Alcohol Use Disorder and Alcohol-Associated Liver Disease: New Definitions, Screening, and Treatment

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Abstract: Alcohol-associated liver disease (ALD) poses a significant global health burden and is a leading cause of liver-related morbidity and mortality. ALD encompasses a spectrum of disease states ranging from asymptomatic steatosis to acute hepatitis and cirrhosis. Alcohol use disorder (AUD) significantly increases the risk of developing ALD, and insight into AUD can provide a more complete understanding of ALD and the patients affected by these interrelated diseases. Accurate and timely identification of AUD, even in primary care, through validated screening tools combined with blood tests and imaging techniques facilitates early detection of ALD. Although liver transplantation (LT) remains the most effective treatment for end-stage ALD, patient outcomes post-LT have evolved because of shifting perspectives on ALD transplant eligibility, comprehensive pre-LT evaluations, and advancements in post-LT ALD detection. Nonetheless, addressing disparities in LT practices for ALD is paramount for ensuring equitable access to this life-saving intervention. This article offers an updated synopsis of ALD definitions, screening methodologies, and contemporary management approaches, particularly in the context of LT.

Keywords
Alcohol, liver transplant, outcomes, alcohol use disorder, diagnosis, management

Alcohol-associated liver disease (ALD) poses a significant global health burden and is one of the leading causes of disability, liver-related morbidity, and mortality worldwide.[1,2] Alcohol consumption increases the risk of the development and progression of ALD in a dose-dependent manner; therefore, it is imperative for health care practitioners to comprehend the interplay between alcohol use disorder (AUD) and ALD.[3,4] Behaviors related to alcohol use are dependent on a complex interaction of individual, psychosocial, and environmental factors that are dynamic across time and social situations.[2,5]

