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The Practice of Retransplantation for Recurrent Alcohol-associated Liver Disease in the United States Is Uncommon With Acceptable Outcomes

Thomas G. Cotter, MD, MS,¹ Matthew A. Odenwald, MD, PhD,² Sarah R. Lieber, MD, MSCR,¹ Nicole E. Rich, MD,¹ Gene Im, MD,³ Michael Charlton, MD,² Amit G. Singal, MD,¹ and Mack C. Mitchell, MD¹

Background. Alcohol-associated liver disease (ALD) is the leading indication for liver transplantation (LT) in the United States. Alcohol use disorder relapse can lead to graft failure and the need for liver retransplantation (re-LT). Despite the rising incidence of LT for ALD, the practice of re-LT for recurrent ALD is not well understood. We aimed to define the practice of re-LT for recurrent ALD during the last 20 y. **Methods.** Using the US national transplant registry, adults who underwent re-LT for recurrent ALD were compared with LT recipients who died from recurrent ALD and propensity score-matched re-LT recipients with non-ALD indications. All groups had at least 1-y survival of their primary graft. Kaplan-Meier analysis was used to calculate 1- and 5-y survivals. **Results.** Between 2000 and 2020, 74 re-LTs were performed for recurrent ALD (1.0% of all re-LTs). There was an increase in recurrent ALD re-LT practice from 2017 to 2020 versus 2014 to 2016 (20 versus 2). At the time of re-LT, patients with recurrent ALD had a significant decrease in body mass index (median 25.1 versus 28.8 kg/m²; $P < 0.001$) versus the index LT. Patient and graft survivals were similar between patients who underwent re-LT for ALD and non-ALD (56.4% versus 56.9% 5-y graft survival, $P = 0.96$; 62.8% versus 59.0% 5-y patient survival, $P = 0.58$). **Conclusions.** The practice of re-LT for recurrent ALD is uncommon in the United States. Graft and patient survivals seem to be acceptable and support the occasional practice of re-LT for recurrent ALD should the patient be deemed an appropriate candidate.

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¹ Division of Digestive and Liver Diseases, UT Southwestern Medical Center, Dallas, TX.

² Division of Gastroenterology and Hepatology, The University of Chicago Medicine, Chicago, IL.

³ Division of Liver Diseases, Recanati-Miller Transplantation Institute, Icahn School of Medicine at Mount Sinai, New York, NY.

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Correspondence: Thomas G. Cotter, MD, Division of Digestive and Liver Diseases, UT Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390. (thomas.cotter@utsouthwestern.edu).

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INTRODUCTION

Alcohol-associated liver disease (ALD) is now the leading indication for liver transplantation (LT) in the United States.¹ Return to sustained alcohol use, defined as either moderate or heavy alcohol that increased over time post-LT, occurs in up to 13% of ALD LT recipients and is associated with increased risk of graft loss and patient death.^{2,3} Notably, transplant recipients had a median time of 3 y of sobriety before LT in the study by DiMartini et al.³ Since the seminal study demonstrating a survival benefit for early LT in patients with medically refractory severe alcohol-associated hepatitis (AH) in 2011,⁴ there has been a noticeable increase of LT for patients with AH in the United States.^{5,6} In contrast to traditional ALD LT recipients, AH LT recipients typically have a shorter period of abstinence, if any, before LT and are typically too sick to complete any formalized alcohol use disorder (AUD) treatment before transplant.⁴ Hence, there is concern for higher risk of return to alcohol use post-LT for severe AH, with the initial US-based studies showing post-LT relapse in ~20% of patients.^{5,7}

With a substantial increase in transplant for ALD and AH, understanding outcomes related to recurrent disease is paramount to not only ensuring improved survival but also maintaining the trust of public in the ethical merits of this practice. Given the risk of accelerated graft failure among ALD LT recipients who return to sustained drinking,^{2,3,7} the question of

liver retransplantation (re-LT) inevitably arises and presents a moral dilemma for transplant providers given the finite donor pool and substantial LT waitlist mortality.⁸ This leads to the question of whether recurrent heavy drinking should preclude re-LT. Although prior studies have shown inferior graft survival in re-LT (for all indications) compared with primary LT recipients,⁹⁻¹² the frequency and outcomes of re-LT for recurrent ALD after late primary graft failure (>1 y after primary LT) remain unknown. Given the rise in LT for ALD and AH, it is critical to describe the burden of the problem of recurrent ALD requiring re-LT and to assess outcomes for re-LT recipients to inform future practice. Therefore, we aimed to ascertain the frequency, demographics, clinical features, and outcomes among patients undergoing re-LT for recurrent ALD.

