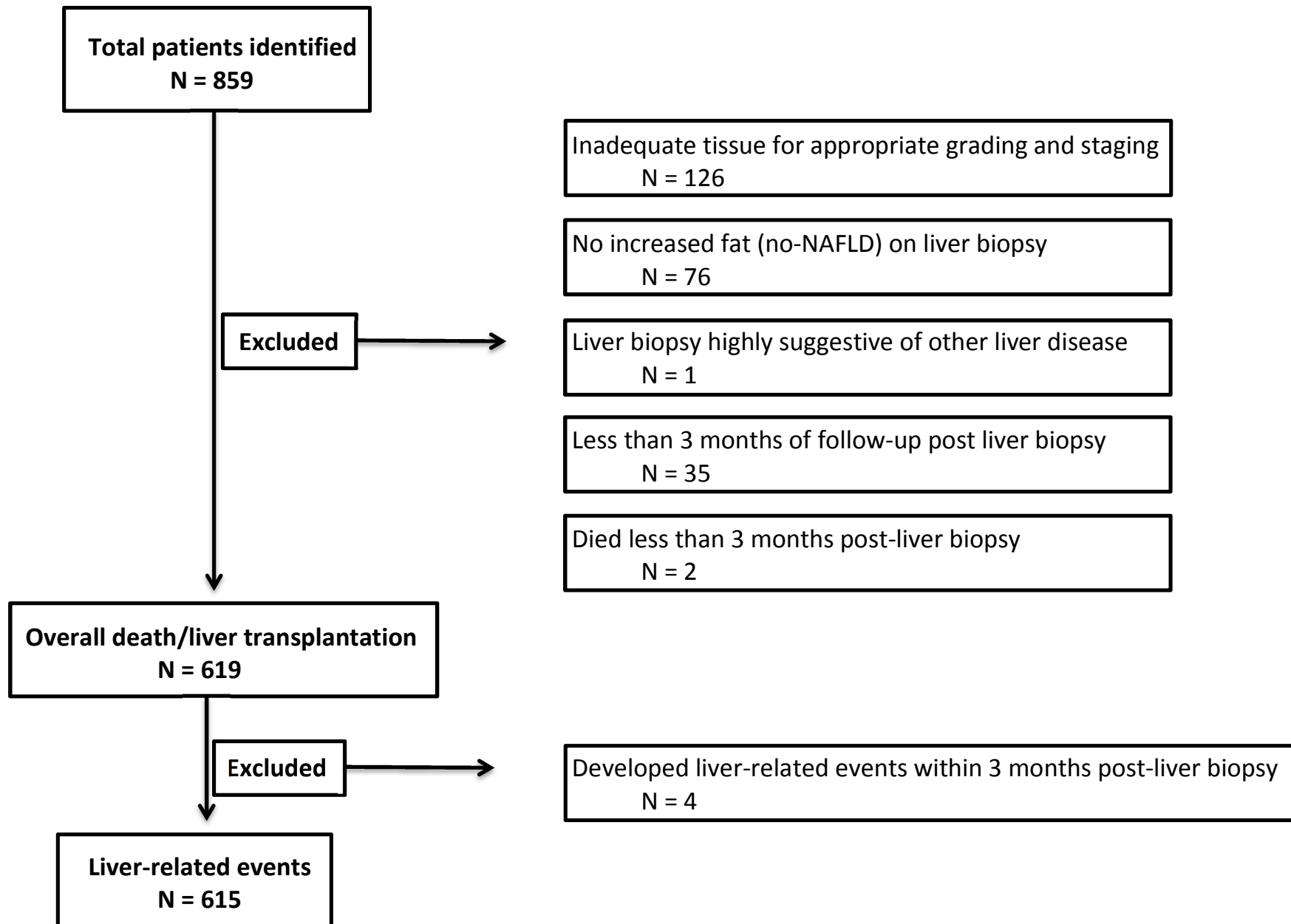
Figure 1. Algorithm of patient selection

Figure 2. Number of liver biopsies by calendar year (decade)