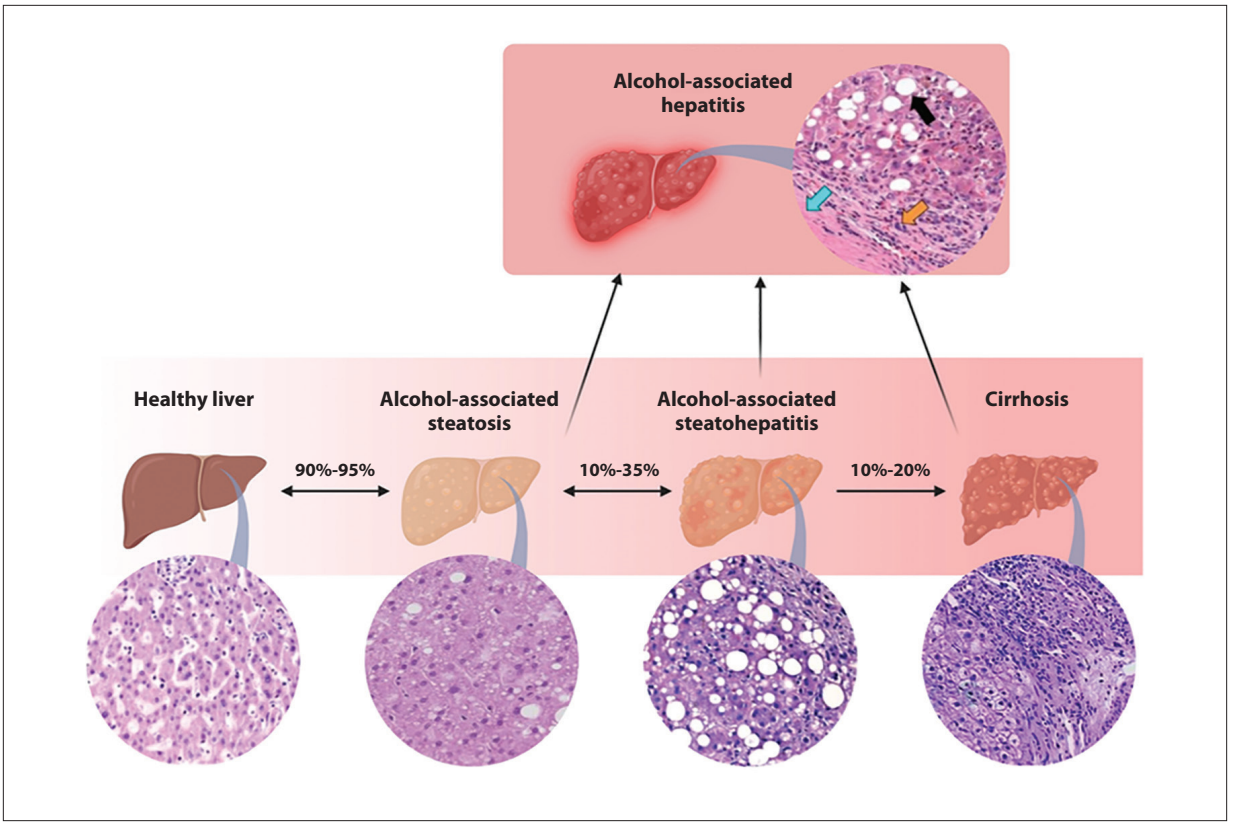

Figure. Risk of progression, clinical spectrum, and histopathologic features of alcohol-associated liver disease. Lipid droplets (black arrow), fibrosis (blue arrow), and immune cell infiltration (orange arrow) are shown in alcohol-associated hepatitis.

Adapted from Ge WS et al,[94] Wang X et al,[70] and Ge X et al[95] and created with BioRender.com.

Despite growing awareness of the health risks of alcohol use, it remains a major public health concern with a rising prevalence, as 43% of the world's population actively engages in drinking behaviors.[6,7] Alcohol consumption has been identified as the seventh leading cause of death worldwide, contributing to 2.2% of female deaths and 6.8% of male deaths, with a more pronounced impact on younger populations.[8] Globally, ALD accounts for 5.1% of all diseases and injuries.[9] In the United States, it is estimated that more than 1 million people will die from ALD between 2019 and 2040, and ALD is now one of the leading indications for liver transplantation (LT).[10,11] ALD has also been observed to have higher costs, liver-related mortality, and poorer survival rates than other causes of chronic liver disease in long-term follow-up studies.[12-15] In addition, concomitant alcohol consumption can accelerate liver damage and fibrosis in individuals with other forms of liver disease.[16] Finally, the COVID-19 pandemic has witnessed a significant surge in alcohol consumption, suggesting that the burden of ALD will likely increase.[2]

ALD is a complex and heterogeneous disease that encompasses a spectrum of histologic and clinical conditions. From a histopathologic perspective, patients may exhibit a continuum of findings, including alcohol-associated steatosis, alcohol-associated steatohepatitis (ASH), and varying degrees of fibrosis culminating in ALD-related cirrhosis (Figure).[17] The risk of progression and mortality varies according to the specific histologic stage.[18] From a clinical standpoint, ALD encompasses a spectrum of presentations, ranging from asymptomatic steatosis (ALD and metabolic dysfunction-associated steatotic liver disease with increased alcohol consumption [MetALD]) to acute alcohol-associated hepatitis (AH), and chronic ALD with or without hepatocellular carcinoma.[19-21] One of the most significant challenges in identifying ALD is that patients can remain asymptomatic throughout most of this spectrum of disease, with the development of symptoms typically indicating advanced stages.[18,22-24]

This article aims to provide an overview of AUD, the current tools and strategies used for its identification, and early detection and diagnosis of the entities within

the spectrum of ALD. The management of AUD extends beyond the scope of this review. This article provides recommendations regarding the management of ALD in the setting of LT, emphasizing the importance of a multidisciplinary approach. By providing a comprehensive understanding of the latest developments in the early detection and diagnosis of ALD, this article intends to equip clinicians with the knowledge necessary to deliver optimal care to individuals with ALD and ultimately reduce its associated morbidity and mortality.

Alcohol Use Disorder

Epidemiology and Definition

AUD encompasses a problematic pattern of alcohol use accompanied by significant impairment or distress.[25] The National Epidemiologic Survey on Alcohol and Related Conditions showed that the 12-month and lifetime prevalence of AUD is 13.9% and 29.1%, respectively, in the adult population of the United States.[26] However, the clinical identification of AUD remains significantly low, with studies indicating that AUD is overlooked in approximately one-third to one-half of patients.[27]

A formal diagnosis of AUD, as defined by the *Diagnostic and Statistical Manual of Mental Disorders,* fifth edition (DSM-5), requires the presence of at least 2 of 11 psychosocial, behavioral, or physiologic criteria within a 12-month period.[25,28] The severity of AUD can be further classified on the basis of the number of criteria met, with 2 to 3 criteria indicating mild AUD, 4 to 5 criteria signifying moderate AUD, and 6 or more criteria representing severe AUD.[25]