MATERIALS AND METHODS

Study Population and Data Acquisition

This was a retrospective study of adult (≥ 18 y) LT and re-LT recipients, including those who, with ALD or AH as the primary listing indication between January 1, 2000, and December 31, 2020, were identified from the United Network for Organ Sharing (UNOS)/Organ Procurement and Transplantation Network database. These data are prospectively collected from organ procurement organizations, transplant programs, and histocompatibility laboratories, complemented by the National Technical Information Service's Death Master File Centers and Medicare and Medicaid Services.¹³ Patients who underwent multiorgan transplantation (apart from simultaneous liver–kidney) were excluded. Only first-time re-LT episodes were considered, with subsequent re-LT episodes ignored ($n = 7$). The primary study group (ie, cases) and comparative groups (ie, controls) were defined as follows.

- Cases (re-LT recipients for recurrent ALD): These were re-LT recipients whose graft survived at least 365 d from the time of the primary transplant and had a primary listing indication of ALD or AH on both occasions. To avoid confounding for technical complications (eg, surgical, perioperative, early posttransplant), we analyzed only re-LTs that occurred >1 y after the primary LT.
- Controls 1 (LT recipients with recurrent ALD who died without re-LT): These were LT recipients who had a primary listing indication of ALD or AH and survived at least 365 d from the time of their initial LT; however, they died because of recurrent disease (ie, recurrent ALD), ascertained from recipient primary cause of death, UNOS code 4604, (recurrent disease of original listing indication) without receiving re-LT.
- Controls 2 (re-LT recipients without ALD): These were propensity score–matched first-time re-LT recipients whose graft survived at least 365 d from the time of the primary transplant and who did not have a listing indication of ALD or AH at the time of primary LT or re-LT.

Statistical Analysis

Continuous variables were summarized with medians and interquartile ranges or with means and SDs and categorical variables with frequencies and percentages. Comparative analysis of continuous variables was based on the 2-sample Wilcoxon rank test, whereas that of categorical variables was based on the 2-sided chi-square test. The coprimary study endpoints were (1) overall survival and (2) graft survival, defined as being free from the occurrence of either recipient death

or removal of the transplanted organ (as per UNOS/Organ Procurement and Transplantation Network). We calculated survival using Kaplan-Meier analysis and compared survival between the recurrent ALD re-LT and non-ALD re-LT groups using the log-rank test. We then compared the recurrent ALD re-LT group with the recurrent ALD group who died without re-LT. In addition, we analyzed how the clinical features of the recurrent ALD LT group changed between the initial LT and the re-LT.

We used propensity score matching (PSM) to match the recurrent ALD re-LT group with the non-ALD re-LT group. PSM can be used to reduce bias, including selection bias and other potential confounders, by simulating a randomized controlled trial-like situation where the treatment and the control groups are matched.¹⁴ The propensity score for each subject was estimated using a logistic regression model for the recurrent ALD re-LT group as a function of variables that are associated with graft failure in the literature.¹⁵⁻¹⁸ These variables were selected a priori and consisted of donor age, body mass index (BMI), recipient age, race, gender, diabetes mellitus, life support requirement at transplant, model for end-stage liver disease score, and retransplant year.¹⁵⁻¹⁸ After estimation of the propensity score for each subject, we performed one-to-one matching using the nearest neighbor method with a caliper width of 0.1 of the SD of the logit of the propensity score. All 74 recurrent ALD re-LT cases were matched. The balance of characteristics between recurrent ALD re-LT and non-ALD re-LT groups in the matched sample was checked by examining standardized percent bias (<10% was desirable) and performing formal comparative analysis between covariates. All analyses were 2-sided and performed at the 5% significance level. All statistical analyses were performed using Stata 16.1 (StataCorp, College Station, TX). Our study qualified for institutional review board exemption, given the presence of de-identified data (IRB20-0804).

