The Effects of Advanced Donor Age on Post-Liver Transplant Prognosis of Patients with Nonalcoholic Steatohepatitis: Analysis of UNOS Registry

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Background and Aims

With the advent of obesity, nonalcoholic steatohepatitis (NASH) has now become one of the leading causes of liver transplant (LT) in the US. To meet the demand, LT donor criteria have expanded to include donors with advanced donor age. However, there is a clinical concern that grafts from aged donors may affect recipient outcomes. This study plans to investigate the prognostic effects of advanced donor age on post-LT prognosis of patients with NASH using a national transplant registry.

Methods

The UNOS-STAR database (2005-2019) was used to select recipients with NASH who underwent LT. Patients that had living donors, multi-organ transplants, or were under 18 years of age were excluded. The resulting recipient sample was stratified using donor age intervals using the following age-delineated categories: quinquagenarians (QU), sexagenarians (SX), septuagenarians (SP), octogenarians (OC). The recipients whose grafts were from donors aged less than 50 were categorized into the reference group (RG). For each comparison, Cox regression iterations that adjusted for MELD and covariates were performed using all-cause mortality as the endpoint. Cumulative risk curves were drawn for each comparison.

Conclusion

This study shows that recipients who received grafts from advanced-age donors have a higher risk of all-cause death and graft failure in NASH-LT patients. Liver grafts from advanced-age donors and their recipients should be carefully assessed prior to LT, in order to mitigate any adverse outcomes.

Results

The RG, QU, SX, SP, and OC donor groups had the following number of recipient populations, respectively: 5953, 2088, 1474, 569, and 78. The median post-LT follow-up time for the study was 3.04 years. The recipient mean ages for each donor category was as follows (RG: 57.1 vs QU: 57.9y p=0.01; SX: 59.2y p<0.001; SP: 60.6y p<0.001; OC: 62.4y p<0.001). The recipient MELD scores for each donor category were as follows (RG: 24.40 ± 8.96 vs QU: 23.20 ± 8.49 p<0.001; SX: 21.70 ± 7.77 p<0.001; SP: 20.00 ± 7.06 p<0.001; OC: 18.10 ± 7.12 p<0.001). Upon performing Cox iterations, the recipients belonging to the advanced donor age groups (except SX) were at a higher risk of all-cause death than the RG (QU: adjusted hazard ratio (aHR) 1.13 95% CI 1.02-1.26; SP: 1.20 95% CI 1.01-1.43; OC: 2.04 95% CI 1.48-2.81). This was also reflected in the higher case-incidence rates found in recipients with advanced aged donors (expressed in per 1000 person-years; RG: 48.72, QU: 55.47, SX: 54.49, SP: 60.65, OC: 113.26). Similarly, recipients belonging to the advanced-age donor groups had higher risks of graft failure (SX: 1.41 95% CI 1.04-1.92; OC: 4.48 95%CI 2.24-9.00) and graft failure incidence rates (in 1000 person-years; RG: 6.86, SX: 8.82, OC: 24.86).