It is crucial to explore other AUD-related concepts defined by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), as they increase the risk of health consequences and the development of ALD. Binge drinking refers to a pattern of alcohol consumption within 2 hours that raises the blood alcohol concentration to 0.08% or higher, typically involving 4 drinks for women or 5 drinks for men.[29,30] In contrast, heavy drinking is defined as consuming more than 3 drinks per day or more than 7 drinks per week for women, and 4 drinks per day or 14 drinks per week for men.[29] Both binge drinking and heavy drinking fall under the category of alcohol misuse, increasing the risk of developing AUD and ALD.[30] Binge drinking is also associated with an increased risk of liver disease independent of average alcohol consumption, highlighting the importance of not only the overall intake of alcohol but also the pattern of alcohol consumption in conferring ALD risk.[29-31]

Of significant importance, studies have demonstrated that even chronic consumption of 1 to 2 drinks per day elevates the risk of ALD and cirrhosis compared with abstaining from alcohol entirely.[24] This suggests that the threshold for safe alcohol consumption may be considerably lower than previously believed. Therefore, it is important to adjust patients' and the public's thinking regarding the quantity and pattern of alcohol consumption that can lead to the development of ALD.

Screening of Alcohol Use Disorder

The initial step for the screening of unhealthy alcohol use and AUD involves the use of validated assessment tools such as the Alcohol Use Disorders Identification Test (AUDIT), the shorter version AUDIT-C, or the NIAAA Single Alcohol Screening Question (SASQ). SASQ has been shown to be a simpler yet still effective tool for AUD screening that can be applied in the primary care setting in less than 1 minute.[32] It evaluates the frequency at which a patient has exceeded the recommended daily drinking limits (4 drinks for men and 3 drinks for women) within the past year. One or more occurrences implies a positive test. Similarly, the AUDIT-C is a concise 3-item version of the AUDIT that can be administered in 1 to 2 minutes to screen for unhealthy alcohol use. Both the SASQ and AUDIT-C are simple, easy to administer, and highly sensitive for detecting unhealthy alcohol use, with sensitivities of 0.73 to 0.88 and 0.73 to 1.00, respectively.[33]

Following a positive SASQ or AUDIT-C result, the US Preventive Services Task Force (USPSTF) recommends follow-up with a more comprehensive 10-question AUDIT, which can be easily administered in 5 to 10 minutes and can confirm unhealthy alcohol use with a high specificity of 0.89 to 0.97 after the higher-sensitivity, lower-specificity screening tools.[33] Furthermore, the full 10-item AUDIT is useful not only for identifying patients with a higher likelihood of harmful drinking but also for risk stratifying patients with unhealthy alcohol use with higher AUDIT scores correlating with more severe AUD as defined by the DSM-5.[34]

Despite the well-documented utility of screening tools and the current recommendation from the USPSTF, these instruments are underutilized in most clinical scenarios, including primary care settings, where all patients aged 18 years and older should undergo screening for unhealthy alcohol use.[33] It is crucial to emphasize the significance of proper screening given the propensity of patients to underreport their alcohol consumption owing to the social stigma associated with AUD.[35]

Alcohol-Associated Liver Disease

Definition and Natural History

ALD represents a diverse spectrum of liver disorders that varies from a histologic and clinical perspective. The factors influencing progression within this continuum

remain incompletely understood. Although patient characteristics, including age, sex, genetics, metabolism, and lifestyle choices, may exert an impact on the development and progression of ALD, alcohol dose always plays a key, modifiable role.

The initial histologic change associated with ALD is the emergence of steatotic liver disease (SLD), which is marked by the accumulation of triglycerides within hepatocytes.[23,24,36] SLD typically arises as a common response to chronic and heavy alcohol consumption, with most heavy drinkers developing this condition after months to years of excessive drinking.[23,37] Notably, even a few weeks of excessive alcohol intake have been found to lead to SLD.[2,38] It is important to highlight that patients with SLD who have cardiometabolic risk factors (CMRFs) and consume 140 to 350 g of alcohol per week for women and 210 to 420 g of alcohol per week for men are now categorized as having MetALD, which is a new subcategory of metabolic dysfunction-associated steatotic liver disease.[21] The proposed CMRFs include obesity, glucose intolerance and diabetes, hypertension, and hyperlipidemia. In the new nomenclature, patients with steatosis are categorized as having ALD if their alcohol consumption is higher than 350 g per week and 420 g per week for women and men, respectively.

