






Meeting Report: The Dallas Consensus Conference on Liver Transplantation for Alcohol Associated Hepatitis

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Liver transplantation (LT) for alcohol associated hepatitis (AH) remains controversial. We convened a consensus conference to examine various aspects of LT for AH. The goal was not to unequivocally endorse LT for AH; instead, it was to propose recommendations for programs that perform or plan to perform LT for AH. Criteria were established to determine candidacy for LT in the setting of AH and included the following: (1) AH patients presenting for the first time with decompensated liver disease that are nonresponders to medical therapy without severe medical or psychiatric comorbidities; (2) a fixed period of abstinence prior to transplantation is not required; and (3) assessment with a multidisciplinary psychosocial team, including a social worker and an addiction specialist/mental health professional with addiction and transplantation expertise. Supporting factors included lack of repeated unsuccessful attempts at addiction rehabilitation, lack of other substance use/dependency, acceptance of diagnosis/insight with a commitment of the patient/family to sobriety, and formalized agreement to adhere to total alcohol abstinence and counseling. LT should be avoided in AH patients who are likely to spontaneously recover. Short-term and long-term survival comparable to other indications for LT must be achieved. There should not be further disparity in LT either by indication, geography, or other sociodemographic factors. Treatment of alcohol-use disorders should be incorporated into pre- and post-LT care. The restrictive and focused evaluation process described in the initial LT experience for AH worldwide may not endure as this indication gains wider acceptance at more LT programs. Transparency in the selection process is crucial and requires the collection of objective data to assess outcomes and minimize center variation in listing. Oversight of program adherence is important to harmonize listing practices and outcomes.

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Abbreviations: AC, alcohol-associated cirrhosis; ACCELERATE, The American Consortium of Early Liver Transplantation for Alcoholic Hepatitis; AH, alcohol associated hepatitis; ALD, alcohol associated liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AUD, alcohol-use disorder; CI, confidence interval; CONSORT, Consolidated Standards of Reporting Trials; DSM-V, Diagnostic and Statistical Manual of Mental Disorders; EtG, urinary ethyl glucuronide; LT, liver transplantation; LTE, liver transplantation evaluation; MELD, Model for End-Stage Liver Disease; MHPA, Mental Health Parity Act; MH/SUD, mental health or substance-use disorder; NIAAA, National Institute on Alcohol Abuse and Alcoholism; PEth, phosphatidylethanol; pt, patient; SIPAT, Stanford Integrated Psychosocial Assessment for Transplant; THC, tetrahydrocannabinol; UNOS, United Network for Organ Sharing.

Summary of Recommendations

GENERAL RECOMMENDATIONS: ALCOHOL ASSOCIATED HEPATITIS

1. There should be efforts to standardize nomenclature and definition of alcohol associated hepatitis (AH) with an emphasis on the use of less stigmatizing terminology (see Tables 1 and 2).
2. Patients with severe AH may be assessed for corticosteroid therapy.

3. Select patients with severe AH that are unresponsive to medical management may be considered for liver transplantation (LT).
4. Predicting response to therapy or mortality before LT is best achieved by assessing the response over time (change in Model for End-Stage Liver Disease [MELD] score or Lille score or a combination of MELD score plus Lille). Mortality is lower for those patients who have a Lille score <0.45, respond to therapy, have a declining bilirubin level, or are abstinent, and these patients may not require LT.
5. An inflexible period of abstinence prior to transplantation is not desirable. Acceptance for LT listing should be based on the severity of liver dysfunction and a comprehensive psychosocial evaluation (see Table 3).

RECOMMENDATIONS FOR LT FOR AH

See Fig. 1 and Table 4 for related recommendations.

Goals of LT for AH

1. Avoiding LT in patients who will recover without it.
2. Avoiding futility and achieving short-term and longterm survival comparable to other indications for LT.
3. Avoiding the creation of a further disparity in LT either by indication (versus other indications),

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TABLE 1. Suggested Changes in Nomenclature

Suggested	Current
Alcohol associated liver disease	Alcoholic liver disease
Relapse	Recidivism
Alcohol associated hepatitis	Alcoholic hepatitis
Alcohol-use disorder	Alcoholic

TABLE 2. Defining AH

Definition	Clinical entity with rapid-onset of jaundice with elevated AST in the background of heavy alcohol use
Pattern of alcohol use	Heavy alcohol use for >6 months, <60 days of abstinence before onset of jaundice
Supporting features	
Biopsy	Steatohepatitis, cholestasis, and severe fibrosis
Presentation	Malaise, tender hepatomegaly, and decompensation
Laboratory values	Bilirubin, mg/dL >3 AST/ALT ratio 1.5, and AST, L <400
Exclude	Drug-induced liver injury, biliary obstruction, viral hepatitis, autoimmune liver disease, and Wilson's disease
Spectrum	AH versus acute-on-chronic liver failure
Presence of cirrhosis	
Definite	Clinical and biopsy proven
Probable	Clinical and exclude competing diagnoses
Possible (biopsy recommended)	Clinically diagnosed but with potential confounding factors (eg, pt denies alcohol)
Other associated diagnoses	Viral hepatitis or others

NOTE: Modified from NIAAA AH clinical trial definition from Crabb et al.⁽¹⁾ (2016).

