ORIGINAL ARTICLE

Alcohol Consumption Patterns and Predictors of Use Following Liver Transplantation for Alcoholic Liver Disease

Andrea DiMartini[1], Nancy Day[1], Mary Amanda Dew[1], Lubna Javed[1], Mary Grace Fitzgerald[1], Ashok Jain[2], John J. Fung[2], and Paulo Fontes[2]

Departments of [1]Psychiatry and [2]Transplantation Surgery, University of Pittsburgh Medical Center and Starzl Transplant Institute, Pittsburgh, PA

For patients who receive a liver transplant (LTX) for alcoholic liver disease (ALD), investigators are focusing beyond survival to determine specific alcohol use outcomes. Studies suggest the use of alcohol ranges from 8 to 22% for the first post-transplant year with cumulative rates reaching 30 to 40% by 5 years following transplantation. Yet while investigators are interested in determining specific rates of alcohol use and predictors of use, only three studies since 1990 have been prospective. In 1998, we began a prospective study of post-LTX alcohol consumption in ALD recipients using multiple repeated measures of alcohol use. After 5 years of follow-up, we found that 22% had used any alcohol by the first year and 42% had a drink by 5 years. By 5 years, 26% drank at a heavier use (binge) pattern and 20% drank in a frequent pattern. In a univariate model, predictors of alcohol use included pre-transplant length of sobriety, a diagnosis of alcohol dependence, a history of other substance use, and prior alcohol rehabilitation. ***Liver Transpl 12:813-820, 2006.*** © **2006 AASLD.**

Received August 4, 2005; Accepted November 29, 2005.

See Editorial on Page 705

Over the past decade, studies have consistently demonstrated the success of liver transplantation (LTX) for alcohol-related liver disease (ALD). Short-term outcomes (1-3 year actuarial survival) of patients transplanted for alcoholic cirrhosis are comparable to[1-3] or better than[4-6] patients transplanted for other types of end-stage liver disease. More recently, investigators are looking beyond survival to focus on two specific areas of post-transplant outcomes in ALD LTX recipients: 1) determining the rates of return to alcohol use and 2) predictors of use post-transplant with the eventual purpose of identifying the impact of alcohol use on post-transplant outcomes. To date, studies which investigated the use of *any* alcohol post-LTX in ALD recipients showed during the first year post-LTX drinking rates range from 8 to 22% .[7] Cumulative rates of any alcohol use are estimated between 30 to 40% by 5 years following LTX.[8] The rate of return to pathologic drinking, defined as drinking that results in withdrawal symptoms or in physical or social injury, is estimated at about 10-13%.[7,9,10]

Unfortunately, most studies of post-LTX alcohol use are not prospective. In fact, in a recent review that identified 21 studies on post-LTX alcohol use published since 1990, only three were prospective.[11] Before estimations of the impact of alcohol use on post-LTX outcomes can be made with certainty, it is crucial to establish clearly the timing and patterns of alcohol use. Therefore, in 1998 we began a prospective study of post-LTX alcohol consumption in ALD recipients using multiple repeated measures of alcohol use. In 2001 we reported on our initial cohort having identified 38% who

Abbreviations: LTX, liver transplantation; ALD, alcohol related liver disease; ATLFB, alcohol-timeline follow-back questionnaire; NIAAA, National Institute on Alcohol Abuse and Alcoholism; CDT, carbohydrate deficient transferrin.

Address reprint requests to: Andrea DiMartini, MD, Western Psychiatric Institute and Clinics, 3811 O'Hara Street, Pittsburgh, PA 15213. Telephone: (412) 383-3166; FAX: (412) 383-4846; E-mail: dimartiniaf@upmc.edu

Supported by grants K23 AA0257 from the National Institute of Alcohol Abuse and Alcoholism and R01 DK066266 from the National Institute of Digestive Disorders and Kidney Diseases Rockville, MD, USA.

DOI 10.1002/lt.20688
Published online in Wiley InterScience (www.interscience.wiley.com).

had at least one drink in the first post-operative year.[12] We now report on our continuing prospective study with up to 5 years follow-up of our cohort. In addition to the first drink, we have identified the onset of other specific drinking outcomes and pre-transplant characteristics that predicted these outcomes.

METHODS

Subjects

Enrollment

All patients transplanted for either a primary or secondary diagnosis of ALD at the Starzl Transplant Institute (STI) from May 1998 to December 2002 were eligible for the study. At the time of enrollment, participants were at least 3 months post-transplant and discharged from the medical facility. Participants were voluntarily enrolled in our study after agreeing to participate and signing informed consent. During the period of study recruitment, 210 transplant recipients were eligible. Of these, 167 participated, 32 (15%) died before enrollment, and 11 (5%) refused to participate.