Approximately 10% to 35% of patients with SLD who persist in heavy alcohol consumption may transition to ASH, which is characterized by hepatocyte injury, ballooning, and inflammation.[23,39] Patients who present with SLD, ASH, and even compensated cirrhosis typically do not exhibit clinical symptoms.[22,23] However, persistently active ASH can further progress to fibrosis, advanced fibrosis, and ultimately cirrhosis in approximately 10% to 20% of cases.[40] Progression to cirrhosis does not occur in all patients and may be influenced by various factors that have not been completely elucidated. For instance, a study found that diabetes increases the risk of ALD-related cirrhosis (odds ratio [OR], 3.68; 95% CI, 2.66-5.08) compared with individuals with similar alcohol exposure but without diabetes.[41] Additionally, the same study found that coffee consumption had a protective effect on cirrhosis development (OR, 0.64; 95% CI, 0.50-0.83). Symptoms of hepatic decompensation, characterized by ascites, variceal bleeding, or hepatic encephalopathy, developed in approximately 25% and 50% of patients 1 and 5 years after diagnosis, respectively.[42] Notably, the 5-year survival rate of patients experiencing cirrhosis with decompensation varies depending on whether they cease alcohol consumption or continue to drink (60% vs 30%, respectively).[42]

AH is an acute symptomatic presentation of ALD characterized by high short-term mortality, estimated to range from 20% to 50%.[43] Patients develop severe liver dysfunction, jaundice, and systemic inflammatory response syndrome.[44] AH may occur either de novo in the setting of ASH, or in individuals with preexisting cirrhosis, leading to a presentation known as acute-on-chronic liver failure. This clinical syndrome manifests as jaundice, fever, abdominal pain, and anorexia in patients with a long history of alcohol use. Often, patients become symptomatic and stop alcohol intake for several weeks before seeking medical care. Histologic findings associated with AH are not specific and include steatosis, hepatocellular ballooning, neutrophilic and lymphocytic infiltration, Mallory-Denk bodies, fibrosis, and cholestasis (Figure).[45] However, severe forms of AH, defined by a Model for End-Stage Liver Disease (MELD) score of 20 or higher or Maddrey discriminant function score of 32 or higher, may benefit from systemic treatment with corticosteroids and N-acetyl cysteine and may require consideration for LT in severe cases that progress despite initial medical therapy.[46-48]

Early Diagnosis of Alcohol-Associated Liver Disease

Within the spectrum of ALD, approximately 90% of patients with early-stage ALD and 70% of those with ALD-related cirrhosis in a compensated state are asymptomatic or have nonspecific symptoms.[49,50] When symptoms arise before decompensation, they often manifest as fatigue, abdominal pain, and lower extremity edema.[50] Physical findings associated with cirrhosis include abdominal wall collateral vessels, palmar erythema, gynecomastia, spider angiomas, and jaundice.

The diagnosis of ALD requires the presence of unhealthy alcohol use or AUD in addition to clinical manifestations, biochemical liver function tests, and imaging modalities. These tests include aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total bilirubin, gamma-glutamyl transferase (GGT), albumin, prothrombin time, and international normalized ratio (INR). These tests were initially complemented by a liver ultrasound.[20,48] If abnormalities are detected, it is important to rule out other causes of liver disease, including viral hepatitis, autoimmune liver diseases, and metabolic liver conditions.

In clinical practice, ALD is often identified in an asymptomatic state and is found incidentally through the detection of abnormal liver test results or abnormal imaging findings of steatosis or coarse liver echotexture during imaging studies obtained for other clinical reasons.[50,51] Although certain laboratory values, such as an AST/ALT ratio greater than 2, elevated mean corpuscular volume (MCV), or GGT, can suggest the diagnosis of ALD and have been employed as surrogate markers, their performance as screening methods has been suboptimal, especially when used without considering the patient's

Table 1. Noninvasive Scoring Systems Assessing Liver Fibrosis and Cirrhosis in Alcohol-Associated Liver Disease

Scoring system	Cutoff	Sensitivity	Specificity
Fibrosis			
APRI	0.5	49%	84%
	>1.50	8%	98%
FIB-4 index	>3.25	16%	99%
	<1.45	42%	83%
ELF score	Moderate	83%	73%
Cirrhosis			
APRI	1.0-1.5	54%	78%
	<1.0	35%	94%
ELF score	N/A	80%	71%

APRI, Aspartate Aminotransferase to Platelet Ratio Index; ELF, Enhanced Liver Fibrosis; FIB-4, Fibrosis-4; N/A, not applicable.