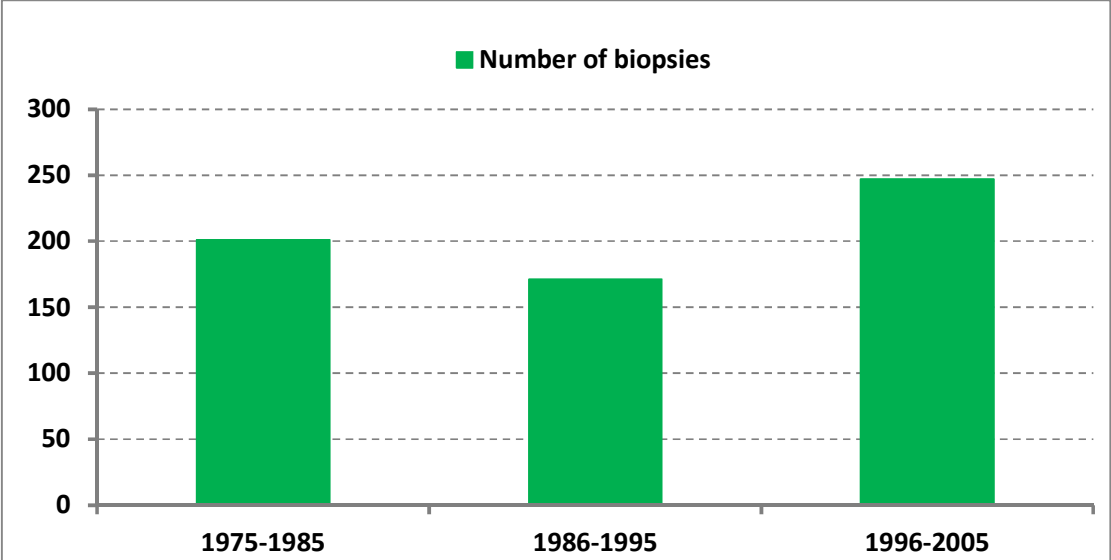
Figure 3. Survival free or liver transplantation based on liver histology features, (A to G)

Figure 4. Survival free of liver-related events based on liver histology features, (A to G)