The pre-LTX diagnosis of alcohol-related liver disease was determined by consensus from interviews and examinations by our transplant surgeons, hepatologists, and psychiatry team (psychiatric nurse clinical specialist-MGF and psychiatrist-AD). Patients with ALD had a history of excessive alcohol use, defined as $\geq$ 20 grams of ethanol per day for women or $\geq$ 60 grams ethanol per day for men.[13] The majority (> 88%) had consumed this amount for 10 years or longer. Psychiatric diagnoses of alcohol dependence or alcohol abuse were made by the psychiatry team using a structured psychiatric clinical interview and the Diagnostic and Statistical Manual of Mental Disorders IV[14] criteria.

PROCEDURES

Interviews and Questionnaires

Three prospective measures of post-transplant alcohol use were obtained. First, every 3 months for the first post-transplant year and every 6 months thereafter, patients completed the Alcohol-Timeline Follow-Back questionnaire (ATLFB).[15] The ATLFB is a calendar instrument that captures a daily profile of alcohol use (quantity, frequency, and pattern of alcohol use) for the intervals between follow-up interviews. The ATLFB measure has good psychometric characteristics and allows the dimensions of drinking to be examined separately. It has high test-retest reliability and validity across multiple populations of drinkers and has been tested on clinical and general population samples.[16] ATLFB questionnaires were completed during a return clinic visit, by telephone interview with the research staff, or by mail. The patients were informed that the information would be strictly confidential, would not become a part of their medical record, and would not be revealed to any member of the transplant team (including the transplant psychiatrist AD or psychiatric nurse clinical specialist MGF). The research staff was not blinded to the patient's diagnosis or history. Completion rates for ATLFB were high at all time points (75-93%). Participants who missed one time point provided data on the missed time period at the next study assessment.

Second, over the same time intervals, a caregiver who knew the patient best and typically lived with the patient (usually a spouse or family member) filled out a quantity-frequency questionnaire, which asked about the patient's alcohol use since transplant. The caregiver questionnaire was patterned after the National Institute on Alcohol Abuse and Alcoholism (NIAAA) Quantity-Frequency measure[17] and asked about the number of drinking days and the amount consumed.

Third, during routine post-transplant clinic appointments, clinical interviews were performed by the transplant psychiatrist (AD) who was blinded to the data obtained by the research staff. Responses to questions about alcohol use from the psychiatrist's interview were corroborated with information given by the patient to the transplant coordinators and surgeons. As this clinic interview was conducted in the transplant clinic in conjunction with the transplant team, information provided to the transplant psychiatrist was revealed to the transplant team. This information was recorded as quantity/frequency of alcohol use with specific dates and amounts of use on a monthly calendar form. Patients are seen in the transplant clinic as medically indicated. However, when possible, most patients are seen twice weekly for the first month after discharge from their hospital admission, then monthly until 3 months post-transplant, and then every 3 to 6 months thereafter.

At each clinic interview, patients are counseled to maintain complete abstinence by the transplant psychiatrist as well as other members of the transplant team. The identification of any alcohol use resulted in further counseling by the transplant psychiatrist and recommendations for professional alcohol counseling. Depending on the circumstances, patients are referred for either inpatient or outpatient addiction rehabilitation. Attendance at AA is also strongly encouraged. Thus after the initial clinical identification of any alcohol use, this was not a naturalistic study in which we only observed the course of the addiction. Instead we practiced the same standard of care as most transplant programs where patients are strongly recommended to remain completely abstinent and addiction counseling is recommend when alcohol use is identified. Information on attendance at rehabilitation is monitored clinically but is not a part of the research dataset.

Biochemical Markers

As part of routine clinical care, random blood alcohol levels were obtained on the patients. Blood alcohol levels (BAL) are performed by gas chromatography with positive levels identified at values $\geq$ 0.01 gm/dL. Using the blood alcohol level and the patient's weight, information on the quantity of alcohol consumed to reach that BAL can be estimated. From the equation $Q = V_d \times$

C_{ss} where Q = loading dose (in grams of ethanol), V_d = volume of distribution (in L) = 0.54 L/kg × patient weight in kg, and C_{ss} = concentration at steady state (in grams/L), we can predict the loading dose of ethanol required to achieve a specific BAL. This BAL can be converted into standard drinks (assuming 10 grams of ethanol/standard drink). This information was used to identify specific alcohol use outcomes (i.e., the time to first drink, the time to six drinks).

