Original Article

Comparison of social support in alcohol hepatitis patients accepted and denied for liver transplantation

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Background: Alcohol associated liver disease (ALD) is on the rise and has become the leading indication for liver transplantation (LT). Severe alcoholic related hepatitis (AH) is a syndrome on the spectrum of ALD with high mortality. Select patients with AH are considered for early LT, with lack of social support (SP) often being a barrier to LT. We aimed to assess the SP network of patients with AH considered for LT.

Methods: A case-control study was conducted among diagnosed AH patients who were accepted and denied for LT at our institution between September 2019 and December 2020. Characteristics such as demographics, comorbidities, laboratory values and SP were compared between patients who were accepted and those who were denied for LT. SP was defined as having 2 caregivers with the ability to understand patient's medical condition, availability for SP and transport with at least 3 months commitment for post-operative care.

Results: Eighty-two patients were evaluated for LT of whom 20 (24%) were accepted for listing. Demographics, insurance and socioeconomic status were similar between patients accepted and denied for LT. Patients who were accepted for LT were more likely to have participated in alcohol rehabilitation programs, compared to those who were denied (22 *vs.* 13, P=0.02). Patients accepted for LT were also more likely to have 1st degree relatives for SP (29/40 *vs.* 60/124).

Conclusions: Participation in alcohol rehabilitation and commitment to sobriety are key in patient selection for LT for AH. SP is an important component of the LT evaluation and selection that is often a barrier for LT. First-degree relatives are less likely to be identified as SP for patients declined for LT for AH.

Keywords: Liver transplant; alcohol hepatitis; patient outcome

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Introduction

The indications for liver transplantation (LT) have evolved over the past decade as a result of the elimination of hepatitis C and increasing consumption of alcohol (1-3). Alcohol has emerged as the leading indication for LT (3,4). Specifically, patients with alcohol associated liver disease (ALD) can have a diagnosis of alcoholic hepatitis and/or alcohol-related cirrhosis. The increase of ALD as an indication for LT appears to be fueled by greater number of young adults presenting with alcohol hepatitis (2,5).

Severe alcoholic related hepatitis (AH) can be associated

with a dismal prognosis (6). For these cases, treatment revolves around alcohol abstinence, supportive care, and corticosteroids (7,8). AH as an indication for LT has only recently been recommended in select patients who do not respond to medical therapy (9). The young age of these patients and their dismal prognosis without transplantation has compelled the medical community to re-examine the long held criteria for six month alcohol sobriety prior to LT. Nevertheless, additional barriers for transplant remain for most patients with AH.

Several studies have identified social and psychiatric contraindications as the most common reason for denial for transplant (6,10,11). Thus, a greater understanding is needed of their social support (SP). Our aim is to define SP in patients in patients evaluated for LT with a diagnosis of AH. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/dmr-21-46).

Methods

Study design

This single-center retrospective study examined inpatients referred for LT for a diagnosis of AH between September 2019 and December 2020. AH was defined according the recent recommend criteria: onset of jaundice within 8 weeks of last alcohol use in patients with ongoing excessive alcohol consumption; AST >50 IU/L, AST:ALT ratio of >1.5 and both values <400 IU/L, and total bilirubin of >3.0 mg/dL (12). Although pathology specimens may be used in the definition of AH, liver biopsies were not performed in our cohort. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of University of California at Los Angeles (IRB#20-002295). Requirement for informed consent was waived due to retrospective nature of the study.

Inclusion criteria in this study included: patients over the age of 18, hospitalized patients with diagnosis of AH, and patients who completed the liver transplant evaluation process. Patients in both case and control group satisfied the inclusion criteria, but only case group underwent LT.