RESULTS

Re-LT for Recurrent ALD: Prevalence and Characteristics

From 2000 to 2020, we identified 120 175 first-time adult LTs, with 32 643 (27.2%) of these LTs performed for ALD (including AH; $n = 750$, 0.6%) and 7142 re-LTs. During this same time period, only 74 patients had a primary listing indication of ALD for both their initial LT (73 for ALD, 1 for AH) and re-LT (71 ALD, 3 AH) (Figure 1). All 74 received deceased-donor LTs, with no living-donor LTs recorded. The annual frequency of this practice is very low and ranged from 0 to 10, accounting for 0% to 2.3% of the annual overall adult re-LTs (Figure 1). There was a slight increase in the number of recurrent ALD re-LTs between 2017 and 2020 compared with 2014 and 2016 (20 versus 2). Nevertheless, even during this time period (2017–2020), the ALD proportion of the overall re-LT practice remained very low (1.0%–2.3%). For context, there were similar numbers of re-LT performed for alpha-1 antitrypsin deficiency ($n = 46$, 0.6%) and Budd-Chiari syndrome (40, 0.5%) for recurrent ALD during the 20-y study period.

The mean primary allograft survival time was 3.6 ± 2.7 y (to time of re-LT) among recurrent ALD re-LT recipients. Clinical characteristics were similar between index LT and re-LT, apart from an age increase from 52.0 (47.0–56.0) to