Elevated levels of carbohydrate deficient transferrin (CDT) can indicate heavy sustained alcohol use.[18] Although we initially measured blood samples for the level of CDT at the study time points, we did not find the CDT values to be accurate in identifying those who were using alcohol and we stopped obtaining these samples (see reference 19).

Pre-Transplant Alcohol and Other Psychosocial Variables

The duration of pre-transplant sobriety was defined as the months from the last reported drink of alcohol to transplantation. Pre-transplant, we calculated the average weekly alcohol usage, by patient report, in standard drinks. Standard drinks were defined as 1 ounce (1 shot) of hard liquor, 1 12-ounce beer, or 6 ounces of wine. Standard drinks were converted into average weekly grams of ethanol assuming that a standard drink has 10 grams of ethanol. This was calculated by converting the ounces of alcoholic beverage to ounces of pure ethanol and then converting into grams of ethanol. Years of drinking was defined as the number of years a patient drank at the average daily amount. During the pre-transplant psychiatric evaluation, we collected information on attendance at alcohol rehabilitation and the type of rehabilitation. We counted any inpatient or outpatient rehabilitation or regular attendance at Alcoholics Anonymous (AA) (defined as at least 12 meetings attended) as pre-transplant rehabilitation. To measure a family history of alcoholism, patients were asked about any first degree biologic relative who had an alcohol use disorder.

Other demographic and psychosocial information collected during the pre-transplant evaluation included current or prior use of other substances, a history of injected drug use, diagnosis of substance use disorders, depressive or anxiety disorders, and treatment for psychiatric disorders. We also calculated the patient's Child-Pugh score at the point of transplantation.

Post-Transplant Alcohol Use Outcomes

Drinking occurs in a wide variety of patterns, defined by quantity, frequency, and duration. We chose three alcohol use outcomes to define drinking events: time to first drink (onset of use), time to six drinks in a day for men and four drinks in a day for women (binge use), and time to four drinking days in a week (frequent use). The alcohol outcomes were calculated using information from each of the four ascertainment measures (clinical interview, ATLFB, caregiver report, and BAL). Time to outcome was calculated from date of discharge from the transplant hospitalization until the outcome was achieved. Since some participants spent several months in the hospital following transplantation, we assumed the individual was not drinking in the hospital, and looked only at the post-hospital time period to measure time to the alcohol outcomes. The time to first alcohol use was defined as the time to first positive report on any of the interview/questionnaires or the first positive BAL. Time to binge use was defined as the time to first interview/questionnaire report of this quantity in a day or a BAL level calculated that was compatible with this quantity. Time to four drinking days in a week was defined by the interview/questionnaires. BALs could not be used as they were not sampled repeatedly within a week. For participants who did not reach the specific alcohol outcomes, we chose date of last follow-up on either the interview or questionnaires, whichever came last.

Statistical Analysis

Continuous variables are presented as the mean ± standard deviation (SD), and categorical variables are presented as proportions. The data on alcohol use outcomes from each patient were included until the end of the observation period or until the event occurred. Event history curves were generated using the Kaplan-Meier method for continuous variables (i.e., the quantity/frequency calendars). Cox proportional hazard modeling was used to investigate which pre-transplant variables predicted alcohol use outcomes. Based on our prior work, we chose five pre-LTX variables for the initial univariate analyses: length of sobriety, attendance at rehabilitation, diagnosis of alcohol dependence, other substance use, and family history of alcoholism. For each primary variable and each outcome, a univariate Cox model was fit to determine if the variable was associated with the specific outcome. All five variables were significantly associated with each alcohol use outcome. Because there were significant correlations (> 0.3) between three of these variables (> 90% participants who attended rehabilitation also had used other substances and had alcohol dependence), we used only alcohol diagnosis, length of sobriety, and family history for the final multivariate Cox model. Since we did not have strong hypotheses about the other psychosocial variables (Table 1), we examined each as a potential predictor of the alcohol use outcomes in an exploratory univariate Cox analysis. Those that achieved a $P \leq 0.05$ were included in the final multivariate analyses. Months sober, average number of drinks/week, and average grams of ethanol/week were log transformed prior to analysis due to positive skewing. A P-value less than 0.05 was considered statistically significant. All analyses were performed using SAS (Statistical Analysis Software) version 8.2.