Evaluation process

The liver transplant evaluation process includes consultations by Hepatologists, Transplant Surgeons, Cardiologists, Pulmonologists, Transplant Coordinator nursing, Social Work, Psychiatrist, and Dieticians. Two care givers are required at our institution. Criteria for SP adequacy include: (I) physical health and robustness of the SP; (II) ability to maintain a therapeutic relationship with the patient; (III) knowledge of the patient's medical care; (IV) availability of the SP; (V) ability to provide transportation for the patient; (VI) dedication of at least three months for post-operative patient care. The type of SP was stratified according to the relationship with the patient. First degree SP was defined as individual's parents, full siblings, children and spouse. Second degree SP included individual's grandparents, grandchildren, aunts, uncles, nephews, nieces or half-siblings. The category 'Other' was identified as hired caregivers, family friends and acquaintances. None was defined as the absence of caregiver support at the time of final committee decision. Psychiatric review consists of assessing patient insight of their liver disease and estimating patient risk of alcohol relapse.

Presence and severity of sarcopenia was estimated by Dieticians using the Nutrition-focused physical exam (13). Estimates of Karnofsky Performance Status scale were determined by the transplant coordinator (14). Hepatology assessed for severity of alcohol related liver disease, indication and likelihood of response to steroid therapy and quantifying amount of alcohol. Conflicts were resolved by consensus during a weekly multi-disciplinary patient selection committee meeting where all above specialties were personally represented.

Laboratory tests included but were not limited to complete blood count, comprehensive metabolic panel, prothrombin time/international normalized ratio (INR), viral and autoimmune serologies. MELD-Na was calculated. Abdominal imaging was performed with abdominal computerized tomography and/or ultrasound.

Statistical analysis

Descriptive statistics were reported using median and interquartile range (IQR) or percentage where appropriate. Median values were used because the data was not normally distributed. We used Chi-square and Fisher's exact test for categorical variables and Wilcoxon rank-sum test for continuous variables. P valued less than 0.05 was considered statistically significant

Results

There were a total of 82 patients evaluated for LT during

Table 1 Demographics of patients with alcohol hepatitis evaluated for liver transplantation

Variable	Combined	Denied	Accepted	P value
Number	82	62	20	
Median age	41.5 [34–51]	42.5 [35–53]	38.5 [34–51]	0.41
Gender				
Male	46 (56%)	33 (53%)	13 (65%)	
Female	36 (44%)	29 (47%)	7 (35%)	
Race/Ethnicity				
Non-Hispanic White	48 (58.54%)	30 (48.39%)	14 (70%)	0.43
Hispanic or Latino	31 (37.8%)	26 (41.9%)	5 (25%)	
Non-Hispanic Asian	6 (7.3%)	5 (8.06%)	1 (5%)	
Non-Hispanic Black	1 (1.2%)	1 (1.6%)	0 (0%)	
Education				
No degree	5 (6.1%)	4 (6.45%)	1 (5%)	0.93
High school	26 (31.7%)	20 (32.3%)	6 (30%)	
Some college	30 (36.6%)	22 (35.5%)	8 (40%)	
4 years of college	8 (9.8%)	6 (9.7%)	2 (10%)	
Graduate school or higher	7 (8.5%)	5 (8.1%)	2 (10%)	
Other	2 (2.4%)	1 (1.6%)	1 (5%)	
Unknown	4 (4.9%)	4 (6.5%)	0 (0%)	
Socioeconomic status				
$35,000 to $49,999	7 (8.54%)	5 (8.06%)	2 (10%)	0.85
$50,000 to $74,999	34 (41.46%)	27 (43.55%)	7 (35%)	
$75,000 to $99,999	31 (37.8%)	22 (35.48%)	9 (45%)	
$100,000 to $149,000	10 (12.20%)	8 (12.9%)	2 (10%)	
Insurance				
HMO	33 (40.24%)	27 (43.55%)	6 (30%)	0.19
PPO	31 (37.8%)	20 (32.26%)	11 (55%)	
Medical	18 (21.95%)	15 (24.19%)	3 (15%)	

HMO, health maintenance organization; PPO, preferred provider organization.

our study period (*Table 1*). Of the 82 patients, 20 were accepted and 62 declined for transplantation. The median (IQR) age of the entire cohort was 41.5 [34–51] years. Most patients in our cohort were men. There were no statistically significant differences between those patients who were denied or accepted in regards to age, gender, race/ethnicity, education level, socioeconomic status and insurance type.

