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ORIGINAL ARTICLE

The landscape of liver transplantation for patients with alcohol-associated liver disease in the United States

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Abstract

Indications for liver transplants have expanded to include patients with alcohol-associated liver disease (ALD) over the last decade. Concurrently, the liver allocation policy was updated in February 2020 replacing the Donor Service Area with Acuity Circles (ACs). The aim is to compare the transplantation rate, waitlist outcomes, and posttransplant survival of candidates with ALD to non-ALD and assess differences in that effect after the implementation of the AC policy. Scientific Registry for Transplant Recipients data for adult candidates for liver transplant were reviewed from the post-AC era (February 4, 2020–March 1, 2022) and compared with an equivalent length of time before ACs were implemented. The adjusted transplant rates were significantly higher for those with ALD before AC, and this difference increased after AC implementation (transplant rate ratio comparing ALD to non-ALD = 1.20, 1.13, 1.61, and 1.32 for the Model for End-Stage Liver Disease categories 37–40, 33–36, 29–32, and 25–28, respectively, in the post-AC era, $p < 0.05$ for all). The adjusted likelihood of death/removal from the waitlist was lower for patients with ALD across all lower Model for End-Stage Liver Disease categories (adjusted subdistribution hazard ratio = 0.70, 0.81, 0.84, and 0.70 for the Model for End-Stage Liver Disease categories 25–28, 20–24, 15–19, 6–14, respectively, $p < 0.05$). Adjusted posttransplant survival was better for those with ALD (adjusted hazard ratio = 0.81, $p < 0.05$). Waiting list and posttransplant mortality tended to improve more for those with ALD since the implementation of AC but not significantly. ALD is a growing indication for liver transplantation. Although patients with ALD continue to have excellent

Abbreviations: AC, Acuity Circles; aHR, adjusted hazard ratio; aIRR, adjusted incidence rate ratio; ALD, alcohol-associated liver disease; aSHR, adjusted subdistribution hazard ratio; HRSA, The Health Resources and Services Administration; LT, liver transplantation; MASLD, metabolic dysfunction–associated liver disease; MELD, Model for End-Stage Liver Disease Sodium Score; OPTN, Organ Procurement and Transplantation Network; SRTR, Scientific Registry for Transplant Recipients.

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posttransplant outcomes and lower waitlist mortality, candidates with ALD have higher adjusted transplant rates, and these differences have increased after AC implementation.

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INTRODUCTION

The success of liver transplantation (LT) coupled with improved organ donation rates has resulted in a significant increase in the number of LTs performed annually in the United States (6342 in 2011 to 9236 in 2021).[1] The landscape for LT in the United States has also dramatically changed in the last decade.[2] Due to the advancement of antiviral treatments, LT for hepatitis C has declined.[2] At the same time, an increase in excessive alcohol consumption has increased the incidence of alcohol-associated liver disease (ALD) in the past decade.[2–4] In 2017, ~2 million individuals in the United States had alcohol-associated cirrhosis.[5] Although the exact incidence of alcohol-associated hepatitis is not well known, the prevalence is increasing, particularly among young adults and women, particularly during the COVID-19 pandemic.[4,6–8] The success of LT for acute alcohol-associated hepatitis and in patients with <6 months of sobriety has been described by several authors.[8–24] Thus, more patients with ALD are being referred for LT,[3] and a recent report from the Scientific Registry for Transplant Recipients (SRTR) notes ALD is the leading indication for adult LT in the United States (Figure 1).[2]

The new liver allocation policy—Acuity Circles (ACs)—was implemented on February 4, 2020, and was designed to reduce the variation in the median Model for End-Stage Liver Disease (MELD) score at transplant between donor service areas in the United States. On a national level, the data suggest that the AC policy has been effective in achieving the goals of increasing the access of patients with the highest MELD scores to transplants, but not much is known about how it impacted specific disease categories, particularly in light of the ongoing increases in LT for patients with ALD.[2,25,26]

The goals of this study were twofold. First, we investigate differences in the transplant rate, waiting list outcomes, and posttransplant survival between candidates and recipients with and without ALD, specifically to understand how the surge in LT for ALD has affected other patients with other primary diagnosis categories including (i) MASLD, (ii) HBV + HCV, (iii) malignant neoplasms (predominantly HCC), (iv) other causes of cirrhosis, and (v) all other diseases in both unadjusted and adjusted models. Second, we sought to assess how differences changed after the implementation of the AC allocation policy. We hypothesized that the AC allocation policy, which sought to increase the access to transplants for those with the highest MELDs, would lead to greater improvements in unadjusted transplant rate and declines in the unadjusted waiting list mortality for those with ALD compared to non-ALD etiologies but similar changes once adjusted for MELD and other candidate characteristics.

METHODS

Data source and inclusion and exclusion criteria

The study used data from the SRTR. The SRTR data system includes data on all donors, waitlisted

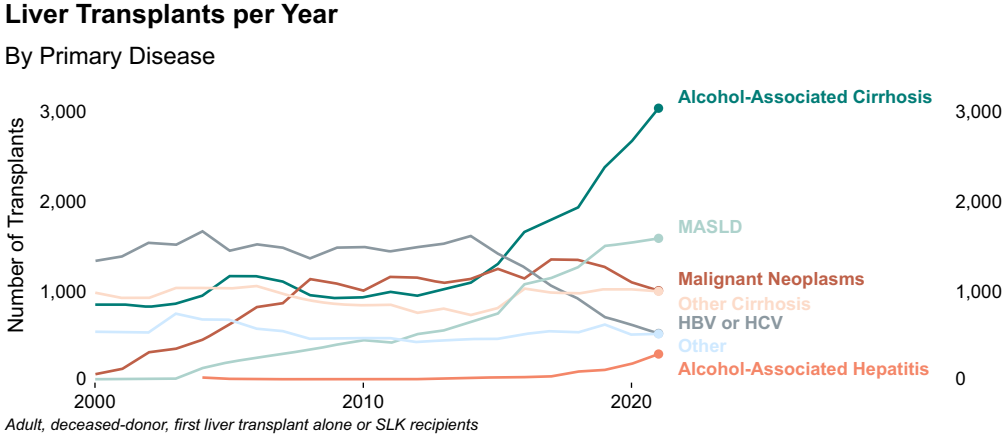

FIGURE 1 Number of liver transplants performed by year and by recipient diagnosis category among adults, deceased-donor, first liver transplant alone, or recipients of simultaneous liver-kidney in the United States.

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candidates, and recipients of transplant in the United States submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA), US Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. This study was exempted from IRB approval.

We compared waitlist dynamics and posttransplant survival among those with ALD and non-ALD and assessed how those comparisons changed with the implementation of AC allocation. We included all adult ($\geq$18 y old), candidates/recipients of first-deceased-donor LT who were actively listed/transplanted during the post-AC era (February 4, 2020, through March 1, 2022) and an equivalent length of time from before AC was implemented (pre-AC, January 8, 2018, through February 3, 2020). We excluded multiorgan listings/recipients except for simultaneous liver-kidney transplants.

Descriptive statistics

We defined candidates/recipients with "alcohol-associated cirrhosis" (with or without hepatitis C) and "alcohol-associated hepatitis " for the primary diagnosis causing liver failure as having ALD. We summarized continuous and categorical characteristics of candidates/recipients by liver disease grouping (alcohol-associated cirrhosis, alcohol-associated hepatitis, and non-ALD) using mean (SD) and frequency (percentage), respectively. Differences in the distribution of the covariates between these groups were summarized using standardized mean difference.