- geography, sex, race, insurance status, or other sociodemographic factors.
4. Identification of LT candidates likely to have longterm abstinence.
5. Incorporation treatment of alcohol-use disorder (AUD) into pre- and post-LT care.
6. Consensus of paramedical and medical staff.

Criteria Related to AH

1. First presentation with decompensated alcohol associated liver disease (ALD).
2. Absence of severe uncontrolled medical or psychiatric comorbidities.
3. Nonresponse to medical therapy.

TABLE 3. Psychosocial Domains to be Assessed in AH Transplant Candidates

	Domain Assessed/Questions Asked	Factors That May Predict Relapse
1. Alcohol-use history	<ul style="list-style-type: none"> • Length of use over time, when did use start, consumption patterns, context of use, periods of abstinence • Diagnostic criteria for alcohol-use disorder (reference Diagnostic and Statistical Manual of Mental Disorders (DSM-V)) • Problems with cravings/urges to drink • Sobriety attempts: voluntary and mandated • Alcohol-use treatment history: types of treatment tried, sobriety duration after treatment, experiences with treatment, successes and failures • Attitudes toward alcohol use: assess insight and acceptance of alcohol as a problem, readiness for change, and commitment to sobriety and alcohol treatment • Recent changes in alcohol use in relation to life stressors with assessment of potential modifiable behaviors and situations 	<ul style="list-style-type: none"> • Younger age at onset of drinking • >10 drinks per day at time of transplant consideration • Multiple failed rehabilitation attempts • History of legal problems due to alcohol use • Shorter pretransplant abstinence • Lack of insight into alcohol-use problems • Lack of acceptance of alcohol use as a problem • Lack of candor and/or deceptive behavior with respect to transplant team • Severe AUD
2. Other substance-use history	<ul style="list-style-type: none"> • Length of use over time, onset of use, consumption patterns, context of use • Diagnostic criteria for substance-use disorder • Treatment history (as above) 	<ul style="list-style-type: none"> • Active, untreated polysubstance use (except marijuana) • Comorbid tobacco use, relapse to tobacco use
3. Mental health history	<ul style="list-style-type: none"> • History of psychiatric diagnoses • Presence of suicide attempts • History of any mental health treatment, including inpatient treatment • Response to mental health treatment 	<ul style="list-style-type: none"> • Active, untreated mental health diagnosis • Recent suicide attempt
4. Treatment adherence history	<ul style="list-style-type: none"> • Past and current adherence to medical and mental health treatment plan • Ability to understand and adhere to transplant treatment plan 	<ul style="list-style-type: none"> • History of extensive nonadherence to medical or mental health treatment
5. Social criteria	<ul style="list-style-type: none"> • Sober support system • Number of support persons, relationship to patient, ability to dedicate time/resources to medical and mental health care 	<ul style="list-style-type: none"> • Lack of sober support network • Only 1 sober support person
Optimal assessment criteria	<ol style="list-style-type: none"> 1. Awake, alert patient (not comatose, altered, or intubated), able to be directly interviewed 2. Psychosocial team to assess patient first to obtain unbiased evaluation of above factors 3. Consistent history and commitment verbalized by patient 4. Multiple assessments over time 5. Active involvement and sober support by family/caregivers 6. Corroboration of history from patient collaterals 	

NOTE: Most of these predictors are for sustained or harmful relapse (not slips).

Criteria Related to AUD

1. Establish acceptable risk of relapse by assessment with a multidisciplinary psychosocial team including a social worker and an addiction medicine specialist/mental health professional with addiction and transplantation expertise.
2. Assessment of a coherent patient (ie, not intubated or floridly encephalopathic) by an addiction specialist.
3. Lack of repeated unsuccessful attempts at addiction rehabilitation.
4. Lack of other current substance use/dependency.
5. Acceptance of ALD diagnosis with insight.