Overall, almost one in five patients in the entire cohort had hypertension and the median (IQR) body mass index was 27.7 (23.7–32.5) (*Table 2*). The median (IQR) Karnofsky score was 50 [40–50] for the entire cohort. The majority of patients in the entire cohort had a liver-related complications, with 79.4% and 74.4% noted to have ascites and encephalopathy, respectively. Medical co-morbidities and liver associated complications were similar between denied or accepted patients for LT. Laboratory values are shown in *Table 3*. The overall median (IQR) MELD-Na was 38 [32–40] for the entire cohort. Specifically, the median

Table 2 Medical co-morbidities and liver associated complication

Variable	Combined	Denied	Accepted	P value
Number	82	62	20	
Medical comorbidities				
Hypertension	15 (18.3%)	12 (19.4%)	3 (15%)	0.66
Diabetes mellitus	5 (6.1%)	5 (8%)	0 (0%)	0.33
Body mass index (kg/m^2)	27.7 (23.7–32.5)	27.6 (23.6–33.0)	28.1 (25.7–32.3)	0.55
Liver associated complications				
Ascites	65 (79.37%)	48 (77.42%)	17 (85%)	0.47
Hepatic encephalopathy	61 (74.4%)	46 (74.19%)	15 (75%)	0.94
Variceal hemorrhage	42 (51.2%)	33 (53.23%)	9 (45%)	0.52
Hepatocellular carcinoma	1 (1.2%)	1 (1.61%)	0 (0%)	1
Karnofsky score	50 [40–50]	50 [40–50]	50 [35–50]	0.25
Wasting				
None	43 (52.44%)	33 (53.22%)	10 (50%)	0.41
Mild	29 (35.37%)	21 (33.87%)	8 (40%)	
Moderate	8 (9.76%)	7 (11.29%)	1 (5%)	
Severe	2 (2.44%)	1 (1.61%)	1 (5%)	

Table 3 Laboratory data*

Laboratory value	Combined	Denied	Accepted	P value
Aspartate transaminase, IU/L	120 (76.5–179.3)	129.5 (78–192)	106 (74.5–161.5)	0.26
Alanine transaminase, IU/L	48.5 [31–90]	53.5 [32–94]	44 [29.5–77.5]	0.41
AST/ALT Ratio	2.6 (1.6–3.7)	2.6 (1.6–3.5)	2.4 (1.7–3.2)	0.64
Alkaline phosphatase, IU/L	149 (113.5–193.3)	148.5 (110–188)	151.5 (121.5–230)	0.67
Bilirubin, mg/dL	26.25 (17.7–32.5)	26 (16.3–29.7)	30.8 (23.1–34.3)	0.08
Platelet count, x10^9/L	93 (59–173)	93.5 (59–172)	93 (62–178)	0.84
Albumin, g/dL	3.1 (2.6–3.5)	3.1 (2.6–3.5)	3.15 (2.75–3.6)	0.42
White blood cell, ×10^9/L	16.29 (11.8–23.5)	17.0 (11.4–24.6)	14.1 (11.9–21.1)	0.50
Hemoglobin, g/dL	8.8 (7.6–10.3)	8.75 (7.4–10.3)	9 (8.0–12.0)	0.21
INR	2.4 (1.9–2.9)	2.3 (1.9–2.9)	2.6 (2.2–2.9)	0.53
MELD Na	38 [32–40]	37.5 [32–40]	38.5 (33.5–40)	0.27

*Median (interquartile range). MELD Na, Model for End-stage Liver Disease Sodium; INR, international normalized ratio.

(IQR) MELD-Na was 37.5 [32–40] and 38.5 f (33.5–40) for patients denied and accepted for LT, respectively. There were no statistically significant differences in laboratory values, including Aspartate Aminotransferase/Alanine Aminotransferase (AST/ALT) ratio and MELD-Na, between the patients denied and accepted for LT.