TABLE 1. Demographic and Clinical Characteristics for 167 Liver Transplant Patients

Variable	N or mean	Percent or S.D.
Age	49.7	7.6
Gender (male)	139	83
Race (% Caucasian)	158	95
Marital status		
Single	21	13
Married	85	51
Divorced	45	27
Education (% high school grad)	139	83
Last occupation (% non-professional)	125	75
Years of heavy drinking	20	9 (range 4-50)
Months sober pre-LTX	40	45 (median 21, range 0-288)
Average number of drinks/week pre-LTX	101	100 (median 63)
Rehab before transplant	77	46
If yes, type:		
Inpatient	45	63
Outpatient	51	74
AA	57	81
Detox only	2	3
Alcohol diagnosis		
Abuse	35	21
Dependence	125	76
No diagnosis	5	3
Family history of alcoholism	104	63
Pre-OLXT: Depressive disorders	67	42
Anxiety disorders	33	21
Other substance use	67	40
IV substance use	45	27
Psychiatric medication	68	41
Any psychiatric dx pre-transplant	105	65
Child-Pugh score at LTX	10	2
Hepatitis B and/or C	86	52

RESULTS

Sample Demographics

The 167 participants were predominately Caucasian males, reflecting the demographics of the transplant population and of patients with end-stage ALD. Table 1 shows their pre-transplant demographic, psychiatric, and medical characteristics. The majority (76%) of participants met pre-LTX lifetime DSM-IV criteria for alcohol dependence, the more severe form of the disorder, and more than 65% had an additional lifetime psychiatric diagnosis, mostly depressive disorders (42%). In addition, 40% had used substances other than alcohol and 27% of the total cohort had used injected drugs (70% of those who used other substances). A majority of the patients (54%) had not participated in any form of addiction rehabilitation prior to transplantation. Most (63%) identified a first-degree biologic relative who also had problems with alcohol use.

Pre-Transplant Alcohol Consumption: Comparison Between Genders

Table 2 shows the differences between men and women with respect to their alcohol use prior to transplantation. Men drank for significantly more years than women (21 vs. 14 years, respectively, $P < 0.0001$), although they consumed similar average weekly amounts. There were no significant differences by gender in the length of pre-transplant sobriety, although it was shorter among women (26 vs. 42 months). Men more often drank beer ($P < 0.0001$), while women were more likely to drink hard liquor ($P = .06$). Men and women were equally likely to have a psychiatric diagnosis of alcohol dependence (75% vs. 82%), and although more men had a history of other non-alcohol substance use this difference was not statistically significant (42% vs. 29%, respectively).

Alcohol Use Outcomes

Figure 1 displays the time to onset for each of the three drinking outcomes (first drink, binge use, and frequent use). By 4.5 years post-discharge, 42% of the subjects had had at least one drink. This outcome is comparable to the often reported statistic of *any* alcohol use following transplantation.[7] Ten percent of the subjects had their first drink within 3.5 months of discharge from the hospital and 1 participant drank within a week of discharge. The next most common outcome, binge use, was reached by 26% of participants by 5 years post-transplant; 10% reached this outcome within the first year. Although we had defined men and women differently with respect to the binge outcome, all subjects

TABLE 2. Comparison Between Male and Female Liver Transplant Patients on Alcohol Use Variables

Variable	Women (n = 28)		Men (n = 139)			
	Mean or n	SD or %	Mean or n	SD or %	χ^2 or t	*P*
Months sober*	26.0	20.6	42.4	48.0	1.48	.15
Average number or drinks per week*	100.0	107.2	101.4	98.7	0.38	.71
Average grams ETOH per week*	999.2	1049.8	1048.5	1047.8	0.40	.69
Years of heavy drinking	13.7	6.5	21.4	8.8	4.14	<.0001
Drank beer	13	52	114	84	13.56	.0002
Drank wine	3	14	17	13	0.02	.91
Drank hard liquor	21	81	83	61	3.70	.06
Dependence diagnosis	23	82	102	75	0.75	.39
Other substance use	8	29	59	42	1.87	.17

*Log-transformed prior to t-test.