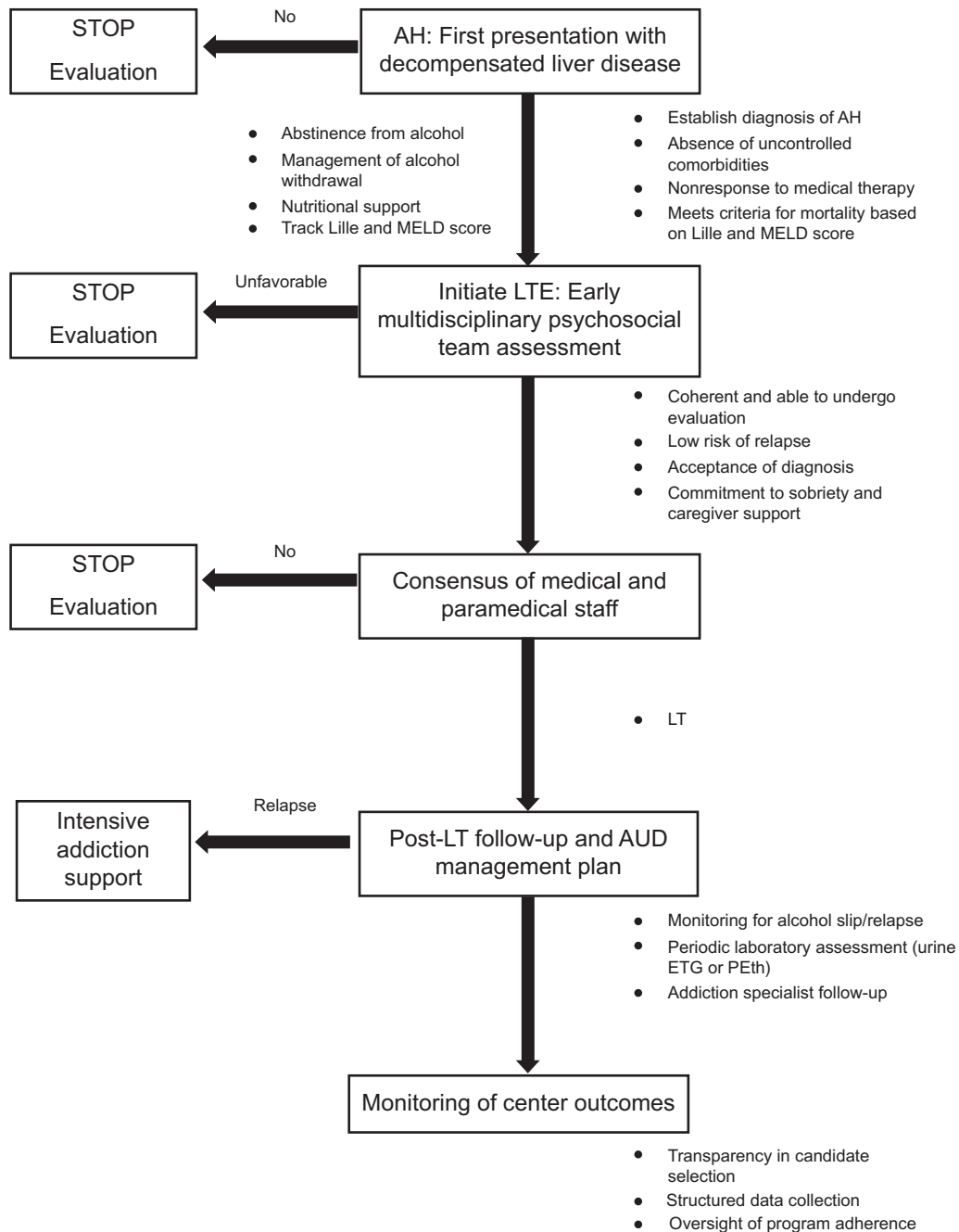


FIG. 1. Listing criteria and program components for LT for AH.

- 6. Commitment of the patient to lifelong sobriety and support of sober caregivers to assist the patient with abstinence goals.
- 7. Presence of close, supportive family members or caregivers.

Post-LT Requirements

- 1. Pre-LT confirmation of plan for AUD treatment after LT.
- 2. Robust posttransplant monitoring for alcohol slips or relapse during post-LT clinic appointments to

TABLE 4. Listing Criteria and Program Components for LT for AH

	Primary criteria	Secondary considerations
AH assessment	<p>First presentation with decompensated AH</p> <p>Absence of severe medical comorbidities</p> <p>Nonresponse to medical therapy</p>	<p>No prior liver-related hospitalization</p> <ul style="list-style-type: none"> • Assessment of frailty, debility, and multiorgan failure • No other contraindications to LT • Contraindications: disease severity, multiorgan failure, infection, renal failure, and low likelihood for response • Consider nonresponders using Lille score ≥ 0.45 or worsening of liver function by days 4 or 7 • Monitor for signs of recovery after listing
AUD assessment	<p>Establish acceptable risk of relapse as assessed by a multidisciplinary psychosocial team composed of a social worker and at least 1 addiction specialist</p> <p>Direct assessment of patient possible by an addiction specialist</p> <p>A maximum of 1 prior failed attempt at rehabilitation</p> <p>Lack of other active substance use/dependency or active untreated psychiatric disorder</p> <p>Acceptance of diagnosis/insight</p> <p>Commitment of patient/family to sobriety and formalized agreement to adhere to lifelong total alcohol abstinence</p> <p>Presence of close, supportive family members or caregivers</p>	<ul style="list-style-type: none"> • Not intubated • Consider independent team of specialists in addiction, social workers, and mental health providers • Ideally first member of LT team to evaluate • Consider independent mechanisms for regional or local review • Not intubated or floridly encephalopathic <p>Establish contract and participation in addiction rehabilitation following transplant</p>
Committee decision making	<p>Consensus of paramedical and medical staff</p>	<p>Consider blinded voting in committee deliberations</p> <p>Consider absolute consensus</p>
Program components	<p>Transparency in selection process</p> <p>Independent psychosocial assessment</p> <p>Structured post-LT follow-up mechanism in place</p> <p>Mental health team</p>	<ul style="list-style-type: none"> • Creation of internal policies/procedures consistently followed by the transplant program • Willingness to share, publish, or have policies/procedures reviewed by outside agents • Documentation of transplant program experiences with AH in CONSORT flow diagram, including those assessed for eligibility, those excluded and reasons for the exclusion, treatment responders, transplant outcomes, and elements of selection criteria • Enhanced reproducibility by use of standard definitions and common data elements • Consistent and timely structured data reporting • Mental health professional with addiction background/training • Mental health professional familiar with transplant process • Documentation of AUD management plan before and after LT • Dedicated addiction specialist/mental health professional for longitudinal management • Commitment for regular monitoring for alcohol use, PEth, and urinary ethyl glucuronide • Structured monitoring program for posttransplant alcohol relapse and, in the event of alcohol relapse, provide resources to assist the patient in recovery • Consider formal addiction education for transplant staff