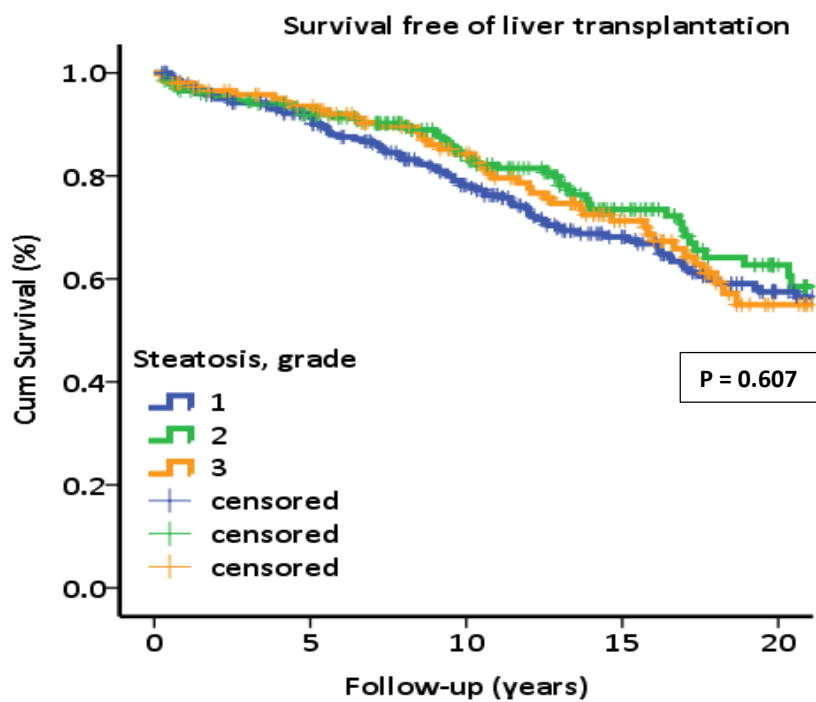
Supplemental Figure 1



Supplemental Figure 2

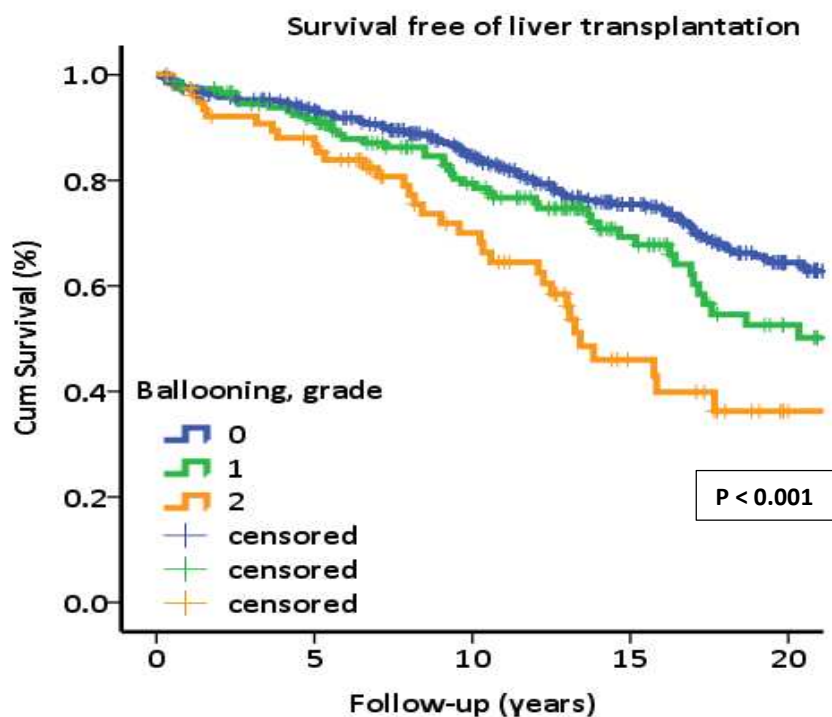


Supplemental Figure 3A



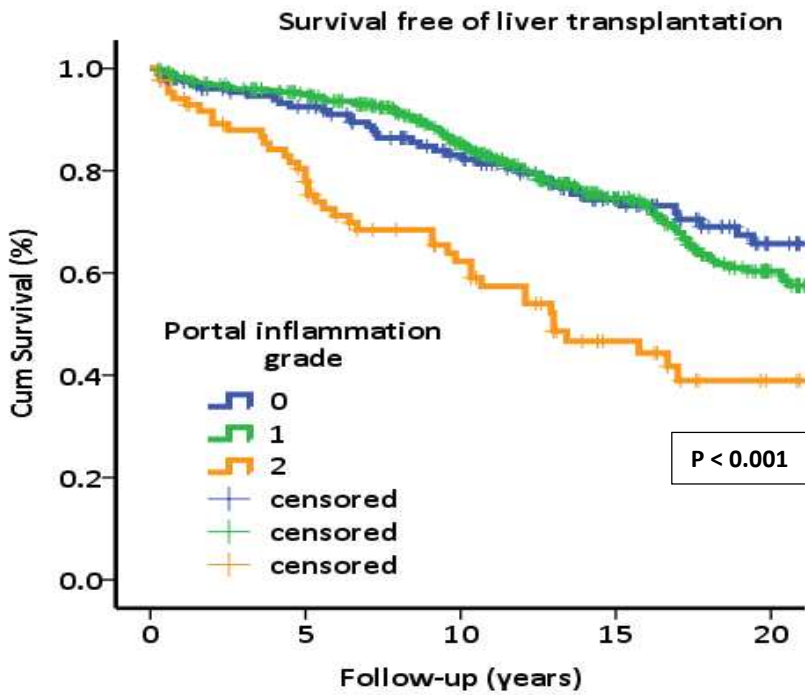
Grade 1	269	222	166	106	59
Grade 2	204	172	122	68	30
Grade 3	146	124	92	57	19

Supplemental Figure 3B



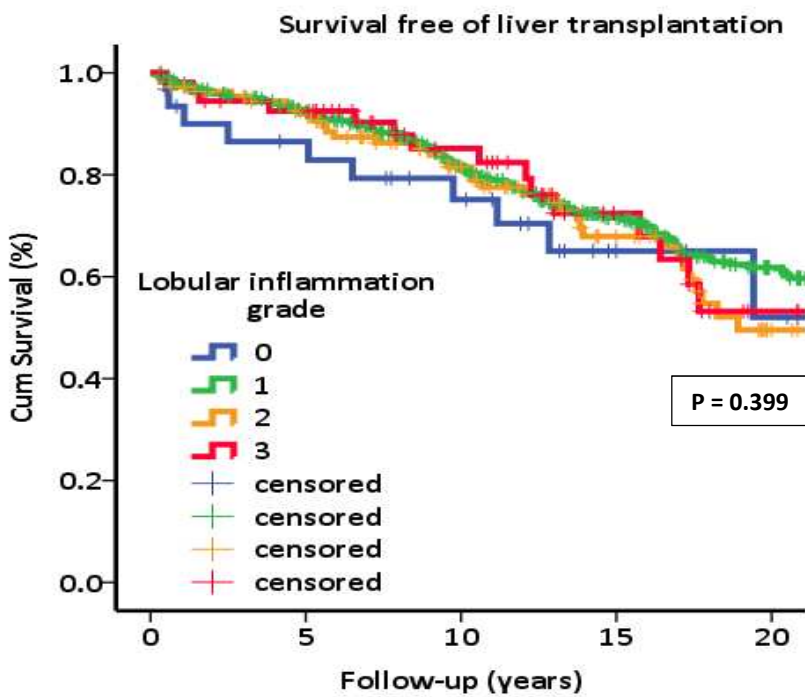
Grade 0	389	326	253	172	85
Grade 1	150	127	89	46	22
Grade 2	80	64	38	15	2