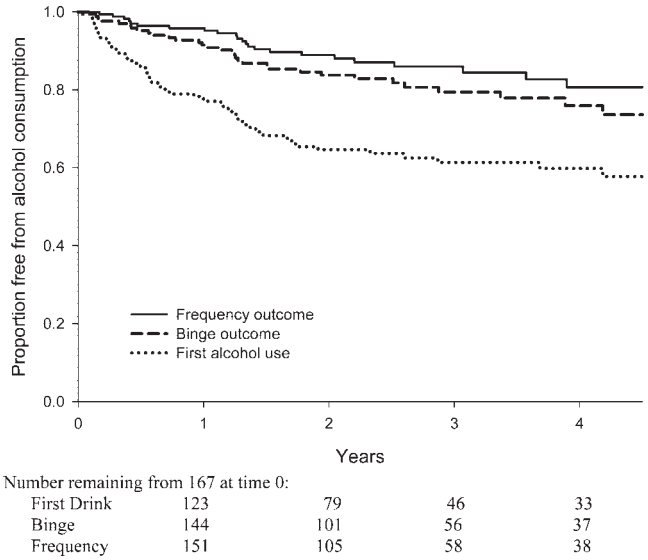

Figure 1. Time to alcohol use outcomes following discharge (N = 167).

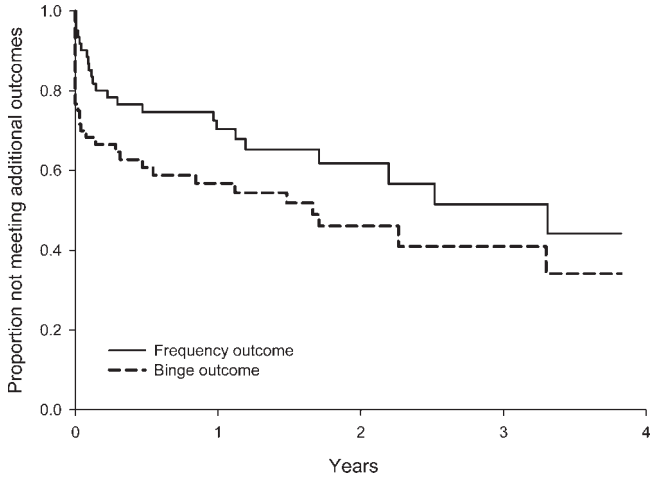

Figure 2. Time from first use to other alcohol outcomes (N = 61).

who binged drank six or more standard drinks for the episodes that defined their binge (range 6-37 drinks, mean = 11 drinks). Twenty percent of the cohort had frequent use by 4 years post-transplant and there were no further cases. Ten percent reached this outcome by 1.5 years post-discharge. Thus, those who return to alcohol use do so early and the rates of alcohol use initiation attenuate with time. While the rate of *any* alcohol use was high, heavy consumption was much less frequent and regular use was uncommon. Among those who went on to binge use, the transition between the first drink and binge use was rapid, with 40% bingeing within 6 months after the first drink (Fig. 2).

Predictors of Alcohol Outcomes

We chose the two most frequent alcohol use outcomes to focus our analysis, the time to first drink and the time to binge use. Based on prior work, we chose five variables for the initial univariate analyses (pre-transplant diagnosis of alcohol dependence, pre-transplant addiction rehabilitation, months sober pre-transplant, family history of alcoholism, and pre-transplant other substance use). In univariate analyses, alcohol dependence (χ^2 =7.34, *P*=0.007), rehabilitation (χ_2 =7.17, *P*=.008), months sober (χ^2 =8.18, *P*=.005), and other substance use (χ^2 =4.43, *P*=.04) were significantly associated with time to first drink. These variables were also significantly associated with the time to binge use and time to frequent use. Interestingly while any pre-transplant substance use predicted those most likely to drink, neither a pre-LTX diagnosis of a substance use disorder nor a diagnosis of substance dependence predicted our alcohol use outcomes. Even amongst those who had alcohol dependence, a co-morbid pre-transplant diagnosis of substance dependence did not predict any alcohol use outcome ($\chi^2 \leq$_0.6, *P* = ns).

Owing to significant overlap in variables only three (alcohol dependence, months sober, and family history) were included in the multivariate Cox analysis. The duration of pre-transplant sobriety was a significant predictor of both time to first drink (*P* = .001) and binge use (*P* = 0.01). Family history was not a significant predictor (Table 3). We also considered the contribution

TABLE 3. Univariate Cox Proportional Hazard Models for Alcohol-Related Outcomes Among Liver Transplant Patients, Excluding Overlapping Variables (N = 162).

	Time to first use			Time to binge		
Effect	HR	χ^2	*P*	HR	χ^2	*P*
Months sober*	0.67	10.76	.001	0.64	6.59	.01
Alcohol Dependence dx†	2.64	6.41	.01			
Family history	1.63	2.96	.09	1.67	1.75	.19

Abbreviation: HR, hazard ratio.
*Log-transformed.
†All participants who had binge use were Alcohol Dependent so this variable was not used in the analysis.