Univariate Analysis

Age Group	Donor Age <50 (Control)	Quinquagenarian Donors		Sexagenarian Donors		Septuagenarian Donors		Octogenarian Donors	
Number of Patients	**5953**	**2088**		**1474**		**569**		**78**	
Recipient Demographics			p		p		p		p
Age, mean ± SD, y	57.10 ± 9.64	57.90 ± 9.08	0.01	59.20 ± 8.34	< 0.001	60.60 ± 7.68	< 0.001	62.40 ± 7.18	< 0.001
Male sex, *n* (%)	3338 (56.10)	1199 (57.40)	0.30	794 (53.90)	0.13	266 (46.70)	< 0.001	36 (46.20)	0.10
Race, *n* (%)			0.31		0.46		0.45 †		0.82 †
White	4736 (79.60)	1701 (81.50)		1171 (79.40)		454 (79.80)		65 (83.30)	
Black	186 (3.12)	56 (2.68)		47 (3.19)		12 (2.11)		2 (2.56)	
Hispanic	841 (14.10)	263 (12.60)		203 (13.80)		85 (14.90)		8 (10.30)	
Asian	117 (1.97)	39 (1.87)		26 (1.76)		14 (2.46)		2 (2.56)	
Other	73 (1.23)	29 (1.39)		27 (1.83)		4 (0.70)		1 (1.28)	
BMI, mean ± SD, kg/m²	31.20 ± 6.24	31.20 ± 6.17	1.00	31.20 ± 6.00	0.97	30.40 ± 6.16	0.002	29.50 ± 5.14	0.01
Hepatic Variables									
MELD Scores, mean ± SD	24.40 ± 8.96	23.20 ± 8.49	< 0.001	21.70 ± 7.77	< 0.001	20.00 ± 7.06	< 0.001	18.10 ± 7.12	< 0.001
Donor Demographics									
Donor Age, mean ± SD, y	32.10 ± 10.60	54.30 ± 2.87	< 0.001	64.00 ± 2.81	< 0.001	73.80 ± 2.73	< 0.001	82.20 ± 2.25	< 0.001
Donor Male sex, *n* (%)	3814 (64.10)	1093 (52.30)	< 0.001	744 (50.50)	< 0.001	243 (42.70)	< 0.001	35 (44.90)	< 0.001
Donor Race, *n* (%)			< 0.001		< 0.001		< 0.001		0.17 †
White	3802 (63.90)	1374 (65.80)		1026 (69.60)		416 (73.10)		58 (74.40)	
Black	1139 (19.10)	438 (21.00)		259 (17.60)		83 (14.60)		10 (12.80)	
Hispanic	766 (12.90)	183 (8.76)		114 (7.73)		41 (7.21)		8 (10.30)	
Asian	112 (1.88)	58 (2.78)		50 (3.39)		14 (2.46)		2 (2.56)	
Other	134 (2.25)	35 (1.68)		25 (1.70)		15 (2.64)		0 (0.00)	
Donor BMI, mean ± SD, kg/m²	27.80 ± 6.71	29.40 ± 7.13	< 0.001	29.10 ± 6.85	< 0.001	27.40 ± 5.83	0.81	26.00 ± 5.97	0.03

† Fisher's Test

Cox Iterations for Primary Endpoints

Quinquagenarian Donors vs Donors Age <50

(A) All-Cause Mortality

Incidence Rates per 1000 Person-Years			
Quinquagenarian Donors	55.47	(50.83 - 60.39)	
Donors Age <50	48.72	(46.11 - 51.43)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.03 *	1.13	(1.01 - 1.25)
2	0.03 *	1.12	(1.01 - 1.25)
3	0.01 *	1.15	(1.03 - 1.27)
†FM	0.02 *	1.13	(1.02 - 1.26)

(B) Graft Failure

Incidence Rates per 1000 Person-Years			
Quinquagenarian Donors	8.10	(6.35 - 10.17)	
Donors Age <50	6.86	(5.88 - 7.95)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.22	1.19	(0.90 - 1.56)
2	0.22	1.19	(0.90 - 1.56)
3	0.16	1.22	(0.93 - 1.60)
†FM	0.12	1.25	(0.95 - 1.65)

Sexagenarian Donors vs Donors Age <50

(C) All-Cause Mortality

Incidence Rates per 1000 Person-Years			
Sexagenarian Donors	54.49	(49.08 - 60.31)	
Donors Age <50	48.72	(46.11 - 51.43)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.30	1.06	(0.95 - 1.20)
2	0.31	1.06	(0.94 - 1.20)
3	0.09	1.11	(0.98 - 1.25)
†FM	0.18	1.09	(0.96 - 1.23)

(D) Graft Failure

Incidence Rates per 1000 Person-Years			
Sexagenarian Donors	8.82	(6.69 - 11.42)	
Donors Age <50	6.86	(5.88 - 7.95)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.08	1.31	(0.97 - 1.77)
2	0.08	1.31	(0.97 - 1.77)
3	0.04 *	1.38	(1.02 - 1.87)
†FM	0.03 *	1.41	(1.04 - 1.92)

Septuagenarian Donors vs Donors Age <50

(E) All-Cause Mortality

Incidence Rates per 1000 Person-Years			
Septuagenarian Donors	60.65	(51.87 - 70.41)	
Donors Age <50	48.72	(46.11 - 51.43)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.09	1.15	(0.98 - 1.36)
2	0.10	1.15	(0.97 - 1.36)
3	0.02 *	1.22	(1.03 - 1.44)
†FM	0.03 *	1.20	(1.01 - 1.43)