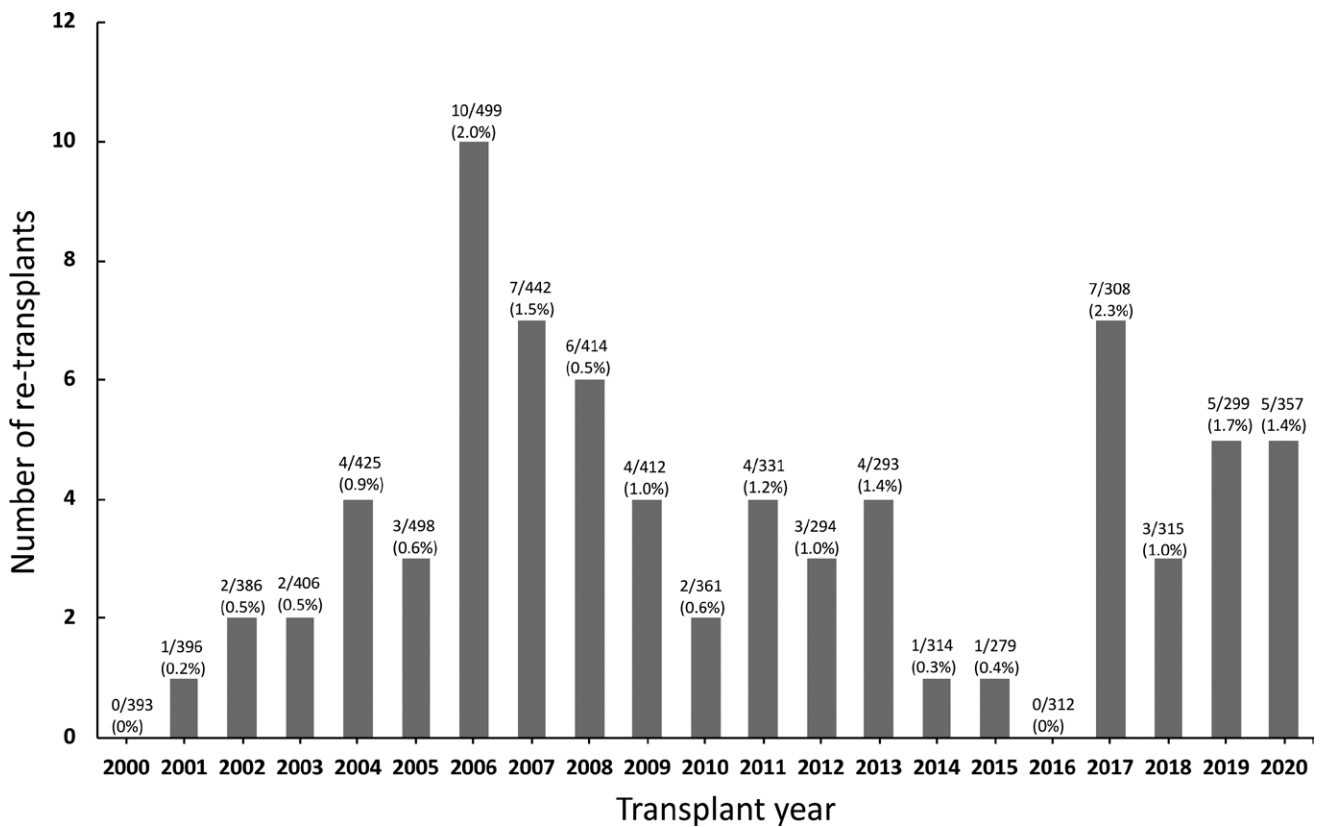


FIGURE 1. The practice of liver retransplantation (re-LT) in patients with ALD (2000–2020) in the United States. The annual number of re-LT recipients with ALD or alcohol-associated hepatitis as the primary diagnosis at the time of both their initial transplant and their retransplant and whose primary graft lasted for >1 y. On top of each bar graph, the number of re-LTs performed for recurrent ALD is shown as a market share of the total number of adult retransplantations in each respective year. ALD, alcohol-associated liver disease.

55.5 (50.0–59.0) y (Table 1). At the time of re-LT, patients with recurrent ALD had a significant decrease in their BMI (median of 25.1 versus 28.8 kg/m²; $P < 0.001$), a significant increase in model for end-stage liver disease scores (median 28.0 versus 22; $P = 0.015$), and a higher proportion with diabetes (29.7% versus 14.9%; $P = 0.030$) than their initial LT (Table 1). There were few patients with hepatocellular carcinoma (<10%), and 39.2% of patients had a positive hepatitis C virus (HCV) antibody serology. Finally, consistent with the inevitable increase in age at the time of the retransplant, more recurrent ALD re-LT recipients became eligible for Medicare (32.4% from 15%), whereas private insurance rates decreased from 68.0% to 50.0%. The highest proportion of re-LTs for ALD occurred in UNOS region 7 (20.3%), whereas UNOS regions 2, 3, 5, and 9 combinedly accounted for 50.0% of all re-LTs, and UNOS region 1 performed no re-LTs. Nearly all the 74 recurrent ALD LTs were performed at the same LT center as the initial LT, except for 4 (5.4%) patients.

Comparative demographics and clinical features of patients with recurrent ALD (who survived at least 1 y from their primary LT) are presented in Table 2, stratified by those who underwent re-LT ($n = 74$) and those who died without receiving re-LT ($n = 89$). The recurrent ALD LT group who died without re-LT had a longer average allograft survival time of 5.2 ± 3.5 y than of 3.6 ± 2.7 y in the recurrent ALD LT group ($P < 0.001$). There were no statistically significant differences between the 2 groups, apart from a lower HCV-positive antibody serology frequency in the group of patients who died without retransplantation.

Survival Outcomes

The covariate balancing of the PSM is presented in Figure S1 (SDC, <http://links.lww.com/TXD/A403>). There was excellent balance achieved between patients retransplanted for ALD versus non-ALD causes with no statistically significant differences observed ($P > 0.05$ for all comparisons) (Table 3). Although cold ischemia time and donation after circulatory death were not specifically matched for, the comparison of these variables between the 2 groups was not statistically different ($P > 0.05$ for both). Primary indications for transplant listing in the non-ALD re-LT group were HCV ($n = 28$; 38%), primary sclerosing cholangitis ($n = 9$; 12%), cryptogenic ($n = 4$; 5%), primary biliary cholangitis ($n = 1$; 1%), hepatitis B ($n = 3$; 4%), and other ($n = 29$; 39%). One- and 5-y graft survival rates were 75.0% and 56.4% in the recurrent ALD liver re-LT recipients, compared with 69.0% and 56.0% in the non-ALD re-LT recipients, respectively ($P = 0.96$) (Figure 2A). One- and 5-y patient survival rates were 80.0% and 62.8% in the recurrent ALD liver re-LT recipients, compared with 70.4% and 59.0% in the non-ALD re-LT recipients, respectively ($P = 0.58$) (Figure 2B).