Transplant rates

We used Poisson regression on data from those on the waitlist during the study period to compare the incidence rate of LT by liver disease grouping before and after AC implementation. We considered both unadjusted models and models that adjusted for allocation MELD and other candidate characteristics. For the adjusted models, we assessed how the effect of liver disease grouping changed with AC implementation within different MELD categories (6–14, 15–19, 20–24, 25–28, 29–32, 33–37, and 37–40, Status 1A). That is, the model included terms for liver disease grouping, MELD category, era (before and after AC), and all 2-way and 3-way interactions of these terms. MELD category and era were allowed to vary over time; thus, the offset in the model was the total time on the waitlist within a MELD category during an allocation era. We also adjusted for relevant candidate characteristics that affect transplant rate, including candidate age, sex, race/ethnicity, ABO blood group, height, body mass index, insurance status (private insurance vs. public/other), educational status (some college or higher vs. high school or less), diabetes, history of malignancy, life support, ascites, dialysis status, simultaneous liver-kidney transplant listing, and listing center.[27–30] Ascites and dialysis were allowed to vary over time. To flexibly model the nonlinear association, we used restricted cubic spline basis expansion for height and age. Based on the fitted model, we estimated the adjusted transplant rate within each era, MELD, and liver disease category (ie, the predicted rate for each era, MELD, and liver disease category averaged across each individual's covariate values). In addition, we summarized differences between the transplant rates of candidates with ALD and without ALD by estimating the adjusted incidence rate ratio (aIRR) of transplants within era and MELD categories.

Waiting list mortality, removal due to deterioration, and removal due to improvement

We estimated the cumulative incidence of (i) removal from the waitlist due to deterioration or death and (ii) removal due to improvement between liver disease groupings with Nelson-Aalen estimators and compared the cumulative incidence between groups using a Fine-Gray regression (competing-risk analogs of the Kaplan-Meier estimator and Cox proportional hazards model, respectively). Transplantation was considered a competing risk. Follow-up in the model was censored at removal for other reasons or on March 1, 2022, whichever was earlier. We considered unadjusted models (which included just liver disease grouping, AC era, and their interaction) and models adjusting for the same factors in the transplant rate models.[27,28,31,32] We assessed whether the effect of liver disease grouping on waitlist mortality differed by AC era and allocation MELD category by including both 2-way and 3-way interactions between liver disease grouping, MELD category, and AC era. Within each era, MELD, and liver disease category, we summarized differences between recipients with ALD and without ALD using the adjusted subdistribution hazard ratio (aSHR).

Posttransplant survival

We estimated the posttransplant survival by liver disease grouping and AC era using Kaplan-Meier estimators. Proportional hazard models were used to compare the posttransplant survival by liver disease grouping. Follow-up was censored at the last known follow-up the recipient had with the transplant center. In addition to unadjusted models, we fit models adjusting

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for relevant characteristics of the recipient (characteristics included in the models for transplant rate as well as medical condition [not hospitalized, hospitalized, and in intensive care], history of transjugular intrahepatic portacaval stent shunt and PVT), donor (age, sex, race, donation after cardiac death, cause of death, insulin use, and ratio of height to recipient), and procedure (ischemia time, procedure type [whole, partial, or split liver], and year of transplant) variables.[27,28,33–35] Transplant center was included as a random effect. As with other outcomes, we examined whether or not differences in survival between liver disease grouping and posttransplant survival differed before and after AC implementation.

MELD trajectory

To better understand the waitlist dynamics and changes in liver function after listing, we modeled the longitudinal trajectory of laboratory MELD on the waitlist by disease group (alcohol-associated cirrhosis vs. alcohol-associated hepatitis vs. non-ALD) using linear mixed-effect models. We included a natural cubic spline basis expansion (with 3 internal knots) for time since listing to flexibly model the trajectory, and we allowed both the intercept and the trajectory to vary by disease group. Random effects were included for both the intercept and the basis expansion of time. Based on the fitted model, we estimated the average longitudinal trajectory within each disease group.

General statistical principles

For all models, we imputed missing covariate information using the full conditional specification (multivariate imputation by chained equations). We imputed 5 complete data sets; parameter estimates from each of the complete data sets were combined by using Rubin's combining rules.

For each model, we, in general, compared all candidates/recipients with ALD to all non-ALD. We then examined subgroups of ALD (alcohol-associated cirrhosis and alcohol-associated hepatitis) in comparison to all non-ALD before comparing outcomes for those with alcohol-associated cirrhosis and alcohol-associated hepatitis to different subgroups of the primary diagnosis causing liver failure among those with non-ALD including (i) MASLD, (ii) HBV + HCV, (iii) malignant neoplasms (predominantly HCC), (iv) other causes of cirrhosis, and (v) all other primary diagnosis.

For all statistical analyses, we used SAS version 9.4 (SAS System) or R version 4.1.1 (R Foundation for Statistical Computing). All statistical tests were 2-sided with $p < 0.05$ indicating statistical significance. Given the large sample size, no variable selection was performed; covariates for adjustment were selected a priori based on clinical judgment and a review of published risk-adjusted models from the SRTR and other groups cited above.[27–35]

RESULTS

Candidates and recipients

During the study period, 49,466 candidates for transplant were listed and met the inclusion and exclusion criteria, 24,614 (49.8%) in the pre-AC era and 24,852 (50.2%) in the post-AC era. Listed candidates with alcohol-associated cirrhosis increased from 7820 (31.7% of pre-AC total) to 9197 (37.0% of post-AC total) and with alcohol-associated hepatitis increased from 308 (1.3%) to 602 (2.4%), whereas the number of listed candidates with non-ALD decreased from 16,486 (67.0%) to 15,053 (60.6%). In general, candidates with alcohol-associated cirrhosis and alcohol-associated hepatitis were more likely to be younger (mean age 53, 43, and 58 years for alcohol-associated cirrhosis, alcohol-associated hepatitis, and non-ALD, respectively), male (70.6%, 65.7%, and 58.0%), White (75.2%, 79.5%, and 67.6%), listed at higher MELD (11.1%, 52.3%, and 4.3% listed at MELD 37–40), and have moderate ascites (38.8%, 52.3%, and 22.3%) (Table 1A and Supplemental Table S1, http://links.lww.com/LVT/A589).

The number of recipients with alcohol-associated cirrhosis and alcohol-associated hepatitis meeting inclusion/exclusion criteria also increased from the pre-AC era to the post-AC era (4473 [29.7% of pre-AC total] vs. 5922 [37.2% of post-AC total] and 205 [1.4%] vs. 474 [3.0%], respectively), whereas the number of recipients without ALD declined (10,360 [68.9%] vs. 9522 [59.8%]). Differences in the characteristics of recipients with ALD and without ALD were in general similar to the patterns observed with candidates (Table 1B). Donor characteristics were generally similar between recipients with ALD and without ALD (Table 1B and Supplemental Table S1, http://links.lww.com/LVT/A589).