include direct interviewing of patient and caregivers about alcohol use.

3. Routine monitoring of alcohol use (eg, with phosphatidylethanol [PEth], urinary ethyl glucuronide) for at least 2 years, with frequency and duration individualized beyond this time period.

Center Requirements

1. Transparency in the candidate selection process and structured collection of objective data to assess outcomes (see Table 5).
2. Ongoing support of abstinence that is integrated into post-LT care, such as concurrent follow-up by

TABLE 5. Data Collection in Programs Performing LT for AH

Timing	Main Component	Subcomponent
Before LT	AH	Definite, probable, and possible
	Number with AH	
	Number evaluated	
	Number listed	
	Medical and psychosocial	Sex, race, MELD, and insurance
	Characteristics of evaluated not listed versus listed	Steroids, other
	Medical treatment	Disease severity
	Contraindication or ineligible for steroids	Multiorgan failure
	Accurate coding for AH	
	AUD diagnosis	Mild, moderate, and severe
	Prior AUD treatment	Types of AUD treatment previously used
	Explant and biopsy characteristics	
	Comorbid psychiatric and/or substance-use disorders	
	Other substance use	
LT	Multidisciplinary team assessment	Addiction specialist Social worker Mental health professional
	Routine testing	Alcohol biomarker testing: PEth and urinary ethyl glucuronide
	Pattern of alcohol use	Slip, relapse, and heavy use
After LT	Documentation of AUD management plan required before and after LT	
	Documentation of urinary ethyl glucuronide (EtG) or PEth testing	
	Survival at 1, 3, and 5 years	

an addiction specialist/mental health professional with addiction and transplantation expertise.

- Oversight of program adherence to harmonizing practices and outcomes.

Introduction

Alcohol is a major cause of liver disease worldwide⁽²⁾ with ALD being one of the most frequent indications for LT in the United States.⁽³⁾ In addition to complications of cirrhosis and hepatocellular carcinoma, AH remains an important cause of liver-related morbidity and mortality. Influenced by small trials showing acceptable outcomes in highly selected patients, transplantation for AH is increasingly performed in the United States and elsewhere.⁽⁴⁻⁹⁾ The percentage of patients transplanted for AH is likely underestimated; in a recent study, only 35% of recipients transplanted for AH were accurately identified.⁽¹⁰⁾

However, LT for AH faces substantial challenges. The medical criteria for AH LT must be carefully defined such that the premature use of LT does not occur for patients likely to recover with supportive care. Additionally, in urgent cases of patients with AH, requirements for specific periods of significant sobriety before LT may vary. The ability to provide the potential benefits of LT for AH patients must be balanced against the potential for alcohol relapse with resulting morbidity and mortality after LT. LT for AH may lead to disparities related to the selection of candidates with AH for LT (ie, may favor patients with resources) as well as impacting LT rates for other indications. Although it is worthy to consider a more compassionate and thoughtful approach to LT for AH patients, the shortened time frame for transplant evaluation in urgent AH cases makes it difficult even for experienced teams to accurately capture the psychosocial aspects that are predictive of outcomes after LT in AH. The public and provider perception of LT for ALD continues to evolve and may not be as controversial as

previously thought.⁽¹¹⁻¹⁹⁾ Furthermore, there is a growing recognition that successful outcomes after LT also depend on appropriate treatment of coexisting AUD. These complexities demand a multidisciplinary team approach to the assessment, selection, and post-LT longitudinal care of AH patients.

To address these issues, Baylor University Medical Center, Dallas, TX, organized a 2-day consensus conference (April 5-6, 2019) endorsed by the International Liver Transplantation Society and American Society of Transplant Surgeons. Overall, 130 participants, including 82 physicians and over 60 transplant and nontransplant university and community programs, were represented. Of these centers, representatives from 9 out of 12 The American Consortium of Early Liver Transplantation for Alcoholic Hepatitis (ACCELERATE) AH consortium centers attended. A survey was not taken of which programs currently performed LT for AH, but the rate varied from none to a few cases per year. Participants included addiction counselors, transplant surgeons, hepatologists, psychiatrists, coordinators (for living donors and for before and after transplant), nurses, program administration, social workers, insurance representatives, and other staff. A draft of the manuscript was sent to all attendees for their collective input and comments.