DISCUSSION

In this 20-y analysis of the UNOS database, we found that re-LT for recurrent ALD is uncommon (0%–2.3% of the entire annual re-LT practice during the past 2 decades). Despite the increasing prevalence of ALD and AH^{19,20} and the marked increase in LT for ALD and AH,^{6,15} re-LT for ALD has remained

TABLE 1.
Sociodemographic and clinical features of LT recipients with recurrent ALD requiring retransplantation in the United States (2000–2020)

	Recurrent ALD requiring retransplantation (n = 74)	
	Index transplantation ^a	Retransplantation
Donor		
Age, y	45.5 (37.0–55.0)	41.5 (25.0–51.0)*
BMI, kg/m ²	27.1 (23.8–30.8)	25.6 (22.7–29.7)
Male gender	45 (61.1)	40 (54.0)*
Caucasian race	54 (73.0)	53 (71.6)
DCD	5 (6.9)	2 (2.7)
Cold ischemia time, h	7.0 (5.3–8.4)	7.0 (5.6–8.8)
Recipient:		
Age, y	52.0 (47.0–56.0)	55.5 (50.0–59.0)**
Male gender	59 (79.7)	59 (79.7)
Caucasian race	54 (73.0)	57 (77.0)
BMI, kg/m ²	28.8 (25.4–32.5)	25.1 (23.4–28.6)***
Posttransplant LOS, d	10.5 (8.0–16.0)	13.0 (8.0–21.0)
Waiting list time, d	54.5 (13.0–213.0)	36.0 (18.0–196.0)
Diabetes	11 (14.9)	22 (29.7)*
MELD score	22.0 (15.0–31.0)	28.0 (20.0–35.0)*
Life support requirement	3 (4.1)	2 (2.7)
ICU	7 (9.5)	7 (9.5)
Dialysis requirement	7 (9.5)	14 (18.9)
Ascites, mild or worse	54 (73.0)	53 (71.6)
Hepatic encephalopathy, grade 1 or worse	47 (63.5)	45 (60.8)
PVT	8 (10.8)	8 (10.8)
HCC	7 (9.5)	2 (2.7)
HCV, positive serology	27 (36.5)	29 (39.2)
Insurance status		
Private	50 (67.6)	37 (50.0)
Medicaid	13 (17.6)	12 (16.2)
Medicare	11 (14.9)	24 (32.4)
VA/other government	0 (0)	0 (0)
Self	0 (0)	1 (1.4)
Donation/free care	0 (0)	0 (0)
Foreign government	0 (0)	0 (0)

Values are n (%) or median (interquartile range). There was 1 patient with alcohol-associated hepatitis in the ALD primary LT group and 3 patients with alcohol-associated hepatitis in the recurrent ALD re-LT group.

Significance codes:

*** $P < 0.001$;

** $0.001 < P \leq 0.01$;

* $0.01 < P \leq 0.05$ (all other P values > 0.05).

^aThe groups are compared by pairwise comparisons via chi-square test for categorical variables and 2-sample Wilcoxon rank test for continuous variables (all continuous variables failed the Shapiro-Wilk normality test).

ALD, alcohol-related liver disease; BMI, body mass index; DCD, donation after circulatory death; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; LOS, length of stay; LT, liver transplantation; MELD, model for end-stage liver disease; PVT, portal vein thrombosis; VA, Veterans Affairs.

stably low during the past decade, perhaps because of a reluctance from transplant programs to perform re-LT in patients with ALD or AH. Regardless of reason, our data indicate that re-LT for recurrent ALD is uncommon and makes up a stable portion of re-LT operations in the United States.

Despite the low number of re-LT for recurrent ALD, our findings indicate that re-LT for ALD has acceptable outcomes compared with re-LT for other indications. When comparing re-LT ALD to non-ALD re-LT, we found similar 1- and 5-y graft and patient survival between groups. Although these

TABLE 2.
Sociodemographic and clinical features of recurrent ALD LT recipients undergoing re-LT compared with those who died without re-LT in the United States (2000–2020)