Transplantation rate

A total of 60,729 candidates for LT were active during the study period and contributed 39,367 person-years on the waitlist. In the pre-AC era, unadjusted transplant rates were 2.1 transplants/1000 waitlist person-days for candidates with ALD compared to 1.9 transplant/1000 waitlist person-days for candidates without ALD. After AC implementation, the difference in unadjusted transplant rates between candidates with ALD and without ALD increased (2.9 vs. 2.1 transplants/1000 waitlist person-days). Figure 2 summarizes the adjusted

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TABLE 1 Summary of key candidate, recipient, and donor characteristics comparing those with alcohol-associated cirrhosis, alcohol-associated hepatitis, and other non-ALD primary diagnoses meeting the inclusion and exclusion criteria

Variable	Levels	Alcohol-associated		Non-ALD	SMD
		Cirrhosis	Hepatitis		
(A) Candidate characteristics					
n		17,017	910	31,539	
Listed organs, n (%)	LTA	15,670 (92.1)	876 (96.3)	29,033 (92.1)	0.12
	SLK	1347 (7.9)	34 (3.7)	2506 (7.9)	
Age (years)		53 (10)	43 (10)	58 (12)	0.944
Sex, n (%)	Female	5001 (29.4)	312 (34.3)	13,388 (42.4)	0.183
	Male	12,016 (70.6)	598 (65.7)	18,151 (57.6)	
Race/ethnicity, n (%)	American Indian/Alaska Native	234 (1.4)	25 (2.7)	264 (0.8)	0.299
	Asian	285 (1.7)	29 (3.2)	1757 (5.6)	
	Black/African American	721 (4.2)	39 (4.3)	2544 (8.1)	
	Hispanic/Latino	2867 (16.8)	89 (9.8)	5569 (17.7)	
	Multiracial	95 (0.6)	5 (0.5)	201 (0.6)	
	Native Hawaiian/Pacific Islander	10 (0.1)	0 (0.0)	83 (0.3)	
	White	12,805 (75.2)	723 (79.5)	21,121 (67.0)	
Insurance status, n (%)	Public insurance/Other	8084 (47.5)	341 (37.5)	16,034 (50.8)	0.181
	Private insurance	8933 (52.5)	569 (62.5)	15,505 (49.2)	
MELD, n (%)	Status 1A	12 (0.1)	10 (1.1)	931 (3.0)	1.393
	MELD 6–14	3237 (19.0)	18 (2.0)	12,465 (39.5)	
	MELD 15–19	3225 (19.0)	23 (2.5)	6144 (19.5)	
	MELD 20–24	3038 (17.9)	39 (4.3)	4679 (14.8)	
	MELD 25–28	1927 (11.3)	63 (6.9)	2274 (7.2)	
	MELD 29–32	1831 (10.8)	107 (11.8)	1657 (5.3)	
	MELD 33–36	1370 (8.1)	154 (16.9)	1027 (3.3)	
	MELD 37–40	1894 (11.1)	476 (52.3)	1350 (4.3)	
	Temp inactive	483 (2.8)	20 (2.2)	1012 (3.2)	
Albumin (g/dL)		3.2 (0.6)	3.1 (0.7)	3.3 (0.7)	0.205
Ascites, n (%)	Absent	1948 (11.5)	110 (12.1)	10,749 (34.1)	0.44
	Slight	8452 (49.7)	403 (44.3)	13,723 (43.5)	
	Moderate	6604 (38.8)	397 (43.6)	7042 (22.3)	
Bilirubin (mg/dL)		8.0 (9.7)	25.4 (13.0)	5.1 (7.9)	1.248
Dialysis, n (%)	No	14,879 (87.5)	593 (65.2)	29,103 (92.3)	0.47
	Yes	2134 (12.5)	317 (34.8)	2419 (7.7)	
Encephalopathy	None	4229 (24.9)	216 (23.7)	14,069 (44.6)	0.378
	1–2	10,740 (63.2)	519 (57.0)	14,958 (47.5)	
	3–4	2035 (12.0)	175 (19.2)	2487 (7.9)	
INR		1.88 (0.82)	2.32 (0.87)	1.64 (1.02)	0.496
Creatinine (mg/dL)		1.56 (1.37)	2.59 (1.99)	1.39 (1.38)	0.476
Sodium (mEq/L)		135 (5)	135 (5)	137 (5)	0.262
Life support, n (%)	No	16,315 (95.9)	802 (88.1)	30,129 (96.9)	0.226
	Yes	698 (4.1)	108 (11.9)	978 (3.1)	
BMI (kg/m^2)		28.4 (5.9)	29.3 (6.4)	29.7 (6.4)	0.143
Diabetes mellitus, n (%)	No	13,956 (82.2)	843 (92.7)	19,649 (63.3)	0.506
	Yes	3031 (17.8)	66 (7.3)	11,403 (36.7)	
Acuity circle era	Pre-AC	7820 (46.0)	308 (33.8)	16,486 (52.3)	0.252
	Post-AC	9197 (54.0)	602 (66.2)	15,053 (47.7)	

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TABLE 1. (*continued*)

Variable	Levels	Alcohol-associated		Non-ALD	SMD
		Cirrhosis	Hepatitis		
(B) Recipient and donor characteristics					
n		10,395	679	19,882	
Transplanted organs, n (%)	LTA	9448 (90.9)	656 (96.6)	18,054 (90.8)	0.161
	SLK	947 (9.1)	23 (3.4)	1828 (9.2)	
Recipient characteristics					
Age (y)		53 (10)	42 (10)	58 (11)	0.998
Sex, n (%)	Female	2891 (27.8)	230 (33.9)	7988 (40.2)	0.175
	Male	7504 (72.2)	449 (66.1)	11,894 (59.8)	
Race/ethnicity, n (%)	American Indian/Alaska Native	143 (1.4)	17 (2.5)	175 (0.9)	0.264
	Asian	182 (1.8)	18 (2.7)	1091 (5.5)	
	Black/African American	473 (4.6)	29 (4.3)	1740 (8.8)	
	Hispanic/Latino	1665 (16.0)	78 (11.5)	3373 (17.0)	
	Multiracial	58 (0.6)	5 (0.7)	118 (0.6)	
	Native Hawaiian/Pacific Islander	7 (0.1)	0 (0.0)	55 (0.3)	
	White	7867 (75.7)	532 (78.4)	13,330 (67.0)	
Insurance status, n (%)	Public insurance/other	4982 (47.9)	257 (37.8)	10,676 (53.7)	0.214
	Private insurance	5413 (52.1)	422 (62.2)	9206 (46.3)	
MELD, n (%)	Status 1A	9 (0.1)	5 (0.7)	660 (3.3)	1.124
	MELD 6–14	313 (3.0)	6 (0.9)	858 (4.3)	
	MELD 15–19	1160 (11.2)	10 (1.5)	2257 (11.4)	
	MELD 20–24	1688 (16.2)	12 (1.8)	3596 (18.1)	
	MELD 25–28	1358 (13.1)	15 (2.2)	4456 (22.4)	
	MELD 29–32	1923 (18.5)	69 (10.2)	3794 (19.1)	
	MELD 33–36	1575 (15.2)	113 (16.6)	1976 (9.9)	
	MELD 37–40	2369 (22.8)	449 (66.1)	2284 (11.5)	
	Temp inactive	0 (0.0)	0 (0.0)	1 (0.0)	
Albumin (g/dL)		3.2 (0.7)	3.0 (0.7)	3.2 (0.7)	0.224
Ascites, n (%)	Absent	1137 (10.9)	71 (10.5)	5908 (29.7)	0.371
	Slight	4494 (43.2)	281 (41.4)	8225 (41.4)	
	Moderate	4764 (45.8)	327 (48.2)	5746 (28.9)	
Bilirubin (mg/dL)		10.7 (11.1)	25.9 (12.7)	7.4 (10.1)	1.071
Dialysis, n (%)	No	8038 (77.3)	343 (50.5)	17,014 (85.6)	0.536
	Yes	2357 (22.7)	336 (49.5)	2865 (14.4)	
Encephalopathy, n (%)	None	2448 (23.5)	157 (23.1)	8116 (40.8)	0.319
	1–2	6138 (59.0)	367 (54.1)	9495 (47.8)	
	3–4	1809 (17.4)	155 (22.8)	2268 (11.4)	
INR		2.18 (1.17)	2.39 (0.91)	1.89 (1.42)	0.277
Creatinine (mg/dL)		1.74 (1.45)	2.68 (1.96)	1.56 (1.48)	0.436
Sodium (mEq/L)		134 (5)	136 (5)	136 (5)	0.239
Life support, n (%)	No	9026 (89.3)	523 (78.6)	18,006 (93.0)	0.282
	Yes	1087 (10.7)	142 (21.4)	1355 (7.0)	
BMI (kg/m^2)		28.3 (5.9)	28.9 (6.3)	29.5 (6.3)	0.131
Diabetes mellitus (at listing), n (%)	No	8626 (83.1)	628 (92.8)	12,528 (63.4)	0.506
	Yes	1758 (16.9)	49 (7.2)	7245 (36.6)	
Acuity circle era, n (%)	Pre-AC	4473 (43.0)	205 (30.2)	10,360 (52.1)	0.303
	Post-AC	5922 (57.0)	474 (69.8)	9522 (47.9)	
Donor characteristics					
Age (y)		41 (15)	39 (14)	42 (16)	0.126