Adapted from Moreno C et al.[59]

clinical history of alcohol misuse.[35,52]

Moreover, it is essential to assess the presence of portal hypertension and hepatic fibrosis in patients suspected of having early ALD. Fibrosis represents a dynamic process in which patients can progress or regress along the fibrosis spectrum over time, depending on the presence or absence of factors causing liver damage. Thus, any assessment of fibrosis represents a snapshot of a specific moment and is subject to change.[53-56] In a retrospective study of 192 patients with ALD, Lackner and colleagues found that in patients with asymptomatic and compensated ALD, long-term prognosis was determined by fibrosis stage but not by clinical or laboratory variables. In this study, the 10-year mortality rate of patients with early ALD and F3 to F4 fibrosis was 45%, compared with 0% in patients with F0 to F2 fibrosis (P<.001).[18] Consequently, the evaluation of fibrosis is an important initial step to accurately assess the staging and risk stratification of patients over time. Although liver biopsy serves as the current gold standard for determining the histologic stage of ALD, it is an invasive and occasionally impractical procedure, particularly in cases where cirrhosis has already been established.[57-59]

Biomarkers of Alcohol-Associated Liver Disease

Numerous laboratory tests serve as tools for the identification and evaluation of ALD, including an elevated AST/ALT ratio, MCV, or GGT. Specifically, an AST/ALT ratio greater than 1, often exceeding 2, suggests ALD. In addition, alterations in platelet count and liver synthetic function, as indicated by an elevation in INR and decreased albumin levels, suggest portal hypertension and advanced ALD.[50,60,61]

However, these conventional tests, while widely available and easy to obtain, exhibit limited specificity for determining ALD-related fibrosis and cirrhosis.[56,62,63] Some scoring systems have been combined to more accurately stage liver fibrosis. Some examples include the AST to Platelet Ratio Index and the Fibrosis-4 (FIB-4) index, which includes age, AST, ALT, and platelet count (Table 1). These indices offer the advantage of being inexpensive because they are assessed on routine laboratory tests. When appropriate cutoff values are applied, these scores effectively and reliably evaluate for advanced fibrosis.[59,64] For instance, a FIB-4 score less than 1.45 has a negative predictive value (NPV) of 94.7% for ruling out advanced fibrosis, whereas a FIB-4 score greater than 3.25 has a positive predictive value (PPV) for advanced fibrosis of 82.1%.[65]

Conversely, commercially available serum tests that measure direct markers of fibrosis, such as the Enhanced Liver Fibrosis (ELF) score and FibroTest, are less widely available, are more costly, and can lack insurance coverage.[56] Nevertheless, they are valuable tools for excluding advanced fibrosis, with NPVs of 94% and 90%, respectively.[66] Notably, the ELF test can predict the histologic stage of fibrosis with a meta-analysis of 9 studies showing a pooled sensitivity and specificity of 83% and 73% for significant fibrosis, 78% and 76% for severe fibrosis, and 80% and 71% for cirrhosis, respectively, with higher numerical ELF score cutoffs predicting a greater extent of fibrosis.[59,67] In a study of patients recruited from the primary care setting with at least 1 year of excessive alcohol use, an ELF score less than 10.5 had a NPV of 98% for ruling out advanced fibrosis (≥F3) on a same-day liver biopsy, illustrating the utility of the ELF score as a noninvasive screening test to identify patients who may be at risk for clinically significant ALD.[66]

The sequential combination of serum fibrosis screening tests followed by imaging has the highest sensitivity and specificity for advanced fibrosis.[64] Therefore, many experts suggest the ELF test, FibroTest, or FIB-4 index as an initial screening test, with high-risk scores prompting referral to a liver specialist and/or performance of advanced imaging such as transient elastography (TE).[50]

Currently, several investigational biomarkers directly measuring fibrosis are under exploration, potentially offering higher specificity by minimizing interference from other clinical variables, although the clinical use of these biomarkers is currently limited by availability and insurance coverage.[56] These include markers of matrix deposition, such as procollagen I peptide, markers of matrix degradation, such as matrix metalloproteinase-2, and cytokines that stimulate fibrogenesis, such as transforming growth factor alpha and beta.[56,68,69] Other novel noninvasive biomarkers of alcohol-related hepatotoxicity

and fibrosis are under active investigation for the diagnosis of AH. These include circulating small noncoding RNA and long noncoding RNAs as well as circulating cytokine levels and cytokeratins as biomarkers of systemic inflammation.[70-72] However, such measurements are in the early stages of study and are not yet available for clinical use.