Supplemental Figure 3C



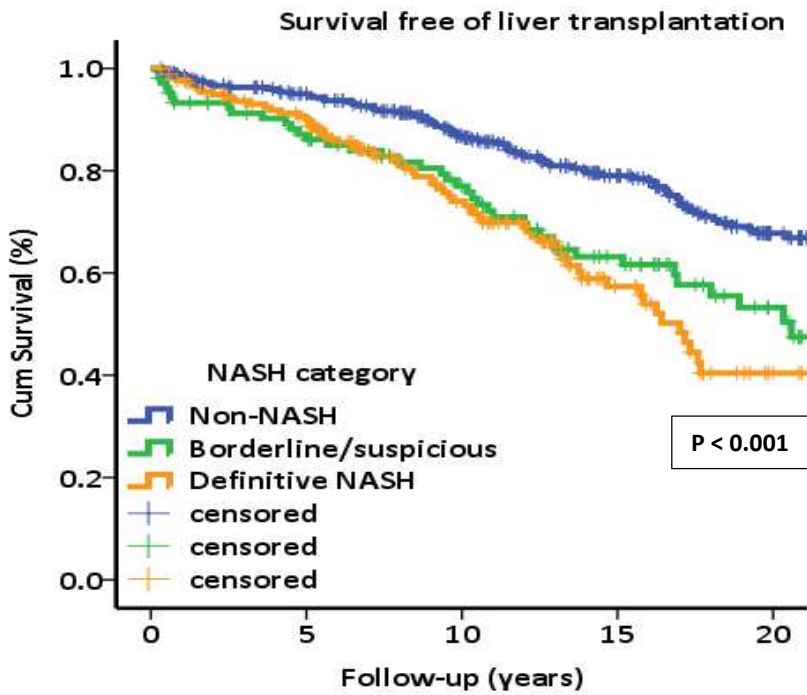
Grade 0	157	128	97	63	33
Grade 1	376	328	245	150	66
Grade 2	86	62	39	20	9

Supplemental Figure 3D



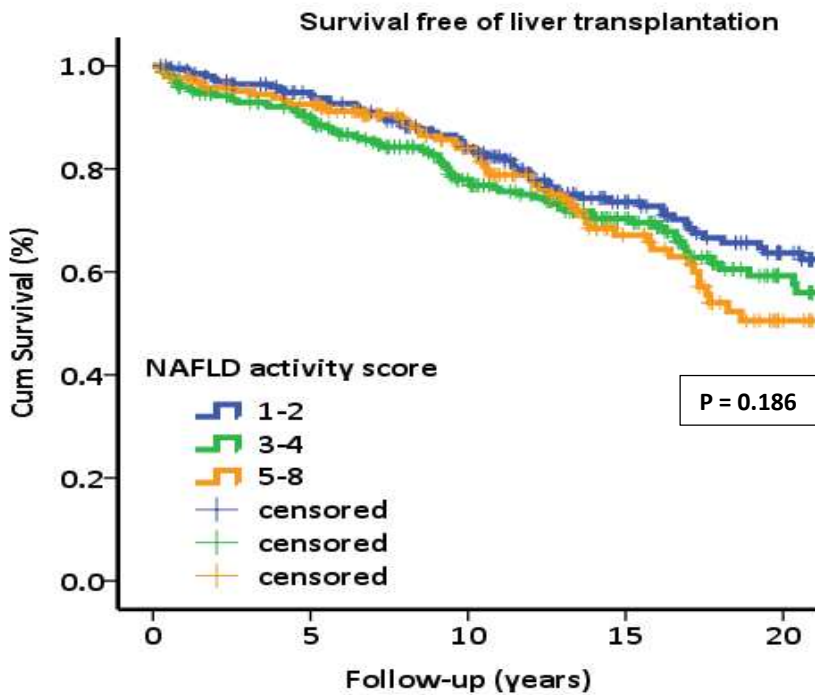
Grade 0	31	24	18	7	4
Grade 1	423	353	268	173	87
Grade 2	110	94	65	37	12
Grade 3	55	48	31	16	6