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TABLE 1. (*continued*)

Variable	Levels	Alcohol-associated		Non-ALD	SMD
		Cirrhosis	Hepatitis		
Sex, n (%)	Female	3840 (36.9)	248 (36.5)	7845 (39.5)	0.04
	Male	6555 (63.1)	431 (63.5)	12,037 (60.5)	
BMI (kg/m^2)		28.6 (6.8)	27.3 (5.3)	28.3 (6.8)	0.141
Cause of death, n (%)	Anoxia	4664 (44.9)	320 (47.1)	8809 (44.3)	0.062
	Cerebrovascular/stroke	2695 (25.9)	165 (24.3)	5474 (27.5)	
	Head trauma	2772 (26.7)	180 (26.5)	5130 (25.8)	
	CNS tumor	36 (0.3)	3 (0.4)	66 (0.3)	
	Other	228 (2.2)	11 (1.6)	403 (2.0)	
Donation after cardiac death, n (%)	No	9392 (90.4)	665 (97.9)	17,785 (89.5)	0.237
	Yes	1003 (9.6)	14 (2.1)	2097 (10.5)	
Hypertension, n (%)	No	6655 (64.8)	473 (70.7)	12,479 (63.6)	0.101
	Yes	3608 (35.2)	196 (29.3)	7142 (36.4)	
Insulin use, n (%)	No	5048 (49.3)	331 (49.4)	9509 (48.5)	0.012
	Yes	5196 (50.7)	339 (50.6)	10,104 (51.5)	
Creatinine (mg/dL)		1.84 (1.98)	1.75 (2.01)	1.80 (1.91)	0.028
Cold ischemia time (h)		5.92 (1.98)	5.94 (1.87)	5.95 (2.11)	0.012
Procedure type, n (%)	Whole liver	10,301 (99.1)	675 (99.4)	19,634 (98.8)	0.05
	Partial liver	4 (0.0)	0 (0.0)	6 (0.0)	
	Split liver	90 (0.9)	4 (0.6)	242 (1.2)	
Recipient/donor height ratio		1.01 (0.08)	1.02 (0.09)	1.00 (0.09)	0.145

Note: Summary of all variables used for adjustment is available in the Supplemental Materials, http://links.lww.com/LVT/A589.
Abbreviations: BMI, body mass index; LTA, liver transplant alone; SLK, simultaneous liver-kidney transplant; SMD, standardized mean difference.

transplant rates (adjusted for factors listed in the Transplant rates section) by MELD category, liver disease group, and AC era. Among those waiting with a current allocation MELD in the highest categories (ie, 37–40, 33–36, 29–32, and 25–28), adjusted transplant rates pre-AC were significantly higher for those with ALD. Specifically, in the pre-AC era, the ratios of the adjusted rates (ie, aIRR) of ALD to non-ALD were 1.07 (95% CI, 0.98–1.16), 1.31 (95% CI,1.19–1.45), 1.34 (95% CI,1.24–1.47), and 1.14 (95% CI, 1.05–1.25) for allocation MELD 37–40, 33–36, 29–32, and 25–28, respectively. Across all MELD and primary disease categories, the rate of transplantation increased in the post-AC era. For example, transplant rates increased from 111.7 to 135.9 transplants per 1000 person-days among candidates without ALD and from 119.4 to 162.9 transplants per 1000 person-days among candidates with ALD with a MELD 37–40. Among those in MELD categories 37–40, 29–32, and 25–28, differences in the transplant rate between ALD and non-ALD were increased after AC implementation (interaction $p < 0.05$ for each MELD category); that is, the aIRR of ALD to non-ALD increased after AC implementation. For example, the aIRR increased to 1.20 (95% CI, 1.11–1.30), 1.61 (95% CI, 1.50–1.74), and 1.32 (95% CI, 1.22–1.45) for MELD categories 37–40, 29–32, and 25–28, respectively, after AC implementation. Interestingly, the aIRR of ALD to non-ALD decreased after AC implementation for MELD 33–36 to 1.13 (95% CI, 1.03–1.24).

The findings were generally consistent when comparing candidates with alcohol-associated cirrhosis and alcohol-associated hepatitis to non-ALD separately (Supplemental Figure S1, http://links.lww.com/LVT/A589) particularly for MELD categories 37–40, 33–36, and 29–32. However, very few candidates with alcohol-associated hepatitis have MELD scores <29 leading to wide confidence intervals comparing transplant rates for alcohol-associated hepatitis to non-ALD for the lower MELD categories. In general, candidates with alcohol-associated cirrhosis and alcohol-associated hepatitis demonstrated consistently higher adjusted transplant rates compared to all subgroups of candidates without ALD (Supplemental Figure S2, http://links.lww.com/LVT/A589).

Waitlist mortality and removal due to deterioration

The cumulative 90-day and 1-year incidence of death on the waiting list or removal from the list due to deterioration in the pre-AC era was 6.2% and 10.8%, respectively, for candidates with ALD and 5.8% and 13.4% for non-ALD. After AC implementation, this cumulative incidence declined to 5.7% and 9.1%,

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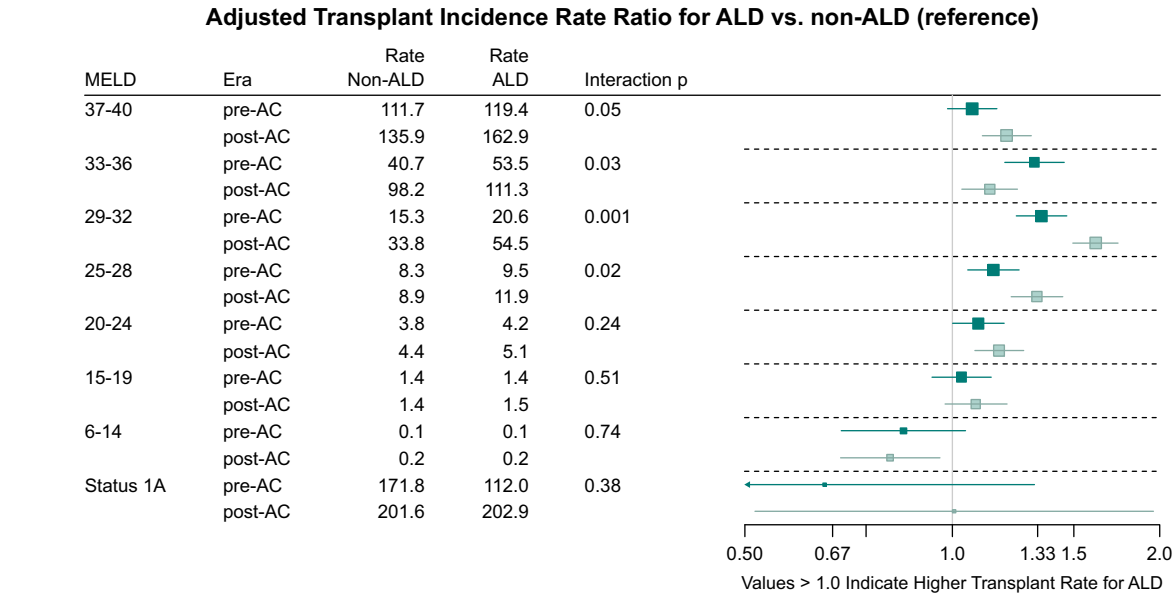