Finally, a fundamental aspect of ALD management includes alcohol cessation, which is strongly associated with long-term survival and posttransplant outcomes. Therefore, direct markers of alcohol metabolism are useful for determining if, and to what extent, a patient has been recently consuming alcohol with a high level of specificity.[40] Examples of these markers include urine levels of ethyl glucuronide and ethyl sulfate, which can be elevated up to 4 to 5 days after alcohol ingestion with a sensitivity of 62% to 89% and specificity of 93% to 99%.[35] Serum phosphatidylethanol (PEth), a recently developed marker that has changed the management of ALD in transplant centers, has an even larger detection window of up to 28 days after alcohol ingestion with superior test characteristics, including a sensitivity of 90% to 99% and a specificity of 100%; however, it has a higher cost.[35] Although these direct markers of alcohol metabolism do not provide information on the degree of ALD, they are invaluable for identifying and risk stratifying patients with ALD who may need additional treatment for their underlying AUD, even after LT.[40]

Imaging in Alcohol-Associated Liver Disease

The most appropriate initial radiologic screening test in ALD is an abdominal ultrasound, which is a noninvasive, inexpensive, and readily available modality with a sensitivity of 60% to 95% and a specificity of 88% to 95% in detecting steatosis.[59] Ultrasound techniques using the attenuation of shear waves, such as controlled attenuation parameter, are more accurate than standard ultrasound in diagnosing SLD.[66] Magnetic resonance imaging (MRI) is even more accurate for the diagnosis of SLD, but is less accessible and much more costly than ultrasound.[40]

Fibrosis is effectively assessed with TE, a technique that measures liver stiffness (LS), which directly correlates with the degree of fibrosis and may be less subject to sampling bias than liver biopsy.[59] TE measures LS in kilopascals as a function of resistance to shear waves.[73] LS as measured by TE correlates with histologic fibrosis stage, with normal values (<6 kPa) excluding significant liver pathology. Values above 12.5 kPa correspond to F4 fibrosis. In the setting of cirrhosis, LS values also correlate with portal pressure and associated complications such as esophageal varices and hepatocellular carcinoma, which are common with values greater than 20 kPa.[59,74] In one study, LS below 10 kPa had a NPV of 99% and LS above 25 kPa had a PPV of 93% for severe fibrosis or cirrhosis in patients with ALD, even with recent or ongoing alcohol consumption.[75]

Technological innovation in elastography has led to new techniques, such as acoustic radiation force impulse imaging and shear wave elastography, which can be performed with conventional ultrasound probes and may be as accurate as TE. Magnetic resonance elastography (MRE), which combines traditional MRI with low-frequency vibrations to evaluate LS, is more accurate than TE in the detection of fibrosis and less affected by the previously mentioned potential confounders. A meta-analysis has shown that MRE has a sensitivity of 94% and a specificity of 95% for identifying greater than F2 fibrosis; however, MRE has yet to supplant TE given its higher cost.[76]

Alcohol-Associated Liver Disease and Liver Transplantation

LT is a life-saving intervention for patients with ALD and end-stage liver disease (ESLD). However, the selection of LT candidates for ALD has been a contentious issue in the medical and public health community because of concerns regarding relapse to harmful alcohol use, organ scarcity, and potential nonadherence to posttransplantation care.[77-79] Despite these potential challenges, it is crucial to acknowledge that AUD is a medical condition that can be treated with various behavioral and pharmacologic therapies. Therefore, when necessary, LT should be considered as part of a comprehensive management plan for patients with decompensated cirrhosis from ALD, and patients should be referred early for LT evaluation.