Supplemental Figure 3E



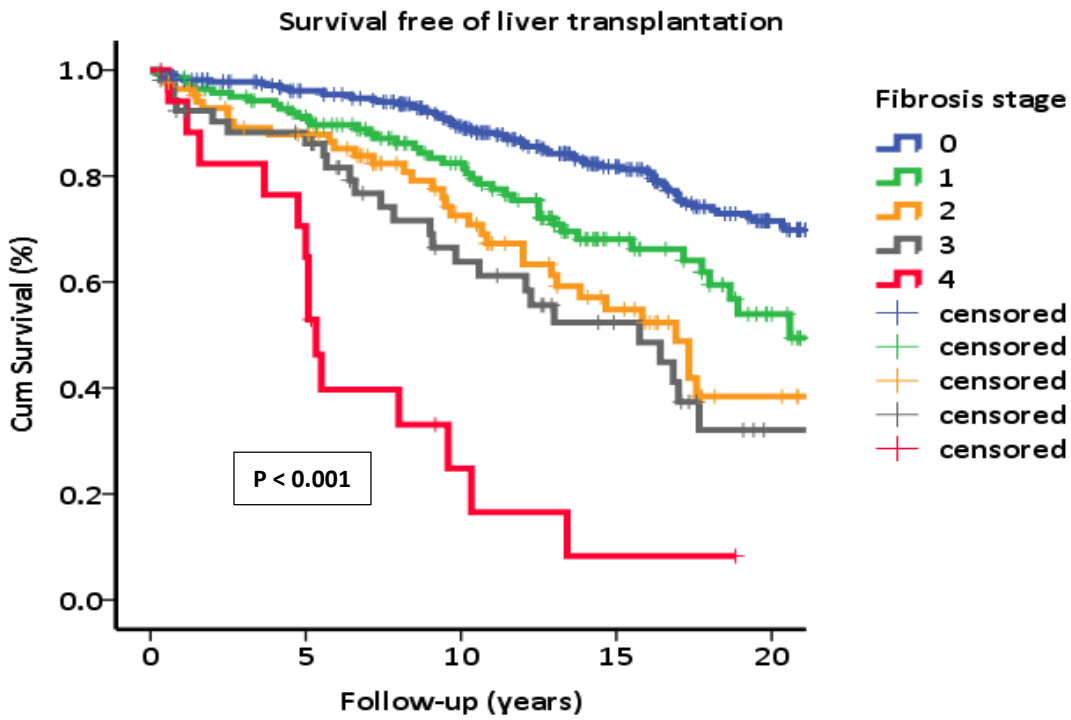
Non-NASH	335	287	227	156	79
Bord/susp	105	84	65	42	19
Def. NASH	179	148	90	36	11

Supplemental Figure 3F



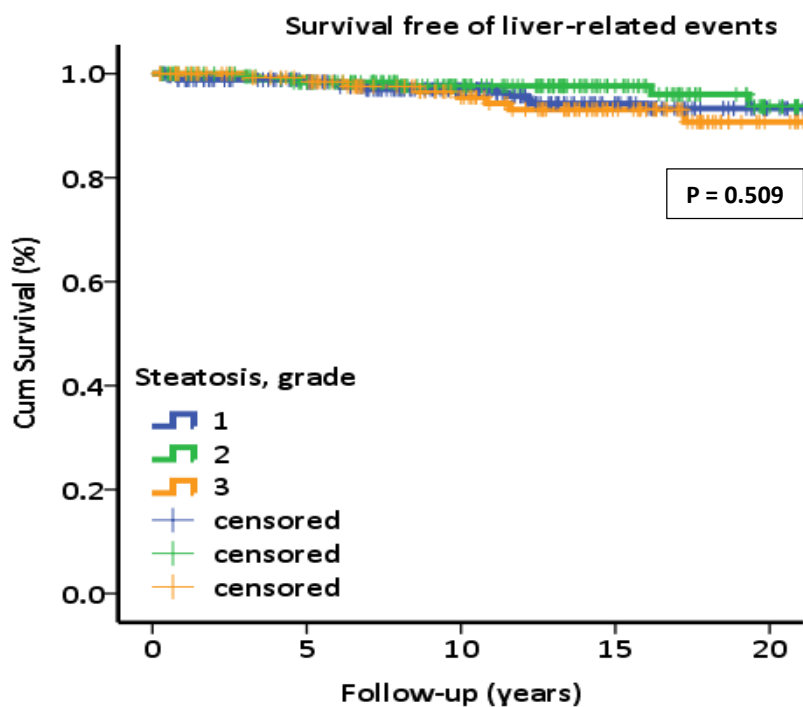
NAS 1-2	205	174	142	94	53
NAS 3-4	247	202	141	89	36
NAS 5-8	167	143	99	51	20