Several contentious points were raised, and therefore, a balanced discussion was presented. This included pros and cons of LT for AH, mandatory requirements for center reporting as well as discussions regarding the financial aspects. The goal was not to unequivocally endorse LT for AH; instead, it was to bring together a multidisciplinary group to discuss AH-related practices at their centers and to consider how clinical assessment, care, and selection for LT could be improved by the collective experiences. The consensus conference expanded on recent recommendations that “liver transplantation may be considered in carefully selected patients with favorable psychosocial profiles in severe AH not responding to medical therapy.”⁽²⁰⁾

General Considerations: AH DEFINITION

Defining AH requires consideration of the pattern of alcohol use, clinical and laboratory presentation, and exclusion of other etiologies of liver dysfunction. Guidance is provided by a recent consensus statement on behalf of the National Institute on Alcohol Abuse and Alcoholism

(NIAAA) though this definition focuses on bringing uniformity to clinical trials and does not address LT (Tables 1 and 2).⁽¹⁾ Liver biopsy should be pursued in cases where the diagnosis of AH is unclear and/or if any alternative diagnosis may affect the treatment plan, especially with regard to eligibility for LT. Considering LT for AH does not obviate the program requirements for chronic liver disease or cirrhosis related to alcohol, which may follow a separate center-specific pathway.

INCIDENCE AND MORTALITY

Population-based estimates in the United States confirm an increase in the incidence of AH mirroring a global increase in ALD.^(2,21-23) There has been an increase among young adults, minorities, and women.^(21,24-26) In national data, the age- and sex-standardized rate of ALD-related mortality has increased by 3-fold in persons aged 25-34 years (CDC accessed March 2019).

MEDICAL THERAPY

The proposed treatment algorithm in AH differentiates management based on disease severity.⁽²⁷⁾ Treatment for AH includes supportive medical therapy in addition to abstinence from alcohol, management of withdrawal symptoms, nutritional support, and consideration of corticosteroid therapy for definite and probable AH. There is a need to accurately identify as early as possible which patients are candidates for corticosteroid therapy, which are ineligible for corticosteroids, or which are nonresponders to therapy. If corticosteroids are used, the absence of a response as defined by the Lille score should lead to their discontinuation. Several investigational compounds are under evaluation for patients with AH, but their role in AH remains to be established.⁽²⁸⁾

PREDICTIVE MODELS

Several predictive models assess treatment response and predict mortality within 1-6 months after diagnosis of AH.⁽²⁹⁻³⁴⁾ Most models have a high negative predictive value (ie, predict those patients who will do well) and do not necessarily identify all patients who will not survive. A model combining a static component (eg, MELD) with a dynamic model (eg, Lille) may be useful to identify nonresponders to medical therapy and/or patients unlikely to recover.⁽³⁵⁾ Extrahepatic complications, most notably

serious infection and renal failure, profoundly affect outcomes.^(3,36-38)

LT for AH

Figure 1 and Tables 3 and 4 summarize recommendations from the consensus conference. The following sections discuss specific recommendations in more detail.

ETHICAL CONSIDERATIONS

LT balances 3 principles of justice: urgency, utility, and equity. Urgency demands that organs go to the “sickest first.” AH patients typically have high MELD scores with 75% mortality at 6 months in those patients not responding to prednisolone.⁽³³⁾ Utility demands that organs be given to patients in whom posttransplant outcomes will be acceptable. Medically, AH patients compare favorably to other diagnoses, with acceptable post-LT patient and graft survival rates.^(6,39) Equity mandates that we adopt principles of LT allocation that are applied similarly to all liver diseases. Where behaviors are responsible for the primary liver disease that requires transplant or for graft loss (such as nonadherence) after transplant, allocation decisions should be made in a similar manner and not applied in a more stringent manner only to those with ALD or AH.⁽⁴⁰⁾

EUROPEAN AND US EXPERIENCE IN LT FOR AH

The initial experience in early “rescue” LT in AH was the French/Belgian trial.⁽⁷⁾ Nonresponders to medical therapy, defined as a Lille model of ≥ 0.45 or a worsening of MELD score at day 7 of therapy, were considered for a rescue LT. Candidates were selected using the following criteria: nonresponse to medical therapy, severe AH as the first liver-decompensating event, presence of close supportive family members, absence of severe coexisting or psychiatric disorders, and an agreement to adhere to lifelong total alcohol abstinence. Complete consensus was required among 4 provider “circles” involved in patient care for LT approval. Ultimately, 26 medical nonresponders underwent LT. A significant survival benefit at 6 months was observed (76.9% versus 23.1% for matched nontransplanted patients). Survival after transplant was similar to random responder controls (85%). The

relapse rate was low; 10% overall had returned to harmful drinking.⁽⁷⁾ These results supported future evaluation in selected patients with severe AH who failed medical therapy.⁽⁴¹⁾