TABLE 4. Multivariate Cox model for Time to First Use, Controlling for Depressive Disorder

Effect	HR	χ^2	*P*
Months sober*	0.65	11.00	.001
Dependence dx	2.34	4.84	.03
Family history	1.62	2.83	.10
Depressive disorder	1.73	4.42	.04

Abbreviation: HR, hazard ratio.
*Log-transformed.

TABLE 5. Multivariate Cox Model for Time to Binge Outcome, Controlling for Marital Status

Effect	HR	χ^2	*P*
Months sober*	0.65	6.52	.01
Family history	1.54	1.23	.27
Married	0.47	4.11	.05

Abbreviation: HR, hazard ratio.
*Log-transformed.
All participants who had binge use were Alcohol Dependent so this variable was not used in the analysis.

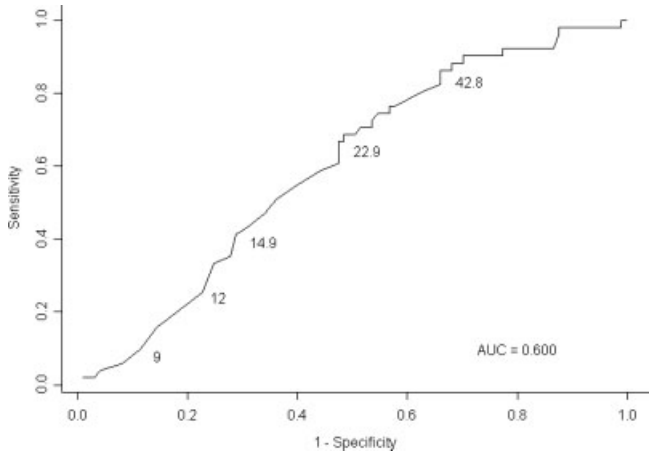

Figure 3. ROC curve for the prediction of relapse (single use) within 18 months of transplant using months sober prior to transplant (selected points on curve labeled with corresponding months sober pre-LTX). *The numbers on the curve are months of pre-LTX sobriety.

of the psychosocial and medical variables. A pre-transplant history of a depressive disorder predicted time to first alcohol use ($P = 0.04$, Hazard Ratio, HR 1.73) (Table 4). Since all of the binge drinkers had prior alcohol dependence, only months sober and family history were included when analyzing the contribution of marital status (Table 5). Being married protected against binge use ($P = 0.05$, HR 0.47).

Since length of sobriety as a continuous variable was a significant predictor of alcohol use, we wondered whether there was a threshold of sobriety that predicted alcohol use. In the transplantation field, a threshold of 6 months pre-LTX sobriety is considered important. However, we only had four participants with 6 months or less pre-LTX sobriety and were not able to analyze this cutpoint as a predictor of post-LTX alcohol use. We explored whether there was a specific sobriety threshold that would predict alcohol use by calculating the area under the curve (AUC) for each alcohol use outcome using ROC curves. Figure 3 shows the results for the outcome of first drink. The curves for all three alcohol use outcomes were similar. The numbers on the curve are months of pre-LTX sobriety. The AUC of 0.60 indicates a somewhat poor predictor and shows that while the true positive rate (sensitivity) increases with time, the false positive rate (1-specificity) also increases almost linearly. For example, 36 months of pre-LTX sobriety is 80% sensitive but only 40% specific in predicting post-LTX abstinence. These findings demonstrate that while there is no clinical cutpoint that can ensure sobriety, longer sobriety predicts less risk of alcohol use.

DISCUSSION

Our study is unique in that it is a prospective study of post-LTX alcohol use using multiple and repeated methods (clinic report, patient report, caregiver report, and biochemical markers) to identify alcohol use. The use of calendars allows us to report on the timing of alcohol use onset using event history analysis curves rather than reporting on yearly rates. Additionally these

calendars allow the characterization of specific drinking outcomes. By contrast, in other studies of post-LTX alcohol use, the characterization of alcohol use outcomes has generally been as a dichotomized variable without regard to the duration of follow-up. We were able to consider the differing lengths of follow-up time for LTX recipients and adjust for this in the analyses.