(F) Graft Failure

Incidence Rates per 1000 Person-Years			
Septuagenarian Donors	9.04	(5.80 - 13.42)	
Donors Age <50	6.86	(5.88 - 7.95)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	0.12	1.40	(0.91 - 2.16)
2	0.12	1.40	(0.91 - 2.16)
3	0.07	1.49	(0.96 - 2.31)
†FM	0.05	1.55	(1.00 - 2.42)

Octogenarian Donors vs Donors Age <50

(G) All-Cause Mortality

Incidence Rates per 1000 Person-Years			
Octogenarian Donors	113.26	(82.52 - 150.50)	
Donors Age <50	48.72	(46.11 - 51.43)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	< 0.001 ***	1.96	(1.43 - 2.69)
2	< 0.001 ***	1.88	(1.37 - 2.58)
3	< 0.001 ***	2.06	(1.50 - 2.82)
†FM	< 0.001 ***	2.04	(1.48 - 2.81)

(H) Graft Failure

Incidence Rates per 1000 Person-Years			
Octogenarian Donors	24.86	(11.43 - 46.67)	
Donors Age <50	6.86	(5.88 - 7.95)	

Sequential Cox Regression Analysis

Model	p-value	aHR	95% CI
1	< 0.001 ***	3.94	(2.00 - 7.76)
2	< 0.001 ***	3.89	(1.96 - 7.71)
3	< 0.001 ***	4.17	(2.09 - 8.32)
†FM	< 0.001 ***	4.48	(2.24 - 9.00)

* p < 0.05, ** p < 0.01, *** p < 0.001

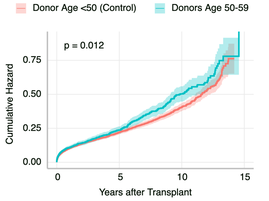
† FM indicates Final Model

Model 1 includes VOI (variable of interest) and demographics, model 2 includes VOI, demographics, comorbidities, and medications, model 3 includes VOI, demographics, comorbidities, medications, and biomarkers, and the final model includes VOI, demographics, comorbidities, medications, biomarkers, and donor information

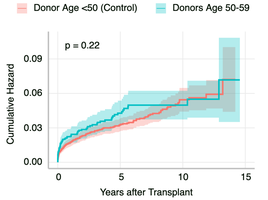
Prognostic Curves for Primary Endpoints

Quinquagenarian Donors vs Donors Age <50

(A) All Cause Mortality

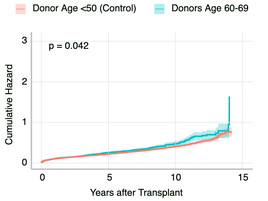


(B) Graft Failure

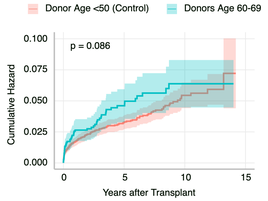


Sexagenarian Donors vs Donors Age <50

(C) All Cause Mortality

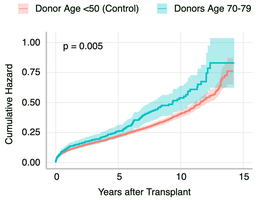


(D) Graft Failure

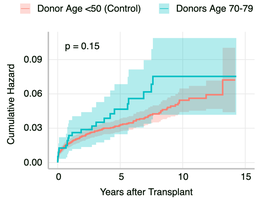


Septuagenarian Donors vs Donors Age <50

(E) All Cause Mortality

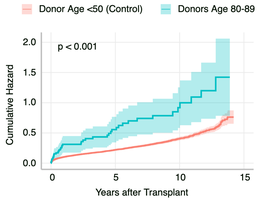


(F) Graft Failure

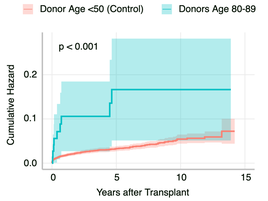


Octogenarian Donors vs Donors Age <50

(G) All Cause Mortality



(H) Graft Failure



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