Studies in the United States were subsequently pursued.⁽⁴⁻⁹⁾ As compared with the European experience where a prospective protocol was followed, the US experience was a mix of center-specific experience and established protocols. In 1 study, 20/94 (21.3%) patients with severe AH refractory to medical therapy were approved for LT, and 9 ultimately underwent LT.⁽⁴⁾ A total of 8 of the 9 (89%) patients survived more than 6 months compared with 30% of the patients who did not undergo LT. Two patients had alcohol relapse, neither leading to adverse outcomes. A second pilot study compared the outcomes of LT for AH and alcohol-associated cirrhosis (AC). At a median follow-up of 532 days (interquartile range, 281-998 days), rates of alcohol use and harmful drinking after LT were similar for AH and AC patients at 28% and 24%, respectively ($P = 0.80$).⁽⁸⁾ ACCELERATE-AH, the largest US experience in LT for AH, was a retrospective review from 12 centers, including the 2 centers that had published the pilot studies.⁽⁶⁾ Each center had its own protocol, and although there were some differences between the sites in terms of the inclusion/exclusion criteria, there were many similarities.⁽⁶⁾ Of the 432 patients evaluated, 155 (35.9%) were accepted as candidates with rates ranging from 13% to 100% across centers.⁽⁶⁾ Psychosocial concerns were the predominant reason for denial of listing for LT. Overall survival after LT for AH was excellent with 1- and 3-year survival rates of 94% (95% confidence interval [CI], 89%-97%) and 84% (95% CI, 75%-90%), respectively. In patients surviving to discharge, 28% resumed alcohol use with 11% returning to harmful drinking. Alcohol relapse after LT had an adverse impact on survival at 3 years when compared with abstainers (75% versus 97%, respectively; $P = 0.03$), and 7 of the 9 deaths that occurred after 1 year were related to alcohol. More than 10 drinks per day, non-Tetrahydrocannabinol (THC) substance use, prior alcohol-related legal difficulties, and more than 1 failed alcohol treatment attempt were associated with sustained alcohol use after LT.⁽⁴²⁾ No longterm follow-up data are available.

ARGUMENTS IN FAVOR OF LT FOR AH

First, LT for ALD has been performed since the 1960s.⁽⁴³⁾ LT for appropriately selected AH patients

prevents premature mortality. In patients with severe AH, failure of medical therapy can be predicted early in the patient's course and is associated with a 6-month survival of approximately 30%.⁽³³⁾ Because most deaths occur within 2 months, early LT is lifesaving. Second, there are effective treatments for AUDs that patients can participate in following LT. Given the stringent criteria used to select AH LT candidates, thus far, relapse rates after LT are similar for patients transplanted for AH versus those with ALD having cirrhosis.⁽⁴⁴⁻⁴⁸⁾ Third, LT for those with AH ensures equity of access to lifesaving transplant, as in other liver diseases. For example, LT is offered to obese individuals with nonalcoholic steatohepatitis even without the demonstration of weight loss before LT and is also offered to carefully selected patients with acute liver failure following a suicide attempt due to medication overdoses with uncontrolled psychiatric disease. Finally, concern that early LT for AH may decrease organ donation is contrary to a survey showing that most potential organ donors were supportive or neutral with regard to this new indication.⁽¹⁷⁾

CONCERNS ABOUT LT FOR AH

First, criteria advocated for LT for AH may not be uniformly adhered to at all centers. There may be a disconnect between the restrictive and focused evaluation process described in the initial experience with LT for AH and its wider acceptance elsewhere across LT programs.⁽⁷⁾ There is already wide variation in acceptance of AH patients for LT, and clarity on what criteria are necessary to ensure good outcomes is lacking. Second, relevant outcomes after LT may be inadequately captured. Although survival rates were acceptable, deaths due to fungal infection were frequent in the European experience with most deaths due to infection within 2 weeks after LT. Survival at 6 months for recipients (77%) was much lower than that for ALD reported to the United Network for Organ Sharing (UNOS; 94%). Variation in medical management (eg, steroid use) among centers may play a role. Third, the cumulative probability of any alcohol use after LT was 25%, 30%, and 34% at 1, 2, and 3 years.⁽⁶⁾ Patterns of alcohol use were worrisome with the median time to the first drink of 160 days (79-346 days), with sustained alcohol use in 38% and binge or frequent drinking in 42%. Hence, there is an obvious need for predictive tools to identify patients at a high risk of relapse, especially for those with harmful drinking patterns.⁽⁴¹⁾ Fourth, a

high MELD score at LT, common among those presenting with AH, may tilt the balance toward bending the rules to transplant these recipients. It is unavoidable that competition between programs will loosen acceptance criteria. The requirements for acceptance should be the same for all patients, regardless of social or financial status. As an example, women increasingly present with AH, though the percent of women undergoing LT for AH is low.⁽⁶⁾ Hence, there may be unrecognized barriers to LT for certain subgroups.

Psychosocial Perspective in LT for AH

In addition to being responsible stewards and gatekeepers, psychosocial assessors of transplant candidates often create intervention or treatment plans to mitigate risk for potentially poor outcomes (Table 3). For patients with an AUD and a short duration of sobriety, this commonly involves engaging the patient in addiction rehabilitation. However, in the urgent AH scenario, because there is no time to provide pre-LT rehabilitation, LT teams rely on more stringent selection criteria for AH candidates in the hope of preventing poor outcomes after LT.