FIGURE 2 Table of adjusted transplant rates by MELD category, liver disease group, and acuity circles era and forest plot of adjusted transplant rate ratio with 95% CI comparing candidates with ALD to candidates without ALD (reference). Rates are adjusted for candidate factors impacting organ offers and suitability and are described in the Transplant rates section. Abbreviations: ALD, alcohol-associated liver disease; MELD, Model for End-Stage Liver Disease.

respectively, for candidates with ALD but nearly unchanged to 5.7% and 13.4% for those without ALD (Figure 3). Figure 4 summarizes the aSHR comparing candidates with ALD to those without ALD by MELD category and AC era. Across the lower MELD categories at listing (ie, 6–14, 15–19, 20–24, 25–28), the adjusted cumulative incidence of death on the waitlist or removal due to deterioration was higher for candidates without ALD than for candidates with ALD (ie, the aSHR <1.0). In general, for most of these lower MELD categories, the point estimate of the aSHR declined in the post-AC era (ie, there was a greater magnitude of differences in waitlist mortality), but differences in the effect of liver disease group were not significant between eras (ie, interaction $p > 0.05$). Pooling the estimate across AC eras, the aSHR was 0.70 (95% CI, 0.57–0.84) for listing MELD 25–28, 0.81 (95% CI, 0.70–0.94) for listing MELD 20–24, 0.84 (95% CI, 0.73–0.96) for listing MELD 15–19, and 0.70 (95% CI, 0.61–0.80) for listing MELD 6–14 (Supplemental Figure S3, http://links.lww.com/LVT/A589). Point estimates were generally similar when comparing candidates with alcohol-associated cirrhosis with non-ALD and alcohol-associated hepatitis with non-ALD (Supplemental Figure S3, http://links.lww.com/LVT/A589 and Supplemental Figure S4, http://links.lww.com/LVT/A589). However, the relatively few numbers of candidates with alcohol-associated hepatitis listed at MELDs <25 leads to very large confidence intervals.

The 90-day and 1-year incidence of removal from the list due to improvement was 0.13% and 1.8% for candidates with ALD and 0.64% and 1.6% for

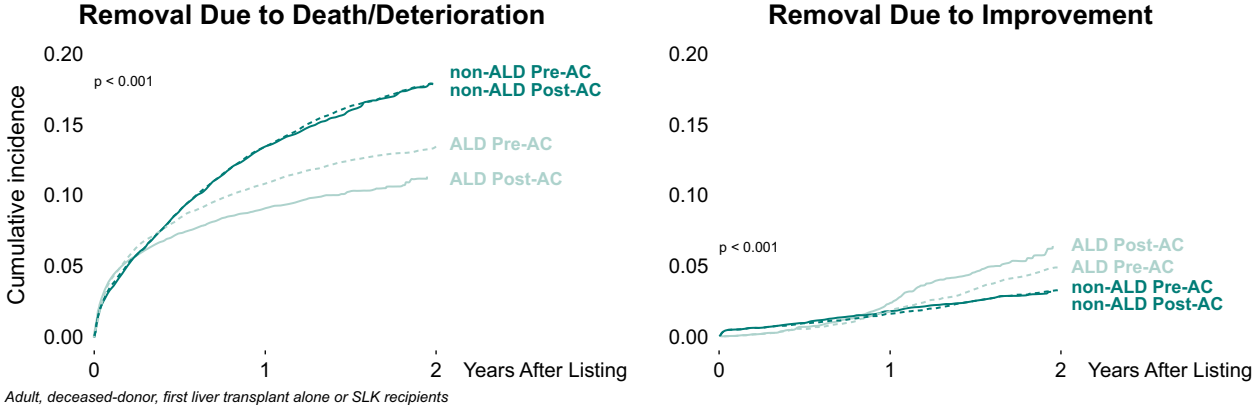

FIGURE 3 Cumulative incidence of removal from the waiting list due to (a) death or deterioration and (b) improvement by liver disease group and acuity circles era.

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candidates without ALD in the pre-AC era. These percentages modestly increased for candidates with ALD in the AC era to 0.17% and 2.4% and for candidates without ALD to 0.65% and 1.8% (Figure 3).

Posttransplant survival

Overall, the 90-day and 1-year posttransplant survival for recipients with ALD was 97.3% and 94.5%, and for recipients without ALD was 96.3% and 93.0% in the pre-AC era. In the post-AC era, posttransplant survival at 90 days and 1 year was 97.0% and 94.2% for recipients with ALD and 95.5% and 90.7% without ALD (Figure 5). Overall, averaged over the follow-up period, posttransplant survival was better for those with ALD (adjusted hazard ratio [aHR] = 0.81, 95% CI, 0.74–0.90). This difference was consistent when follow-up was limited to 1 year (aHR = 0.77, 95% CI, 0.69–0.87) and when examining 1-year survival conditioned on surviving 90 days after transplant (aHR = 0.78, 95% CI, 0.65–0.92). The difference in adjusted posttransplant survival between ALD and non-ALD was somewhat exacerbated after the implementation of AC. Specifically, in the pre-AC era, the aHR for ALD compared to non-ALD for overall survival, 1-year survival, and 1-year survival conditioned on surviving 90 days was 0.87 (95% CI, 0.78–0.98), 0.85 (95% CI, 0.73–0.99), and 0.90 (95% CI, 0.73–1.12), respectively. The magnitude of the effect increased to 0.72 (95% CI, 0.63–0.84, interaction $p = 0.04$), 0.70 (95% CI, 0.60–0.83, interaction $p = 0.08$), and 0.63 (95% CI, 0.49–0.82, interaction $p = 0.03$) for overall survival, 1-year survival, and 1-year survival conditioned on surviving 90 days after the implementation of AC, respectively.

Point estimates for the comparison of alcohol-associated cirrhosis to non-ALD and alcohol-associated hepatitis to non-ALD on adjusted overall survival, 1-year survival, and 1-year survival conditioned on 90-day survival were generally similar but the CIs for alcohol-associated hepatitis were wide (Supplemental Figure S5, http://links.lww.com/LVT/A589). Adjusted posttransplant survival was significantly higher for alcohol-associated cirrhosis compared to each subgroup of non-ALD (Supplemental Figure S6, http://links.lww.com/LVT/A589). Point estimates for comparing alcohol-associated hepatitis to each subgroup of non-ALD on posttransplant survival favored alcohol-associated hepatitis but CIs were wide and nonsignificant (Supplemental Figure S6, http://links.lww.com/LVT/A589).