The overall median number (IQR) of days from liver transplant referral to final liver transplant decision was 8

Table 4 Social support

Social support source	Denied	Accepted
Number	124	40
Social support		
1st degree	60 (48.39%)	29 (72.5%)
2nd degree	7 (5.7%)	3 (7.5%)
Other*	13 (10.48%)	8 (20%)
None	44 (35.5%)	0 (0%)

*Other includes partner, hired caregiver and friend.

(4–16.8), with the time being longer for patients accepted than those denied. For instance, the media (IQR) number of days was 7 [4–11] and 11 (8–32.5) for patients denied and accepted, respectively (P=0.003). Similarly, the number of presentations between the denied and accepted was also statistically significant (P<0.001). Patients denied were presented 2 (1–2.5) times to the patients selection committee, whereas those accepted were presented a median (IQR) of 1 [1] times. Three quarters of SP individuals for the accepted patients were identified as first degree relatives. In contrast, less than half the individuals identified for SP were first degree relatives for patients denied for LT. The source of first degree relatives was similar for patients denied and accepted transplantation (*Table 4*).

The median (IQR) overall period of sobriety was 28 [6–54] for the entire cohort, with no statistically significant differences between those patients denied {21.5 [6–49]} days) and those accepted {36.5 [8.5–71]} (P=0.33) (*Table 5*). The proportion of patients with a history of Driving Under the Influence was similar between those patients denied and those accepted for transplantation (P=0.63). However, the proportion of patients who were involved in alcohol rehabilitation program and history of lack of alcohol relapses were greater in the patients accepted for LT (P=0.02 and <0.001, respectively. Substance use was similar between the two groups.

Discussion

Despite the controversy surrounding the subject of LT for AH patients, careful consideration of LT is necessary to improve survival of patients experiencing from severe AH (15). Our results show that the decision by the multidisciplinary patient selection committee to deny LT to patients after referral occurred significantly faster than the decision to accept patients for LT. This may be influenced by the complicated and in-depth nature of the psychosocial evaluation portion of the LT evaluation process which involved gathering information regarding a patient's substance use and SP system. Denied patients required twice as many presentations to the patient selection committee compared to accepted patients which may reflect the difficult and often devastating decision to deny potentially life-saving treatment to patients.

Our study results corroborate previous research that exclusion from LT is more likely for patients with a predisposition to addiction and insufficient SP (6,10). The resistance to perform LT on patients with a history of alcohol relapse stems from the legitimate concern that these patients will continue using alcohol post-transplantation (6). The literature estimates that 20–25% of patients transplanted for alcohol cirrhosis relapse (16,17). The continued significant use of alcohol post liver transplant is associated with poor long-term survival (18,19). However, it is important to note that the pattern of drinking is not homogenous, varying based on onset, quantity and duration. One study identified 4 distinct alcohol use trajectories of minimal use over time, early onset moderate to heavy consumption, and late onset moderate use (20). The results of another study showed that by 5 years, 26% drank in binge patterns and 20% drank in a frequent pattern (21). These are not insignificant numbers and if anything, likely underestimate alcohol relapse since our ability to assess post LT alcohol use improved with the increased utilization of the Phosphatidylethanol blood tests which identifies alcohol use in the past 28 days (22). This may explain the added weight given to specific criteria when selecting patients for LT, such as the commitment to alcohol rehabilitation and lack of alcohol relapse. The data validates this as patients accepted for LT were significantly more likely to

Table 5 Alcohol and other substance use in patients denied for liver transplantation

