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## Short Communication

## Life expectancy after liver transplantation for metabolic disease: Alpha-1-antitrypsin deficiency, Wilson's disease, or hemochromatosis



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Metabolic disease is an uncommon etiology for liver transplantation, representing less than 1% of all such transplants worldwide [1]. The most frequent in this rare group are three genetic conditions: Alpha-1-Antitrypsin (AAT) Deficiency (inability to produce the AAT protein), Wilson's Disease (a rare disorder characterized by excess copper storage), and Hemochromatosis (genetic iron overload).

Several studies have reported on life expectancy after liver transplantation for some of the more common etiologies such as HCC [2], and also for some unusual ones including primary biliary cirrhosis, primary sclerosing cholangitis, or Hepatitis B cirrhosis [3]. We here examine survival after transplant for the aforementioned three metabolic causes, and investigate whether survival in these groups has improved since 2002.

The data and methods used here are the same as those in the prior studies [2,3]. Briefly, we analyzed de-identified data from the OPTN database, which contains information on 130,665 first time, single organ liver transplants. We restricted attention to patients meeting three

criteria: (1) reason for transplant as AAT (etiology code 4300), Wilson's (4301), or Hemochromatosis (4302), (2) age 35 to 74 years, and (3) transplanted during the MELD era, calendar years 2002 to 2018.

Demographic and medical characteristics of the patients are given in Supplemental Table 1, and the multivariate Cox (proportional hazards regression) survival models in Supplemental Table 2. Long-term survival was similar comparing the AAT and Wilson's cohorts (hazard ratio [HR] 0.97,  $P=0.88$ ), but was much worse in Hemochromatosis (HR=1.67,  $P<0.001$ ). Over the 17-year study period, there was evidence of improvement in survival during the first year post transplant (HR=0.96 per calendar year;  $P=0.013$ ). Amongst those who had already survived one year post transplant, however, and as shown in the prior studies, there was no evidence of improvement (HR=1.03,  $P=0.26$ ).

The resulting life expectancies by age, sex, and group are shown in Table 1 below. Overall, life expectancy was much reduced from that of the general population (GP), and varied according to age, medical

**Table 1**  
Life expectancies based on the multivariate model of Supplemental Table 2.

Starting Time	CurrentAge	Male			Female		
		AAT/Wilson's	Hemo-chromatosis	GP	AAT/Wilson's	Hemo-chromatosis	GP
<b>From tx</b>	40	19	15	39	19	14	43
	50	17	13	30	16	12	33
	60	14	11	22	14	10	25
	70	12	9	15	12	9	17
<b>1-yr post</b>	41	19	15	38	19	15	42
	51	17	13	29	16	13	33
	61	15	12	21	14	11	24
	71	13	10	14	13	10	16
<b>5-yrs post</b>	45	16	13	34	16	12	38
	55	14	11	26	14	10	29
	65	12	9	18	12	9	21
	75	10	8	11	10	8	13

risk factors, and health status. Such information may prove helpful in medical decision-making regarding treatment for both liver disease and other medical conditions.

### Conflicts of Interest

None.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.liver.2021.100062](https://doi.org/10.1016/j.liver.2021.100062).

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Robert M. Shavelle\*

Ji Hun Kwak

Jordan C. Brooks

Rachel C. Saur

*Life Expectancy Project, San Francisco, CA, United States*

\*Corresponding author.

E-mail address: [Shavelle@LifeExpectancy.org](mailto:Shavelle@LifeExpectancy.org) (R.M. Shavelle).

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**Supplemental Table 1. Patient demographics and medical risk factors (figures are column percentages)**

<b>Variable</b>	<b>Categories</b>	<b>AAT N=1,112</b>	<b>Wilson's N= 163</b>	<b>Hemo N= 387</b>
Age (years)	35-44	12	44	11
	45-54	31	37	30
	55-64	40	17	42
	65-74	17	2	17
Sex	Male	73	59	82
Race	White	94	79	87
Transplant year	2002-2005	18	18	26
	2006-2009	22	18	27
	2010-2013	22	28	18
	2014-2018	38	36	29
MELD score at transplant	6-10	2	3	7
	11-18	23	18	29
	19-24	27	17	20
	25-40	41	39	36
	Missing/Other	7	23	8
Donor type	Living	3	4	3
Weight	Underweight (BMI<18)	1	1	1
	Normal weight (18-25)	17	27	21
	Overweight (25-30)	33	38	39
	Obese (30+)	49	34	39
Presence of Hepatitis C	Yes	3	4	7
Diabetes	Yes	22	7	31
Functional status at transplant (Karnofsky Performance Status)	100% (normal)	1	2	2
	90% - Minor symptoms of disease	2	1	3
	80% - Normal activity with effort	8	7	10
	70% - Cares for self, but unable to carry on normal activity	12	9	14
	60% - Requires occasional assistance	13	10	7
	50% - Requires considerable assistance	13	10	12
	40% - Disabled	10	8	6
	30% - Severely disabled	9	7	8
	20% - Very sick	15	20	14
	10% - Moribund	3	12	4
Missing/Other	14	14	20	
Ascites	Yes	91	80	83
Hepatic encephalopathy	No	24	32	28
	Mild (1-2)	62	53	57
	Severe (3-4)	13	15	14
	Unknown/missing	1	0	1