Laboratory MELD trajectory

In general, the longitudinal trajectory of laboratory MELD differed substantially among liver disease groups (Figure 6). The laboratory MELD at listing was significantly higher on average for ALD with acute hepatitis (35.9; 95% CI, 35.3–36.6) and cirrhosis (23.8;

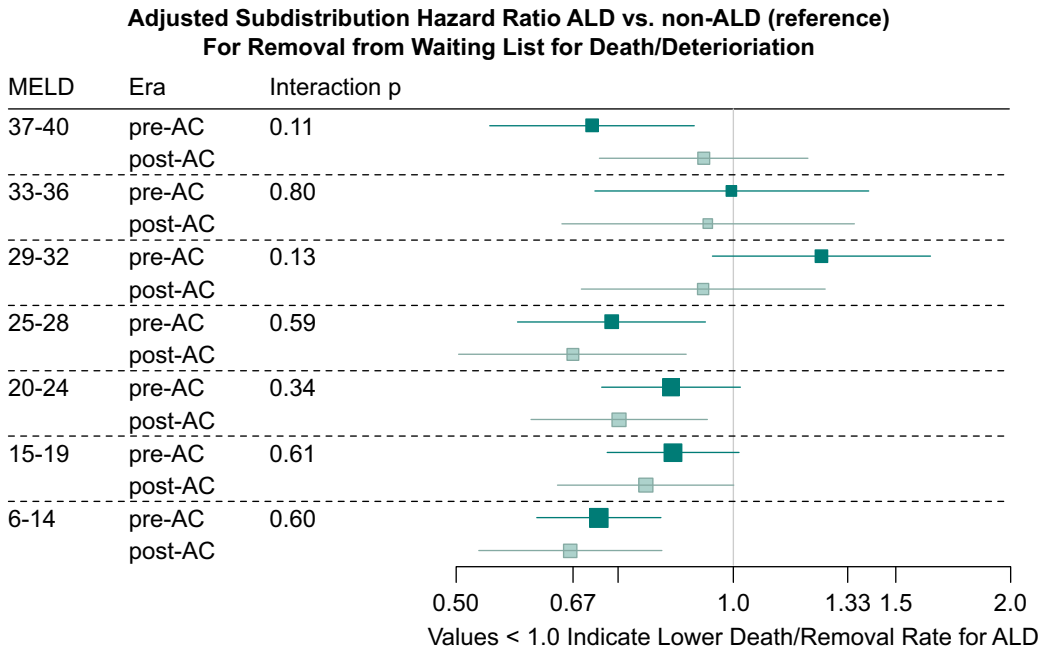

FIGURE 4 Forest plot of adjusted subdistribution HR with 95% CI comparing candidates with ALD to candidates without ALD (reference) by MELD category at listing and acuity circles era. Rates are adjusted for candidate factors impacting organ offers and waiting list mortality and are described in the waiting list mortality, removal due to deterioration, and removal due to improvement section. Abbreviations: ALD, alcohol-associated liver disease; MELD, Model for End-Stage Liver Disease.

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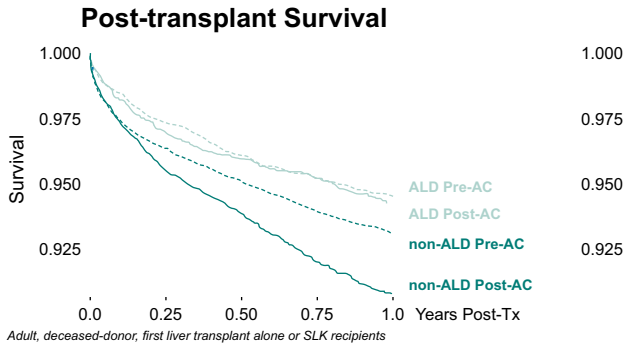

FIGURE 5 Posttransplant survival by liver disease group and acuity circles era.

95% CI, 23.7–24.0) than for non-ALD (18.5; 95% CI,18.4–18.6). These differences were sustained over the first 180 days of listing, but the average changes from the listing MELD differed significantly among groups ($p < 0.001$). In particular, the average MELD declined for those with alcohol-associated hepatitis (32.0 at 180 days after listing, 95% CI, 30.8–33.2) but increased for those with non-ALD (20.6, 95% CI, 20.5–20.7) and was relatively consistent for alcohol-associated cirrhosis (24.6, 95% CI, 24.4–24.8).

We found that candidates with alcohol-associated cirrhosis and hepatitis had higher laboratory average MELD over the first 180 days of listing when comparing to each subgroup of non-ALD with the exception that candidates with alcohol-associated cirrhosis and other non-ALD had nearly identical trajectories (Supplemental Figure S7, http://links.lww.com/LVT/A589).

DISCUSSION

In the present study, we examined the transplant rates, waiting list outcomes, and posttransplant survival of patients with ALD and assessed how those differences changed after the implementation of the AC liver allocation policy on LT and compared to patients without ALD.

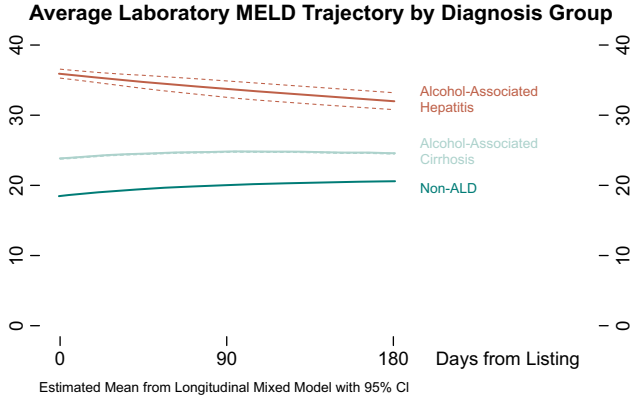

FIGURE 6 The longitudinal trajectory of average laboratory MELD with pointwise 95% CIs among liver disease groups.

Transplantation rates

We found that patients with ALDs have higher rates of transplantation even after adjusting for patient urgency (eg, MELD) and other factors related to organ availability (eg, transplant center and ABO blood type). These adjusted differences in transplant rate tended to increase after the implementation of AC liver allocation. The findings were broadly consistent across different subgroups of ALD (alcohol-associated cirrhosis and alcohol-associated hepatitis) and in comparison, to different subgroups of non-ALD (HBV/HCV, malignancy, MASLD, and other cirrhosis). For most donations after brain death, after prioritizing compatible Status 1A and 1B candidates within 500 nautical miles of the donor hospital, AC prioritizes candidates with the highest medical urgency (ie, MELD scores 37–40) first within 150 nautical miles of the donor hospital and then 250 and 500 nautical miles before prioritizing lower candidates with lower medical urgency (ie, MELD 34–36, 29–33, etc.) up to 500 nautical miles away. This change in allocation gives patients with MELD scores of 29–34 much wider access than patients with MELD scores of 15–28. Patients with ALD have higher MELD scores at listing and consistently maintain their higher trajectory scores (Figure 6). This advantages them for liver offers, thus resulting in an increase in *unadjusted* transplantation rate for ALD after AC implementation (unadjusted transplant rate 2.1 vs. 2.9 transplants/1000 waitlist person-days before and after AC) but relatively stagnant *unadjusted* transplantation rate for non-ALD. Kwon et al[36] reported a similar dramatic increase in deceased-donor LTs for alcohol-associated hepatitis in Korea after the implementation of an allocation system that prioritized patients with the highest MELD. These data suggest that the AC model of liver allocation is functioning well and allocating livers to the sickest patients (as determined by a higher MELD score).