CHALLENGES IN EVALUATION OF AUD IN AN URGENT SETTING

Evaluation and treatment of AUD that coexists in patients with AH is crucial. During an expedited evaluation, AUD may be inadequately addressed, assessment and selection occurs in a limited and expedited time, and treatment for AUD, a chronic disorder with the need for ongoing management, is often not accorded priority. In a life-threatening medical condition, it is difficult to expect a patient to contemplate hypotheticals (eg, lifelong abstinence, willingness to attend addiction rehabilitation, and adherence to transplant directives) with no to little evidence they will or can do so. In addition, there is no opportunity to reassess a candidate's response after the initiation of addiction treatment. Patients and families may try to manage impressions about or to minimize their alcohol-use history. Patients may be difficult to interview due to being in denial or feeling ashamed, guilty, overwhelmed, scared, or in pain. In this context, the establishment of an

effective therapeutic relationship to manage AUD can be challenging.

NECESSARY COMPONENTS OF THE PSYCHOSOCIAL ASSESSMENT

Optimally, the patient should be directly interviewed by the social worker and mental health and/or addiction professionals. Thus, the request for these evaluations should occur early in the hospital course prior to the development of encephalopathy. The composition of the mental health/social work team and competencies matter and may dictate the quality and strength of recommendations. Transplant centers considering AH transplant should have in place a multidisciplinary psychosocial team composed, at a minimum, of a transplant social worker and a mental health professional preferably with addiction and transplant experience. An addiction specialist may be helpful in ensuring that AH patients receive the full spectrum of AUD care. Psychometric scales and instruments can be used to aid the collection and integration of data but should not be used to determine candidacy. Scales may be helpful for tracking treatment response and anticipating further treatment needs. Collateral information should be sought from family members, LT team members, and other clinical care providers to provide a comprehensive picture of the patient's history. Active family or caregiver support is paramount for current and future care. Biochemical markers may also be needed to corroborate drinking history. Patients with AUDs often have other psychiatric comorbidities. In circumstances where an AH candidate has another comorbid psychiatric disorder, additional evaluation by a psychiatrist is indicated. That may be a decision that takes place at the program level based on the following:

1. The comfort and psychiatric expertise of the referring team and social worker.
2. Potential meeting of a threshold on a standardized scale (eg, Stanford Integrated Psychosocial Assessment for Transplant [SIPAT]).
3. Resource availability.

FACTORS ASSOCIATED WITH RISK FOR POST-LT ALCOHOL USE

Until a larger experience is developed with AH alcohol-use outcomes, the LT field draws on the substantial

experience of predictors of relapse for ALD LT and from the general non-LT population of AUD patients. It is critical to recognize that the presence of a factor associated with alcohol use means that the likelihood of alcohol use is greater, not that it is certain.^(6,8,49-52) Whether a single criterion or cumulative factors are used to determine AH LT candidacy is not settled. Proposed criteria or risk scores have high negative predictive value and predict those who will not return to harmful patterns of alcohol use rather than identify those who will.⁽⁴²⁾

DURATION OF SOBRIETY

Aside from allowing a period of observation to ensure that an AH patient has adequate time to respond to medical therapy avoiding preemptive LT, the notion of waiting a specific number of days or months of abstinence to demonstrate the patient's ability to maintain sobriety is ill-conceived. In AH, such a mandated wait could allow the patient to deteriorate, increasing the surgical risk, but each month sober only incrementally reduces risk. There is limited support for a specific 6-month cutoff point.⁽⁵⁰⁾ Furthermore, in the natural history of AUD, stable abstinence is measured in years not months. Recently, expert guidelines no longer recommend a fixed period of abstinence prior to transplantation^(27,53) and have stopped listing AH as an absolute contraindication to LT⁽⁵³⁾ contrary to the recommendations from the preceding decade.⁽⁵⁴⁾

POSTTRANSPLANTATION NEEDS

After transplantation, the AH LT recipient should be assisted in beginning addiction treatment as soon as medically feasible. This critical requirement should not be lost among the other post-LT care needs. Psychosocial evaluation and treatment should be integrated in the flow of post-LT care and should be mandated by the center. There should be agreement for the LT team to facilitate post-LT participation in addiction treatment and in rigorous collection of alcohol-use outcome data. To improve adherence, treatment and monitoring expectations should be developed prior to LT. LT teams may need significant assistance from their social worker and behavioral health provider to overcome potential barriers to addiction treatment: lack of local care, lack of adequate or appropriate resources, lack of monitoring (biochemical or collateral), and insurance issues.