While our physicians/clinicians strongly advise abstinence post-LTX, by 4.5 years post-LTX, 42% of our patients had had at least one drink. While the rates of more problematic drinking patterns, binge and frequent use, were less common (26% and 20% respectively), a substantial percentage of those who drank any alcohol quickly advanced to heavier use. In fact, for 20% of those who binged, their first drinking episode was a binge episode, which demonstrates that controlled or light consumption is not possible for these patients. In addition, all of the binge drinkers drank six or more standard drinks at their binge episode. Our finding that the rates of alcohol use initiation attenuate with time post-LTX may be explained by increasing stability of sobriety over time. Thus the longer a patient remains sober post-LTX, the less likely they are to begin to drink.

The clinical notion that a short length of pre-LTX sobriety can guarantee post-LTX sobriety is misguided. In long-term studies of persons with alcohol dependence, stable sobriety is measured in years, not months. In these studies, after 5 years of abstinence, subsequent relapse becomes unlikely.[20] It is likely that the 6 month time frame often reported in the transplant literature has been chosen as a sobriety benchmark due to the medical severity of some candidates who would not survive longer prior to transplantation. We found that each additional month of pre-LTX sobriety lowered the risk of drinking post-LTX by 33%. However, we could not identify a specific length of pre-LTX sobriety that predicted abstinence. ALD candidates with a short pre-LTX sobriety need addiction rehabilitation prior to transplantation, as well as strong and sober family supports. In addition, all candidates with ALD should be periodically reassessed on the wait-list as two studies have reported relapse rates of up to 25% for wait-listed ALD candidates.[21,22]

While the significant correlation between alcohol dependence and other non-alcohol substance use precluded including both in the multivariate model, in the univariate analyses other substance use was a strong predictor of post-LTX alcohol use although a diagnosis of a substance use disorder did not predict alcohol use outcomes. We consider any substance use to be problematic. Perhaps individuals who used other substances pre-LTX are less likely to take seriously the health risks of alcohol use post-LTX. Illicit substance use is an important issue in LTX as increasing numbers of transplant candidates have hepatitis C or B, which are most often contracted from injected and/or illicit drug use. In our cohort, 40% of the subjects had used drugs other than alcohol and 27% had used injected drugs. These patients may require specialized psychiatric care including ongoing addiction counseling post-LTX and monitoring for other substance use in addition to alcohol.

We found that a history of a pre-LTX depressive disorder was associated with greater risk to drink post-LTX. Although we did not know if the patient was depressed at the point they started drinking, in non-transplant alcohol dependent patients depression can increase the risk for drinking and decrease the responsiveness to alcoholism treatment.[23] Transplant candidates and recipients should be carefully monitored for depressive symptoms and treatment should be provided when a depressive disorder occurs. Social support is also critical for transplant recipients. In our study, being married provided protection against binge alcohol use. This coincides with data from a large US epidemiologic study that found being married was positively associated with recovery for alcohol-dependent individuals.[24]

While the rates of alcohol use are disturbing, given that these patients were strongly and repeatedly advised against any alcohol use, it is important to understand the clinical course of alcohol dependence. Alcohol dependence is a chronic medical illness. Prior to achieving stable abstinence, patients can have a relapsing-remitting course. These rates compare favorably with the general population of alcohol-dependent individuals for whom 2-year relapse rates of 60 to 80% are common following alcohol treatment.[20] Additionally, in our clinical experience with this population, we found that many of those who binge drank or drank frequently spontaneously revealed their use to us and requested assistance with alcohol rehabilitation. Thus many who drank actively sought help to stop and no patient denied the potential harmful effects of alcohol on their health. For LTX recipients who drink any alcohol at all, addiction counseling is strongly recommended. The transplant team should assist the patient in locating an appropriate referral. Ignoring or minimizing the consumption of even small amounts of alcohol or occasional use may suggest to the patient that this is acceptable and is a missed opportunity for education and treatment. The use of pharmacotherapy, while potentially beneficial, should be undertaken by a psychiatrist knowledgeable of these medications, their risks, and potential interactions with other drugs.[25]

A potential limitation of our study is the lack of a measure of duration for each of the alcohol outcomes. In the future, we will have prospective data on daily alcohol use post-LTX and will be able to map alcohol consumption patterns onto post-LTX outcomes. Trajectory analyses can model alcohol use over time using the quantity, frequency, and duration of use. Thus we plan to report on this population using the defined trajectories of alcohol use as predictors of specific medical outcomes.

REFERENCES

1. DiMartini AF, Jain A, Irish W, Fitzgerald MG, Fung JJ. Liver Transplantation in alcoholic and non-alcoholic cirrhosis: survival according to UNOS status, medical variables, and sobriety. Transplantation 1998;66:298-302.