Supplemental Figure 3G



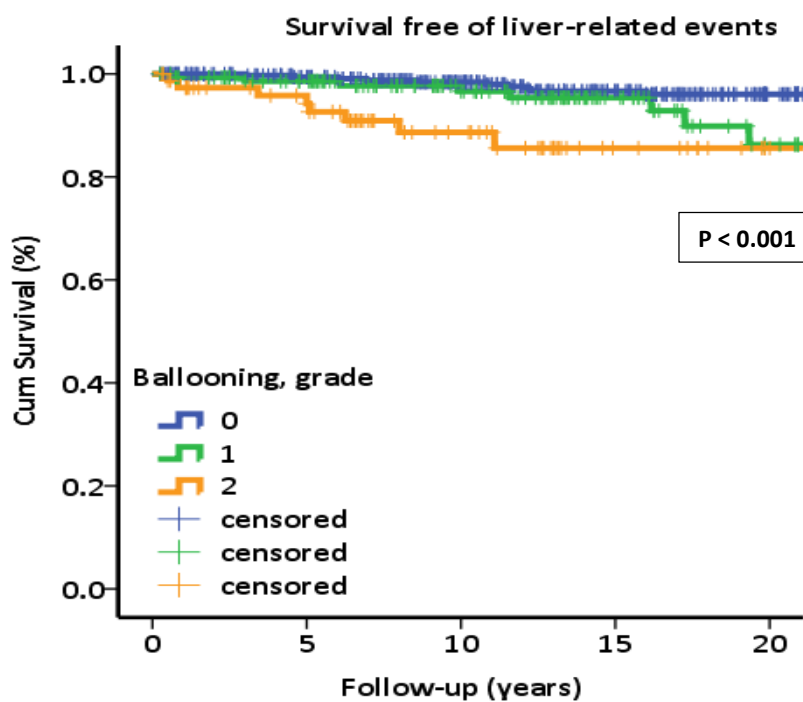
Stage 0	322	276	228	157	84
Stage 1	141	120	85	38	14
Stage 2	85	69	42	24	8
Stage 3	53	42	24	14	3
Stage 4	18	12	3	1	0

Supplemental Figure 4A



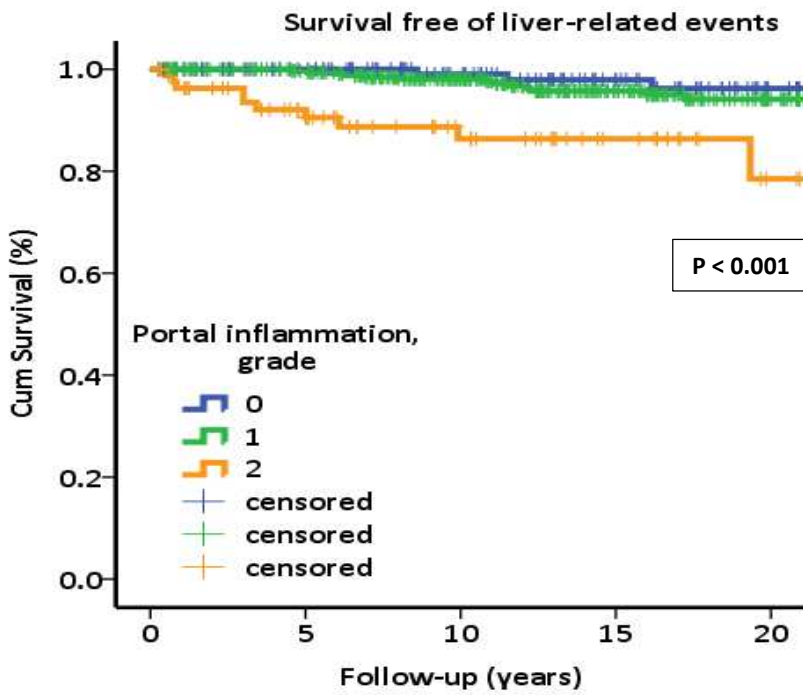
Grade 1	269	222	167	107	58
Grade 2	202	170	121	69	30
Grade 3	144	122	89	54	19