Variables	Re-LT ^a (n = 74)	Died without re-LT (n = 89)
Donor		
Age, y	45.0 (37.0–55.0)	50.0 (42.0–61.0)
BMI, kg/m ²	27.1 (23.8–30.8)	27.3 (24.2–30.7)
Male gender	45 (61.1)	58 (65.2)
Caucasian race	54 (73.0)	65 (73.0)
DCD	5 (6.9)	5 (5.8)
Cold ischemic time, h	7.0 (5.3–8.4)	7.0 (5.4–8.7)
Recipient		
Age, y	52.0 (47.0–56.0)	50.0 (44.0–57.0)
Male gender	59 (79.7)	62 (69.7)
Caucasian race	54 (73.0)	67 (75.3)
BMI, kg/m ²	28.8 (25.4–32.5)	29.0 (25.3–32.2)
Posttransplant LOS, d	10.5 (8.0–16.0)	10.0 (8.0–15.0)
Waiting list time, d	54.5 (13.0–213.0)	49.0 (13.0–213.0)
Diabetes	11 (14.9)	12 (13.5)
MELD score	22.0 (15.0–31.0)	25.0 (17.0–32.0)
Life support requirement	3 (4.1)	3 (3.4)
ICU	7 (9.5)	13 (14.6)
Dialysis requirement	7 (9.5)	10 (11.2)
Ascites, mild or worse	54 (73.0)	64 (71.9)
Hepatic encephalopathy, grade 1 or worse	47 (63.5)	52 (58.4)
PVT	8 (10.8)	4 (4.5)
HCC	7 (9.0%)	17 (19.1)
HCV, positive serology	27 (36.5)	15 (16.9)*
Insurance status		
Private	50 (67.6)	57 (64.0)
Medicaid	13 (17.6)	16 (18.0)
Medicare	11 (14.9)	14 (15.7)
VA/other government	0 (0)	2 (2.2)

Values are n (%) or median (interquartile range).

Significance code:

*** $P < 0.001$;

** $0.001 < P \leq 0.01$;

* $0.01 < P \leq 0.05$ (all other P values > 0.05). The data set contained $< 1\%$ of missing data: Missing values of continuous variables were ignored, whereas missing values of categorical variables were assumed to be negative.

^aThe groups are compared by pairwise comparisons via chi-square test for categorical variables and 2-sample Wilcoxon rank test for continuous variables (all continuous variables failed the Shapiro-Wilk normality test).

ALD, alcohol-related liver disease; BMI, body mass index; DCD, donation after circulatory death; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; LOS, length of stay; LT, liver transplantation; MELD, model for end-stage liver disease; PVT, portal vein thrombosis; VA, Veterans Affairs.

recurrent ALD re-LT outcomes are inferior to ALD primary LT recipients,⁶ the re-LT outcomes are consistent with prior studies comparing re-LTs and primary indications of other indications.¹² These similar outcomes support the practice based on patient survival if a LT recipient with recurrent ALD presents for re-LT consideration. Notably, these good outcomes are presumably with careful patient selection that transplant providers should bear mind. As AUD is typically a chronic relapsing, remitting condition, the clinical conundrum of whether to retransplant an individual with recurrent ALD is almost certain to arise. Importantly, the candidate's AUD should be assessed and determined to be well treated before retransplantation given the ethical issues surrounding the decision. With this expected rise in incidence, it will be

TABLE 3.**Clinical features of recurrent ALD recipients at the time of re-LT compared with propensity score–matched non-ALD re-LT recipients in the United States (2000–2019)**

Variables	Recurrent ALD at time of re-LT ^a (n = 74)	Non-ALD re-LT recipients (n = 74)
Donor		
<i>Age, y</i>	41.5 (25.0–51.0)	39.0 (26.0–51.0)
<i>BMI, kg/m²</i>	25.6 (22.7–29.7)	25.0 (22.1–29.4)
Male gender	40 (54.0)	42 (57.0)
Caucasian race	53 (71.6)	50 (68.0)
DCD	2 (2.7)	1 (1.4)
Cold ischemic time, h	7.0 (5.6–8.8)	6.4 (5.3–8.0)
Recipient		
<i>Age, y</i>	55.5 (50.0–59.0)	57.0 (51.0–60.0)
<i>Male gender</i>	59 (79.7)	63 (85.0)
<i>Caucasian race</i>	57 (77.0)	54 (73.0)
<i>BMI, kg/m²</i>	25.1 (23.4–28.6)	24.9 (22.5–29.0)
Posttransplant LOS, d	13.0 (8.0–21.0)	12.0 (8.0–30.0)
Waiting list time, d	36.0 (18.0–196.0)	48.5 (14.0–220.0)
<i>Diabetes</i>	22 (29.7)	18 (24.0)
<i>MELD score</i>	28.0 (20.0–35.0)	28.0 (22.0–34.0)
<i>Life support requirement</i>	2 (2.7)	2 (2.7)
ICU	7 (9.5)	13 (18.0)
Dialysis requirement	14 (18.9)	7 (9.0)
Ascites, mild or worse	53 (71.6)	53 (71.6)
Hepatic encephalopathy, grade 1 or worse	45 (60.8)	41 (55.0)
PVT	2 (2.7)	2 (2.7)
HCC	7 (9.5)	2 (3.0)
HCV, positive serology	29 (39.7)	33 (45.2)
Karnofsky Performance Status, ≥60	35/67 (52.2)	44/66 (66.7)
Employed with monetary income	10/66 (15.2)	10/62 (16.1)
Insurance status		
Private	37 (50.0)	42 (56.8)
Medicaid	12 (16.2)	5 (6.8)
Medicare	24 (32.4)	21 (28.4)
VA/other government	0 (0)	5 (6.8)
Self	1 (1.4)	0 (0.0)
Donation/free care	0 (0)	1 (1.4)