Variable	Combined	Denied	Accepted	P value
Number	82	62	20	
Duration of sobriety*	28 [6–54]	21.5 [6–49]	36.5 (8.5–71)	0.33
<30 days	42 (51.22%)	35 (56.45%)	7 (35%)	0.19
30–90 days	28 (34.15%)	18 (29.03%)	10 (50%)	
>90 days	12 (14.63%)	9 (14.25%)	3 (15%)	
History of driving under influence	24 (29.27%)	19 (30.65%)	5 (25%)	0.63
Rehabilitation programs (AA/NA)	35 (42.68%)	22 (35.48%)	13 (65%)	0.02
Previous alcohol relapses	35 (42.68%)	35 (100%)	0 (0%)	<0.001
Tobacco use				
Current	15 (18.29%)	13 (20.97%)	2 (10%)	0.09
Previous	22 (26.83%)	13 (20.97%)	9 (45%)	
No	45 (54.88%)	36 (58.06%)	9 (45%)	
Other substance used				
Current	9 (10.98%)	7 (11.29%)	2 (10%)	0.99
Previous	24 (29.27%)	18 (29.03%)	6 (30%)	
No	49 (59.76%)	37 (59.68%)	12 (60%)	
Substance used				
THC	16	11	5	0.02
Cocaine	4	1	3	0.04
Meth	6	3	3	0.15
Meth/THC	3	2	1	1
Meth/THC/Cocaine	2	1	1	0.43

* Median (interquartile range). AA, alcoholics anonymous; NA, narcotics anonymous; THC, tetrahydrocannabinol.

be involved in alcohol rehabilitation programs and to lack a history of alcohol relapse. Additionally, the results of our study align with previous research by confirming that poor SP and unfavorable psychosocial profiles are key reasons for LT denial compared to other evaluation criteria (6,10-15).

Approximately three quarters of patients accepted for LT had some form of primary SP whereas half of denied patients had other forms of SP or an absence of SP entirely (*Table 5*). Our findings raise questions about the merit of emphasizing SP in the LT evaluation process and whether this contributes to disparities in access to LT. Moreover, our social and psychiatric evaluation may fail to account for variations in strength among the differing degrees of SP. For example, for some patients, secondary SP from grandparents may be a subjectively stronger form of support compared to existing primary support from parents. Providing the patient selection committee with more information regarding the strength of support unique to each patient may better guide the decisions of committee members. Although clear guidelines for SP were listed in our LT evaluation process, potential revisions to our psychosocial evaluation may be necessary to increase uniformity in evaluation and reduce barriers to LT access.

Our study is not without limitations. This was a retrospective study performed at a single tertiary care center in the US with a comprehensive evaluation team. The retrospective nature of our study limited our ability to detect statistically significant differences between accepted and denied AH patients in demographics, insurance, and

socioeconomic status. Moreover, our study is descriptive in nature and does not provide any insight around association of factors like SP with LT status. Larger prospective studies may better evaluate if an emphasis on SP in selection criteria favors patients belonging to particular demographics over others. Replications of this study in different centers with varying patient populations are needed in the future to assess the generalizability and value of our results (6,11). More studies exploring how the differing degrees and sufficiency of SP influence long-term, post-transplant outcomes for AH patients are required. Further insight into how varying clinicians weigh the importance of SP for LT candidacy would also bring clarity to our current data. Specifically, analyzing the attitudes of psychosocial clinicians (e.g., Psychiatrists, Social work) versus other medical clinicians (e.g., Hepatologists, Transplant surgeons) on the selection committee is crucial for exposing any variation in patient experiences and potential evaluation biases that may impact equity in access to LT (23,24).

In conclusion, this study examines the LT evaluation process for patients with AH. The evaluation process favored patients with a higher degree of SP, participation in alcohol rehabilitation programs, and patients with a history of no previous alcohol relapses. Future studies investigating how often SP affects LT denial decisions and whether particular groups of patients are more impacted by these decisions will expand upon our current findings. Re-examination of varying clinician attitudes in the selection committee and the psychosocial component of LT evaluation by future groups will be instrumental in increasing equity, uniformity, and transparency in the LT evaluation process with the ultimate hope of improving long-term survival outcomes for AH patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/dmr-21-46

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