Supplemental Figure 4B



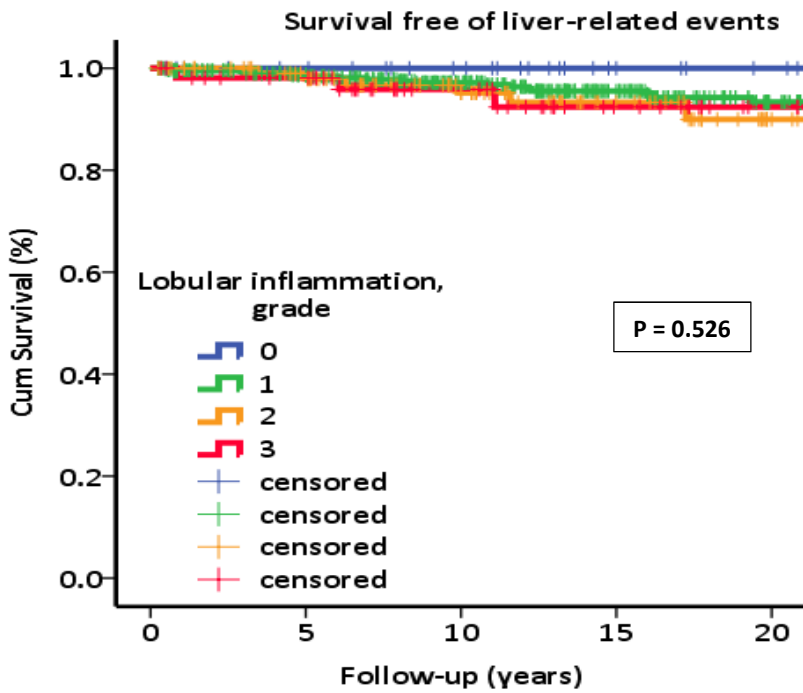
Grade 0	387	327	254	172	84
Grade 1	150	126	89	46	21
Grade 2	78	61	34	12	2

Supplemental Figure 4C



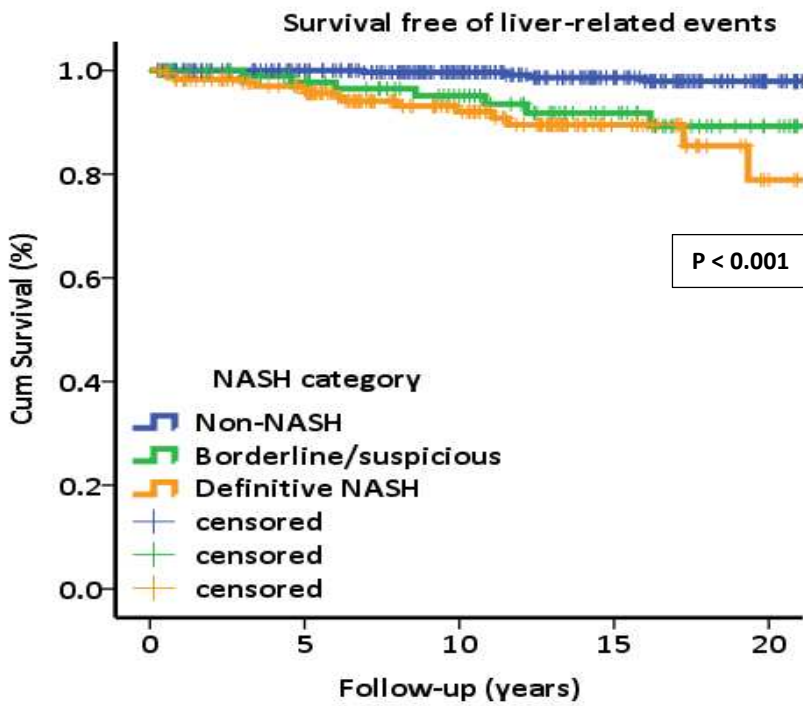
Grade 0	156	128	97	64	33
Grade 1	374	326	243	146	66
Grade 2	85	60	37	20	8