However, why candidates with ALD have higher adjusted rates of transplantation (ie, adjusting for MELD and other characteristics including transplant center) and why this difference has increased with the latest changes to the liver allocation system is not clear, but further studies are needed to understand this difference in adjusted transplantation rates. Perhaps, there is a perception that patients with ALD are technically easier, have lesser comorbidities (have lower rates of diabetes, PVT, TIPS, and previous abdominal surgery), and have superior survival and, therefore, are more likely to be selected for transplant than patients with the same score, similar position on the waitlist, and different etiologies. In addition, patients with ALD are frequently hospitalized before transplant which may facilitate placement of an organ offer that is made outside of the match run due to, for example, a late turndown.

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Waitlist mortality and removal

We also found that ALD candidates and recipients had decreased waitlists (for those listed in MELD categories <28) in both unadjusted models and models adjusted for relevant candidate/recipient and donor characteristics. These differences in outcomes were generally greater in the AC era. Differences in transplant rates may be driving differences in the proportion dying on the waitlist between those with ALD and non-ALD even after adjusting for candidate characteristics (Figure 4). In particular, higher rates for candidates with ALD at higher MELD scores might enable those candidates with ALD listed at lower MELD scores who then rapidly deteriorate to receive a donor organ before dying on the waiting list. In addition, patients with ALD might be more likely to avoid the progressive sarcopenia and frailty associated with refractory ascites due to shorter waitlist periods thus improving posttransplant survival.

It is important to note that the average MELD score declined for patients with alcohol-associated hepatitis while they were on the waiting list, suggesting that this improvement in liver function could be from the alcohol abstinence, and perhaps there is an urgent need to improve recipient evaluation criteria beyond MELD for alcohol-associated hepatitis to identify patients who are likely to improve and, thus, do not need LTs. Bittermann et al,[7] similar to our study, analyzed transplantation trends in patients with alcohol-associated hepatitis, compared to patients listed with MELD ≥ 30, and noted that patients with alcohol-associated hepatitis had a higher transplantation rate and lower waitlist mortality. Interestingly, patients with alcohol-associated hepatitis only had a 3.3% delisting due to improvement.

Posttransplant survival

Patients with ALD have posttransplant outcomes similar to or better than those of patients undergoing LT for other indications. We surmise that there are several potential explanations. Perhaps this improved survival reflects an improvement in patient selection (patients with ALD have lower rates of diabetes, PVT, TIPS, and previous abdominal surgery). The difference in improved survival of patients with ALD was exacerbated after the implementation of AC, perhaps reflecting that the shorter prelisting times may also have led to fewer consequences such as less frailty, sarcopenia, or malnutrition. Better perioperative multidisciplinary management to reduce the risk of alcohol use disorder relapse may also have contributed to better survival thus validating the indication of LT for ALD.[23]

Potential implications of our findings

Accurate assessment of the prevalence of ALD in the United States is challenging due to underreporting. A recent study reviewing data from 2015 through 2019 estimated that mean annual deaths due to excessive alcohol use were 43.2 per 100,000 population, with 22,472 deaths attributed annually to ALD.[37] For severe alcohol-associated hepatitis, the current therapies other than LT have suboptimal results.[38] Concurrent with this increase in deaths due to excessive alcohol use, there has been a greater acceptance of treating patients with ALD undergoing LT.[39] A recent survey of transplantation centers in the United States showed that over 70% of programs reported no minimum sobriety requirement. LT for alcohol-associated hepatitis was performed at 85% of the centers.[40] These 2 factors have led to explosive growth in the number of LT for patients with ALD over the last decade (Figure 1). If this trend of increasing ALD incidence and the use of LT as a treatment modality were to continue, there could be increases in the number of patients dying on the waiting list across all etiologies of liver disease. An estimated 15% of patients on the waitlist already die before a liver becomes available.[1,2]

Indeed, the purpose of the allocation algorithm is to equalize the waitlist mortality among candidates. That there are subgroups of candidates with increased or decreased waitlist mortality with the same MELD score suggests that either the model for medical urgency or the allocation algorithm should be revised to be more aligned with the Final Rule. Perhaps, the primary diagnosis should be added as a coefficient based on the transplantation rate to the “continuous distribution” model of allocation currently being evaluated by UNOS to provide similar transplant opportunities for candidates with ALD and non-ALD diagnosis.

Limitations of the study

Our study is limited by its retrospective design. We were unable to evaluate specific patient and donor offers, center variability, and center-specific factors that could influence listing, donor acceptance, and follow-up prevention for alcohol use relapse. We also do not have the outcomes of alcohol use disorder relapse, if any, in the ALD group. In addition, as this study uses data from a national registry, we lack granular data on liver candidates/recipients and donors (eg, the use of machine perfusion). Although we adjusted for a wide variety of candidate/recipient and donor characteristics, we may have missed variables not available in the registry that could have influenced these results.

While we presented results comparing candidates/recipients with and without ALD before and after AC

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implementation, some of the differences observed after AC implementation may have been due to ongoing secular trends or other concurrent factors.

Most prominently, the implementation of AC occurred nearly concurrently with the onset of the COVID-19 pandemic and public health emergency in the United States. The COVID epidemic may have caused an increase in ALD incidence particularly among those already with alcohol use disorders at high risk of relapse who no longer had access to in-person behavioral counseling programs or other events without alcohol.[8] The emergence of COVID-19 potentially confounded our study findings. The pandemic affected different parts of the country at different times.[41,42] Trying to carve out data from different parts of the country at different times would be challenging and geographic differences could not be evaluated owing to sample size constraints. However, our data show that even before the pandemic, patients with ALD had increased transplantation rates and lower waitlist mortality; thus, the COVID-19 pandemic is unlikely to explain the current higher transplantation rates for ALD.

CONCLUSIONS

In summary, ALD is a rapidly growing indication for LT. Candidates with ALD, compared to other etiologies of liver disease, are transplanted at higher rates even after adjusting for MELD and other allocation factors, and this difference has increased after the implementation of the AC policy. However, patients with ALD continue to have excellent posttransplant outcomes and lower waitlist mortality.

AUTHOR CONTRIBUTIONS

David M. Vock and Srinath Chinnakotla: participated in the research design, writing of the paper, performance of the research, and data analysis. Vanessa Humphreville, Karthik V. Ramanathan, Andrew B. Adams, Nicholas Lim, Vinh H. Nguyen, and Jillian K. Wothe: participated in the research design and writing of the paper.

CONFLICTS OF INTEREST

The authors have no conflicts to report.