Living Donor LT for AH

AH patients listed for deceased donor LT may also be considered candidates for living donor LT. The medical risks to the donor are the same regardless of recipient etiology of disease. However, there may be increased psychological risks to donors for recipients with AH related to relapse and graft loss especially in the long term once routine follow-up ends. Adherence to autonomy for both the donor and recipient through the process of informed consent and disclosure is equally important. With AH, the recipient's etiology of disease and potential for relapse might affect the donor candidate's decision about donation, so centers must have a policy in place regarding disclosure of issues unique to LT for AH. The transplant program must ensure that the urgency of need is not interfering with information disclosure, processing, or the ultimate decisions of donors. The informed consent process also requires voluntariness in decision making. Voluntariness is defined as the absence of coercion, unwarranted persuasion, or undue manipulation. Potential living donors for AH recipients may be victims of unwarranted persuasion because they are asked to decide in a time-pressured manner to help a loved one who is at an imminent risk of dying. All transplant centers are required to provide an independent living donor advocate for living donor evaluation. For individuals considering living donation to AH recipients, the independent living donor advocate, along with the rest of the donor evaluation team, must ensure that the decision meets the standards of voluntariness.

Payer Coverage

The 6-month rule has been enforced and reflected in the medical policy set forth by most payers. With recent data and a more definitive set of professional statements and modification of specific institutional criteria referring the 6-month rule, changes in payer coverage policies must follow. This would result in a coverage that better reflects the evolving standard of care. A commitment by payers for addiction counseling after transplantation is equally important. From a resource allocation standpoint, advocating for insurance payer coverage for AUD treatment is crucial. In addition, centers may experiment with unique ways of bridging coverage gaps, resource deficits, and

insurance disparities. These may include telemedicine, provider-to-provider consultation models, collaborative care models, cross-disciplinary training, and community outreach efforts. Programs need to invest not only in coordinators and nutrition specialists for medical management but also in addiction specialists.

Payer limitation of coverage continues to be an issue. There has been increased attention to mental health benefits because there continues to be concern about the adequacy of coverage under most health plans. The Mental Health Parity Act (MHPA) of 1996 aimed to prevent group health plans and health insurance issuers that provide mental health or substance-use disorder (MH/SUD) benefits from imposing less-favorable benefit limitations on MH/SUD benefits than on medical/surgical benefits. Mental Health Parity and Addiction Equity Act of 2008 preserves the MHPA protections and adds significant new protections, such as extending the parity requirements to substance-use disorders. It was amended by the Health Care and Education Reconciliation Act of 2010 (collectively referred to as the "Affordable Care Act") to also apply to individual health insurance coverage. A concerted effort by national liver societies and patient advocacy groups may be needed to harmonize this coverage across centers.

Role of the Transplant Center

LT centers are likely only seeing the tip of the iceberg, with many AH patients never being evaluated by or even discussed with LT centers. Transparency in center practices and oversight is paramount. Oversight of structural components of the program is needed. This includes the presence of adequate psychosocial and addiction personnel at centers with patients undergoing LT for AH, monitoring of pretransplant and posttransplant outcomes, and structured data collection. The transplant community needs to consider mandated collection of AH-specific elements, and centers should be open to sharing center-specific practices to improve outcomes (Table 5). Local or regional review boards may need to be involved to ensure transparency, and third-party adjudication or oversight, such as that provided by UNOS, may be needed.

The need to streamline processes and the anticipated burden to the system (eg, psychosocial assessments, expansion of teams, and increased hospital volume) is clear. Centers need to invest and ensure having mental health professionals/addiction specialists available not only for pretransplant evaluation but also for posttransplant assessment and active follow-up after discharge. Frustration and burnout for members of the provider team may feature prominently as more patients with AH are evaluated. This will require teams to monitor and address the mental health, burnout, and cynicism of their providers and staff. Teams need to insist on and expect psychosocial providers to meet frequently and to thoroughly collaborate among themselves.

Expansion of LT for AH will affect center activity. Issues may arise about the number of donor offers, offers accepted for AH candidates but transplanted in other patients, and how LT for AH might impact LT for other indications, particularly within the new acuity circle policy. There may be financial gain in transplanting patients with AH; a high MELD patient with AH may inherently have better short-term outcomes than high-MELD patients without AH, though further data are needed. This could be partially mitigated by requiring centers to meet a 2-year survival criterion for AH because relapse to harmful alcohol use beyond the first year typically leads to deaths.

Competition between centers for these patients is a concern. Within a region, there may be market pressures for other centers to follow suit. Hence, failure to offer transplant for patients with AH may reduce referrals for this and other indications. In addition, referral physicians often view an “active plan,” such as transplant, as a better option than a “passive plan,” ie, supportive care. So, the perception of the transplant center within the community as an “aggressive” or “forward-thinking” or “cutting-edge” center plays heavily on the treatment plan for these patients. There is a clear need for community education on this topic so that limited LT center resources can be optimally used and so that patient dissatisfaction and associated provider burnout/cynicism are limited.

It needs to be reiterated that only a very small number of patients are expected to fulfill this very strict criteria.

Conclusion

LT for ALD has evolved over the last 40 years, starting from an absolute contraindication to an accepted

routine reason for LT. Following in its footsteps, LT for AH remains contentious. With a measured approach that collectively considers and respects the perspectives of all stakeholders in the transplant process, consensus and progress are possible to improve the outcomes of our sickest wait-listed patients, regardless of etiology.

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