Supplemental Figure 4D



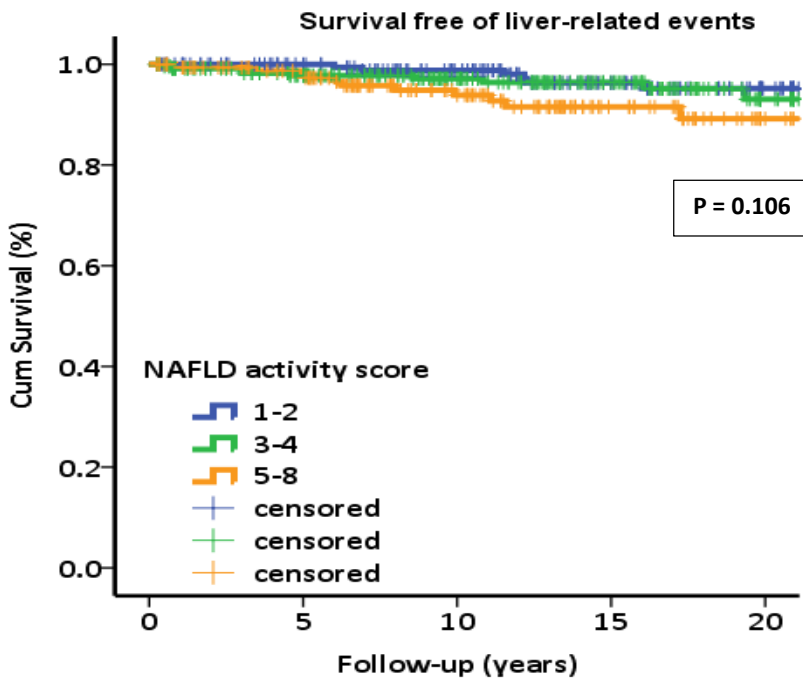
Grade 0	30	24	18	8	4
Grade 1	421	350	266	170	85
Grade 2	109	92	62	36	12
Grade 3	55	48	31	16	6

Supplemental Figure 4E



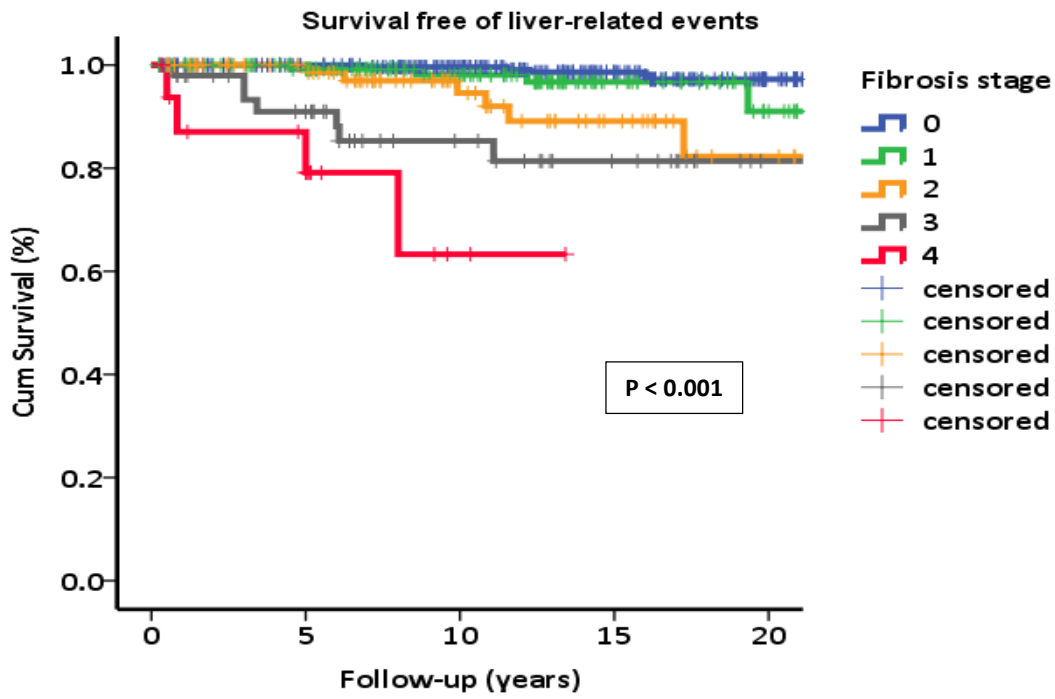
Non-NASH	334	287	227	156	79
Bord/susp	104	83	65	41	18
Def. NASH	177	144	85	33	10

Supplemental Figure 4F



NAS 1-2	205	174	142	93	52
NAS 3-4	245	200	141	89	35
NAS 5-8	165	140	94	48	20

Supplemental Figure 4G



Stage 0	321	276	228	157	84
Stage 1	141	120	85	37	12
Stage 2	85	69	39	22	8
Stage 3	51	38	23	14	3
Stage 4	17	11	2	0	0