REFERENCES

1. UNOS data and policy. 2023. Accessed February 10, 2023. www.unos.org.
2. Kwong AJ, Ebel NH, Kim WR, Lake JR, Smith JM, Schladt DP, et al. OPTN/SRTR 2020 Annual Data Report: Liver. Am J Transplant. 2022;22(suppl 2):204–309.
3. Wong RJ, Singal AK. Trends in liver disease etiology among adults awaiting liver transplantation in the United States, 2014-2019. JAMA Netw Open. 2020;3:e1920294.
4. Singal AK, Arsalan A, Dunn W, Arab JP, Wong RJ, Kuo YF, et al. Alcohol-associated liver disease in the United States is associated with severe forms of disease among young, females and Hispanics. Aliment Pharmacol Ther. 2021;54:451–61.
5. GBD 2017 Cirrhosis Collaborators. The global, regional and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: A systemic analysis for the Global Burden of Disease Study. Lancet Gastroenterol Hepatol. 2020;5:245–66.
6. Lee BP, Dodge JL, Terrault NA. Liver transplantation for alcohol-associated liver disease continues to rise 2 years into COVID-19 pandemic especially among younger adults. J Hepatol. 2023;78:e139–41.
7. Bittermann T, Mahmud N, Abt P. Trends in liver transplantation for acute alcohol-associated hepatitis during the COVID-19 pandemic in the US. JAMA Netw Open. 2021;4:e2118713.
8. Cholankeril G, Goli K, Rana A, Hernaez R, Podboy A, Jalal P, et al. Impact of COVID-19 pandemic on liver transplantation and alcohol-associated liver disease in the USA. Hepatology. 2021;74:3316–29.
9. Mathurin P, Moreno C, Samuel D, Dumortier J, Salleron J, Durand F, et al. Early liver transplantation for severe alcoholic hepatitis. N Engl J Med. 2011;365:1790–800.
10. Hasanin M, Dubay DA, McGuire BM, Schiano T, Singal AK. Liver transplantation for alcoholic hepatitis: A survey of liver transplant centers. Liver Transpl. 2015;21:1449–52.
11. Im GY, Kim-Schluger L, Shenoy A, Schubert E, Goel A, Friedman SL, et al. Early liver transplantation for severe alcoholic hepatitis in the United States—A single-center experience. Am J Transplant. 2016;16:841–9.
12. Cotter TG, Sandıkçı B, Paul S, Gampa A, Wang J, Te H, et al. Liver transplantation for alcoholic hepatitis in the United States: Excellent outcomes with profound temporal and geographic variation in frequency. Am J Transplant. 2021;21:1039–55.
13. Im GY, Cameron AM, Lucey MR. Liver transplantation for alcoholic hepatitis. J Hepatol. 2019;70:328–34.
14. Bataller R, Arab JP, Shah VH. Alcohol-associated hepatitis. N Engl J Med. 2022;387:2436–48.
15. Marroni CA, Jr AMF Jr., Fernandes SA, Galant LH, Mucenic M, Meine MHM, et al. Liver transplantation and alcoholic liver disease: History, controversies, and considerations. World J Gastroenterol. 2018;24:2785–805.
16. Lucey M. Liver transplantation in the alcoholic patientIn: Maddrey W, Schiff E, Sorell M, eds. Transplantation of the Liver. Lippincott Williams; 2002:319–26.
17. Starzl TE. Orthotopic liver transplantation for alcoholic cirrhosis. JAMA. 1988;260:2542–44.
18. Testino G. Acute alcoholic hepatitis, end stage alcoholic liver disease and liver transplantation: An Italian position statement. World J Gastroenterol. 2014;20:14642–51.
19. Dutkowski P, Linecker M, DeOliveira ML, Müllhaupt B, Clavien PA. Challenges to liver transplantation and strategies to improve outcomes. Gastroenterology. 2015;148:307–23.
20. Rustad JK, Stern TA, Prabhakar M, Musselman D. Risk factors for alcohol relapse following orthotopic liver transplantation: A systematic review. Psychosomatics. 2015;56:21–35.
21. European Association for the Study of the Liver. EASL clinical practical guidelines: Management of alcoholic liver disease. J Hepatol. 2012;57:399–420.
22. Singal AK. Liver transplantation in alcoholic liver disease current status and controversies. World J Gastroenterol. 2013;19:5953–63.
23. Puri P, Cholankeril G, Myint TY, Goel A, Sarin SK, Harper AM, et al. Early liver transplantation is a viable treatment option in severe acute alcoholic hepatitis. Alcohol Alcohol. 2018;53:716–8.
24. Lee BP, Mehta N, Platt L, Gurakar A, Rice JP, Lucey MR, et al. Outcomes of early liver transplantation for patients with severe alcoholic hepatitis. Gastroenterology. 2018;155:422–430e421.
25. Wey A, Noreen S, Gentry S, Cafarella M, Trotter J, Salkowski N, et al. The effect of acuity circles on deceased donor transplant

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and offer rates across model for end-stage liver disease scores and exception statuses. Liver Transpl. 2022;28:363–75.
26. OPTN Liver & Intestinal Transplantation Committee. Two year monitoring report of liver and intestine acuity circle allocation removal of DSA and region as units of allocation. 2022. Accessed March 27, 2024. https://optn.transplant.hrsa.gov/media/k5yi4jvl/data_report_liver_full_2yrallocation_20220805_final_508_compliant.pdf
27. SRTR risk adjustment models. 2023. Accessed February 10, 2023. www.srtr.org.
28. Snyder JJ, Salkowski N, Kim SJ, Zaun D, Xiong H, Israni AK, et al. Developing statistical models to assess transplant outcomes using national registries: The process in the United States. Transplantation. 2016;100:288–94.
29. Hart A, Schladt DP, Zeglin J, Pyke J, Kim WR, Lake JR, et al. Predicting outcomes on the liver transplant waiting list in the United States: Accounting for large regional variation in organ availability and priority allocation points. Transplantation. 2016;100:2153–59.
30. Trieu JA, Bilal M, Hmoud B. Factors associated with waiting time on the liver transplant list: An analysis of the United Network for Organ Sharing (UNOS) database. Ann Gastroenterol. 2018;31:84–9.
31. Bertsimas D, Kung J, Trichakis N, Wang Y, Hirose R, Vagefi PA. Development and validation of an optimized prediction of mortality for candidates awaiting liver transplantation. Am J Transplant. 2019;19:1109–18.
32. Kim WR, Therneau TM, Benson JT, Kremers WK, Rosen CB, Gores GJ, et al. Deaths on the liver transplant waiting list: An analysis of competing risks. Hepatology. 2006;43:345–51.
33. Molinari M, Ayloo S, Tsung A, Jorgensen D, Tevar A, Rahman SH, et al. Prediction of perioperative mortality of cadaveric liver transplant recipients during their evaluations. Transplantation. 2019;103:e297–e307.
34. Nitski O, Azhie A, Qazi-Arisar FA, Wang X, Ma S, Lilly L, et al. Long-term mortality risk stratification of liver transplant recipients: Real-time application of deep learning algorithms on longitudinal data. Lancet Digit Health. 2021;3:e295–e305.
35. Evans MD, Diaz J, Adamusiak AM, Pruett TL, Kirchner VA, Kandaswamy R, et al. Predictors of survival after liver transplantation in patients with the highest acuity (MELD ≥40). Ann Surg. 2020;272:458–66.
36. Kwon TJ, Kang W, Gwak GY, Paik YH, Choi MS, Lee JH, et al. Outcome of patients with severe alcoholic hepatitis after Model for End-Stage Liver Disease-based allocation system implementation in Korea. Korean J Transplant. 2021;35:24–32.
37. Esser MB, Leung G, Sherk A, Bohm MK, Liu Y, Lu H, et al. Estimated deaths attributable to excessive alcohol use among US adults aged 20 to 64 years, 2015 to 2019. JAMA Netw Open. 2022;5:e2239485.
38. Singal AK, Mathurin P. Diagnosis and treatment of alcohol-associated liver disease: A review. JAMA. 2021;326:165–176.
39. Sedki M, Ahmed A, Goel A. Ethical and allocation issues in liver transplant candidates with alcohol related liver disease. Transl Gastroenterol Hepatol. 2022;7:26.
40. Lim N, Kwong AJ, Jafri SM, Jesse MT, Kriss M, Nair K, et al. Heterogeneity in center practices in liver transplantation for alcohol-associated liver disease in the United States. Am J Gastroenterol. 2022;117:1530–5.
41. Pei S, Yamana TK, Kandula S, Galanti M, Shaman J. Burden and characteristics of COVID-19 in the United States during 2020. Nature. 2021;598:338–41.
42. Subramanian V, Anderson C, Karp S, Pastan S, Gerber D, Locke J, et al. COVID-19 and transplantation-data censoring. Am J Transplant. 2022;22:1958–62.

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