Donor age	0-19	11	12	10
	20-49	54	57	54
	50-79	35	31	36
	80+	0	0	0
Portal Vein Thrombosis	Yes	10	7	10
Time spent on waitlist	<180 days	71	81	73
	181-365 days	15	6	12
	> 365 days	14	13	15
Length of Hospital Stay Post Transplant	0-10 days	52	52	48
	11 to 30 days	37	40	37
	31+ days	10	7	14
	Missing	1	1	1
Previous malignancy	Yes	9	2	10
Ventilator use at transplant	Yes	4	14	4
Working at time of transplant	Yes	13	19	14
Dialysis within 1 week of tx	Yes	9	19	11

**Supplemental Table 2. Hazard ratios (P-values) -- from Cox Proportional Hazards Regression models.§**

Variable	Categories	Univariate	Multivariate
Age (years)§	(Continuous)	1.03 (<0.0001)	1.03 (<0.0001)
Sex§	Male	0.96 (0.73)	1.00 (0.96)
Race§	White	1.02 (0.93)	0.88 (0.51)
Transplant year§	(Continuous)	0.98 (0.18)	0.98 (0.08)
Etiology	Hemochromatosis	1.76 (<0.0001)	1.67 (<0.0001)
MELD score at transplant	6-10	1 (ref)	1 (ref)
	11-18	0.60 (0.03)	0.57 (0.02)
	19-24	0.60 (0.04)	0.62 (0.05)
	25-40	0.68 (0.10)	0.72 (0.16)
Donor type	Living	0.67 (0.27)	0.66 (0.25)
Weight	Underweight	3.60 (0.01)	3.53 (0.01)
	Normal weight	1 (ref)	1 (ref)
	Overweight	0.79 (0.08)	0.78 (0.08)
	Obese	0.75 (0.04)	0.77 (0.05)
Presence of Hepatitis C	Yes	1.26 (0.35)	1.37 (0.20)
Diabetes	Yes	1.38 (0.01)	1.27 (0.04)
Functional status at transplant	70-100%	1 (ref)	1 (ref)
	0-60%	1.22 (0.07)	1.44 (0.004)
Ascites	Yes	1.12 (0.49)	1.13 (0.46)
Hepatic encephalopathy	Yes	0.99 (0.90)	1.00 (0.99)
Donor age	<20	0.85 (0.35)	0.84 (0.29)
	20 and up	1 (ref)	1 (ref)
Portal Vein Thrombosis	Yes	1.18 (0.37)	1.21 (0.31)
Time spent on waitlist	<180 days	1 (ref)	1 (ref)
	180-365 days	0.91 (0.57)	0.89 (0.46)
	>365 days	0.85 (0.30)	0.86 (0.32)
Length of Hospital Stay	0-10 days	1 (ref)	1 (ref)
	11-30 days	1.12 (0.35)	1.11 (0.40)
	31+	3.37 (<0.0001)	3.28 (<0.0001)
Previous malignancy	Yes	1.20 (0.31)	1.02 (0.93)
Ventilator use	Yes	1.92 (0.001)	2.19 (<0.0001)
Working at transplant	Yes	0.69 (0.05)	0.75 (0.13)
Dialysis within 1 wk of tx	Yes	1.54 (0.01)	1.63 (0.003)

§ The univariate results are based on models with only the one stated variable. The multivariate results are based on multiple models, each of which includes terms for age, sex, race and transplant year. For example, the hazard ratios for MELD scores are based on a model with five factors. Of course the multivariate hazard ratios for age, sex, race, and transplant year each vary by model. For simplicity, the values shown here are the ones for the model with MELD score.