Values are n (%) or median (interquartile range).

There are 9 propensity score–matched variables presented in italics in this table. In addition, recipients were also matched on transplant year.

Significance codes:

*** $P < 0.001$;

** $0.001 < P \leq 0.01$;

* $0.01 < P \leq 0.05$ (all other P values > 0.05). There were no significant differences observed.

The data set contained $< 1\%$ of missing data: Missing values of continuous variables were ignored, whereas missing values of categorical variables were assumed to be negative.

^aThe groups are compared by pairwise comparisons via chi-square test for categorical variables and 2-sample Wilcoxon rank test for continuous variables (all continuous variables failed the Shapiro-Wilk normality test).

ALD, alcohol-associated liver disease; BMI, body mass index; DCD, donation after circulatory death; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; LOS, length of stay; LT, liver transplantation; MELD, model for end-stage liver disease; PVT, portal vein thrombosis; VA, Veterans Affairs.

important to continue to measure outcomes while also assessing provider, patient, and public attitudes toward the practice.

One of the unique aspects of our study encompassing 20 y of national data is the fact that it provides insight into the natural history of LT recipients with ALD who undergo re-LT for recurrent ALD after their primary graft survives beyond 1 y. In a French study, ~20% (n = 162) of ALD LT recipients experienced severe alcohol relapse at a median of 1.5 y, with

the vast majority relapsing by year 3 posttransplant. Of these 162 patients, over one third progressed to recurrent ALD that resulted in an accelerated rate of subsequent decompensation.²¹ A single-center study from Wisconsin, United States, also demonstrated that heavy drinking after LT is associated with decreased graft survival and advanced allograft fibrosis.²² At 4 y post-LT, the graft survival curves diverged with LT recipients who continuously consumed heavy alcohol experiencing accelerated graft failure compared with those who did not consume heavy alcohol posttransplant.²² In our study, the median time of 3.6 y to re-LT is broadly consistent with the aforementioned studies in addition to being congruent with the index natural history study from DiMartini et al³ on when to expect significant graft failure from recurrent ALD; however, it is on the shorter than expected side that may reflect an element of misclassification bias that is elaborated further below.

Interestingly, individuals requiring re-LT for recurrent ALD had a significantly lower BMI than index LT, despite the frequency of ascites remaining stable between the 2 groups. Given that weight gain and subsequent metabolic syndrome are well-documented consequences of LT,²³ we suspect that the decrease in BMI between index and retransplantation can be explained in 2 ways: Patients may have experienced an initial posttransplant weight gain that was not captured in our analysis or, alternatively, the drop in BMI corresponds with more progressive malnutrition and frailty in the setting of relapsed AUD and recurrent end-stage liver disease. If the latter is true, decreasing BMI in the setting of hepatic dysfunction could potentially be an important marker for recurrent AUD. Although our analysis from this large data set was not granular enough to determine the exact timing or cause of the observed BMI decline, it highlights the importance of close outpatient follow-up for monitoring of AUD relapse and nutritional status post-LT.