2. McCurry KR, Baliga P, Merion RM, Ham JM, Lucey MR, Beresford TP, et al. Resource utilization and outcome of liver transplantation for alcoholic cirrhosis. Arch Surg 1992;127:772-777.
3. Lucey MR, Merion RM, Henley KS, Campbell DA, Turcotte JG, Nostrant TT, et al. Selection for and outcome of liver transplantation in alcoholic liver disease. Gastroenterology 1992;102:1736-1741.
4. Poynard T, Naveau S, Doffoel M, Boudjema K, Vanlemmens C, Mantion G, et al. Evaluation of efficacy of liver transplantation in alcoholic cirrhosis using matched and simulated controls: 5-year survival. Multi-centre group. J Hepatol 1999;30:1130-1137.
5. Belle SH, Beringer KC, Deter KM. Liver transplantation for alcoholic liver disease in the United States 1988 to 1995. Liver Transpl Surg 1997;3:212-219.
6. Gish RG, Lee AH, Keefe EB, Rome H, Concepcio W, Esquivel C. Liver transplantation for patients with Alcoholism and end-stage liver disease. Am J Gastroenterol 1993; 88:1337-1342.
7. Everson G, Bharadhwaj G, House R, Talamantes M, Bilir B, Shrestha R, et al. Long-term follow-up of patients with alcoholic liver disease who underwent hepatic transplantation. Liver Transpl Surg 1997;3:263-274.
8. Lucey M. Liver transplantation for alcoholic liver disease: a progress report. Graft 1999;2:S73–S79.
9. Fireman M. Outcome of liver transplantation in patients with alcohol and polysubstance dependence. Presentation at Research Society on Alcoholism: Symposium on Liver Transplantation for the Alcohol Dependent Patient. Denver, CO. June, 2000.
10. Pageaux GP, Bismuth M, Perney P, Costes V, Jaber S, Posçoz P, et al. Alcohol relapse after liver transplantation for alcoholic liver disease: does it matter? J Hepatol 2003; 38:629-634.
11. Tome S. Lucey MR. Timing of liver transplantation in alcoholic cirrhosis. J Hepatol 2003; 39:302-307.
12. DiMartini A, Day N, Dew M, Lane T, Fitzgerald MG, Magill J, Jain A. Alcohol use following liver transplantation: a comparison of follow-up methods. Psychosomatics 2001; 42:55-62.
13. Diehl AM. Alcoholic liver disease. Liver Transpl Surg 1997; 3:206-211.
14. First, Michael, ed. Diagnostic and statistical manual for mental disorders, 4th ed. Washington, DC: APA Press, 1994.
15. Sobell LC, Sobell MB. Timeline follow-back: a technique for assessing self-reported alcohol consumption, Measuring Alcohol Consumption. New York: The Humana Press, Inc., 1992.
16. Sobell LC, Sobell MB. Timeline followback: a calendar method for assessing alcohol and drug use (User's Guide). New York: Addiction Research Foundation, 1996.
17. Armor, DJ, Polich JM, Stambul HB. Alcoholism and treatment. New York: John Wiley & Sons, 1978.
18. Axis Biochemical ASA. Manual on directions for use, 1998. pp 1-6.
19. DiMartini A, Day N, Lane T, Beisler A, Dew MA, Anton R. Carbohydrate deficient transferrin in abstaining patients with end-stage liver disease. Alcoholism: Clin Exp Res 2001;25:1729-1733.
20. Vaillant GE. The natural history of alcoholism and its relationship to liver transplantation. Liver Transpl Surg 1997;3:304-310.
21. Iasi MS, Vieira A, Anez CI, Trindale R, Codorani NT, Favero SS, et al. Recurrence of alcohol ingestion in liver transplantation candidates. Transpl Proc 2003;35:1123-1124.
22. Weinrieb R, Van Horn D, Lin Y-T, DePiano M, Massoth K, Lucey M. A controlled study of motivation enhancement therapy vs. community alcoholism treatment for alcoholic liver transplant candidates. Alcoholism: Clin Exp Res 2005;29:76A.
23. Thase ME, Salloum IM, **Cornelius** JD. Comorbid alcoholism and depression: treatment issues. J Clin Psychiatry 2001;62:32-41.
24. Dawson D, Grant B, Stinson F, Chou P, Huang B, Ruan WJ. Recovery from DSM-IV Alcohol Dependence: United States, 2001-2002. Addiction 2005;100:281-292.
25. Krahn LE, DiMartini A. Psychiatric and psychosocial aspects of liver transplantation. Liver Transpl 2005;11: 1157-1168.