These results should be understood in the context of the UNOS database. First, there is a risk of misclassification bias that may have increased the numbers of the recurrent ALD re-LT recipient cohort; therefore, the practice may be even rarer than described. The recurrent ALD re-LT did have a comparatively increased positive HCV serology rate; therefore, recurrent HCV infection may have been the primary reason for re-LT rather than recurrent ALD. It is also possible that the original indication for LT may also have been carried over from the initial LT when the episode was being recorded in UNOS, and a proportion of patients may have had an alternative surgical or medical complication as the primary indication for re-LT. Second, the database lacks granular data on alcohol consumption pre- and post-LT and poorly captures “recurrent ALD” as a cause of graft failure/death among ALD LT recipients. It is likely that > 89 recurrent ALD LT recipients died without re-LT during our study period; however, we believe that the latter control group is a worthy comparative group, acknowledging the limitations. Finally, the low numbers of recurrent ALD re-LT recipients (and, by extension, low number of graft failures) precluded any analysis on associations with graft failure in this important population. Another point to consider is that our non-ALD re-LT control group may not be wholly representative of the current patient population that undergoes liver re-LT retransplantation given the high proportion of patients whose primary listing indication was HCV infection. HCV as a listing indication for re-LT has drastically reduced since the approval

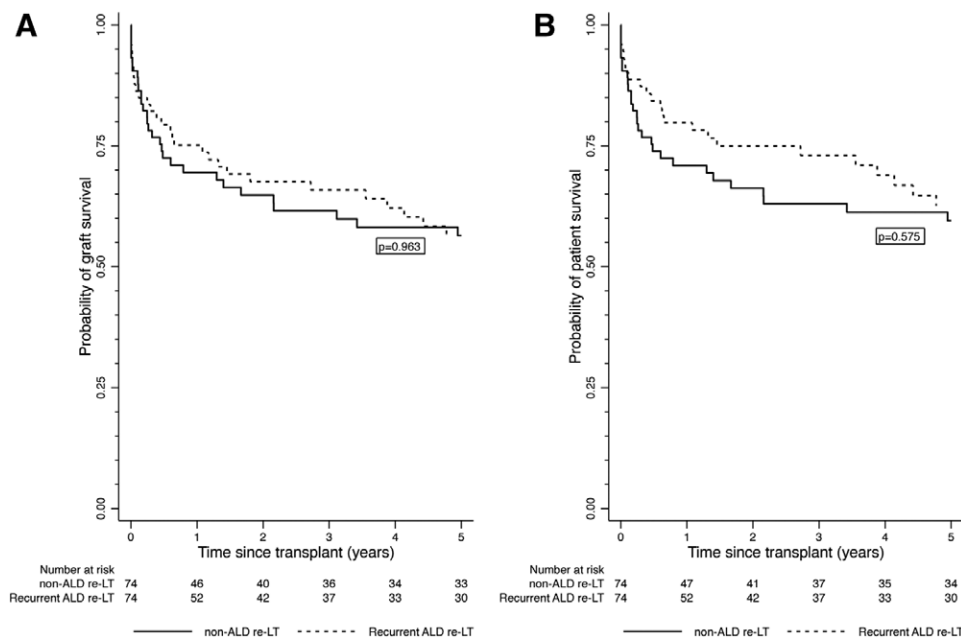


FIGURE 2. Graft (A) and (B) patient survivals are shown in the recurrent ALD re-LT group and compared with propensity score-matched non-ALD re-LT recipients in the United States (2000–2020). Initial allograft of both groups survived for at least 365 d. ALD, alcohol-associated liver disease; LT, liver transplantation.

of direct-acting antiviral agents. The generalizability of our results outside of the United States is uncertain given the variability of LT practice around the world and absence of similar data to ours; however, our results outline the characteristics of the ALD re-LT recipients in detail, enabling inferences to be made should similar re-LT candidates present for evaluation in other countries outside of the United States.

In conclusion, our study suggests a nationwide reluctance by LT centers for re-LT for recurrent ALD despite a significant increase in AUD, ALD, and initial LT for ALD and AH^{21,22}; however, our results show acceptable outcomes in recurrent ALD re-LT and support the practice (from a survival perspective) should a recurrent ALD LT candidate be deemed appropriate. Future studies will be needed with particular attention to the optimal preretransplant patient selection and postretransplant care given the anticipated increase in recurrent ALD re-LT practice.

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