Recent studies have demonstrated that the outcomes of LT for ALD are comparable or even superior to those for non–alcohol-associated etiologies of cirrhosis.[35,77] In fact, there has been significant improvement in both graft and patient survival rates after LT for ALD over the past few decades, with reported 5-year survival rates ranging from 73% to 84%.[77,80,81] Additionally, even at 10 years after LT, patient and graft survival rates for ALD were 75% and 69%, respectively, which were not significantly different from those transplanted for non-ALD indications.[82]

Despite the success of LT in patients with ALD, there is a risk of posttransplant relapse of alcohol use and AUD, with reported rates ranging from 15% to 50%.[35,77,80] Several demographic and AUD-related factors have been identified in patients who relapse to alcohol use after LT compared with those who remain abstinent. These factors include younger age, being single, shorter duration of sobriety before transplantation, family history of alcoholism, presence of other psychiatric comorbidities, and use of other substances.[80,82,83] Therefore, adequate pre-LT

Table 2. Psychosocial Questionnaire for Patients With Alcohol-Associated Liver Disease Being Evaluated for Liver Transplant

Psychosocial screening for liver transplant evaluation
1. Do you believe you have a problem with alcohol?
2. Are you willing to stop alcohol use for the rest of your life?
3. Are you willing to participate in alcohol (or addiction) treatment?
4. Have you attended 2 or more formal alcohol treatment programs or rehabilitations?
5. Are you currently using recreational or street drugs other than marijuana and tobacco?
6. Have you undergone addiction treatment for substances other than alcohol?
7. Have you been hospitalized for a mental health illness other than addiction?
8. Have you attempted suicide?
9. Is a family or care provider available within 48 hours of patient admission?
10. Can the caregiver provide 24/7 care for up to 3 weeks?
Additional questions:
A. Upon interview, does the patient exhibit signs of encephalopathy? If so, what is the West Haven HE grade (0, 1, 2, 3, or 4)?
B. Are there discrepancies between the patient report and history from other sources?
C. Are there discrepancies between the alcohol report and toxicology (PEth)?

HE, hepatic encephalopathy; PEth, phosphatidylethanol.

Adapted from DiMartini A et al.[80]

screening and the management of AUD in patients with ALD can lead to low relapse rates after LT for ALD.

Evaluation and Selection of Liver Transplant Candidates for Alcohol-Associated Liver Disease

In the realm of LT for ALD, the significance of a comprehensive pretransplant evaluation cannot be overstated. This crucial step in the LT process necessitates the involvement of a multidisciplinary team comprising a diverse range of specialists, such as hepatologists, transplant surgeons, psychiatrists, psychologists, social workers, and addiction specialists. By working collaboratively, the team can diligently assess several key factors, including the patient's suitability for the surgical procedure, capacity to withstand posttransplant care, presence of a robust social support system, and willingness to adhere to treatment programs.

In the context of LT for ALD, the psychosocial assessment is of the utmost importance.[84,85] Beyond the standardized clinical evaluation, this assessment plays a critical role in comprehending the patient's perspective and behavioral aspects. It encompasses evaluating their understanding of the disease and its associated risks, assessing their level of motivation, and determining their ability to maintain sobriety. Furthermore, it delves into the patient's personal history of substance use disorders, including any previous attempts at rehabilitation, and considers the availability of reliable social support networks (Table 2). By conducting an all-encompassing pretransplant evaluation, transplant providers can effectively identify patients who are more likely to achieve favorable outcomes while simultaneously minimizing the risk of relapse.

The traditional approach of employing the 6-month sobriety rule, which aimed to identify patients at a heightened risk of relapse and allow for the possibility of liver recovery from alcohol-related injury, is undergoing a transformative shift owing to advancing expertise in LT for ALD. Recent data have revealed comparable graft and patient survival outcomes between individuals with and without a specified sobriety period. In a study conducted by Ursic-Bedoya and colleagues, the survival outcomes of patients with positive blood or urine alcohol levels on the day of transplantation were compared with those with negative alcohol tests. After a follow-up period of 12.9 years, the study revealed that patients with positive alcohol tests exhibited survival rates similar to those of the control group with negative alcohol tests.[86] However, patients with positive alcohol tests demonstrated higher and more rapid rates of relapse, as well as increased rates of recurrent cirrhosis.

Although rigid adherence to a sobriety period may no longer be deemed imperative, it remains beneficial for patients to undergo alcohol treatment whenever possible before undergoing LT. Furthermore, the clinical and objective monitoring of alcohol use through the use of questionnaires and laboratory tests such as PEth should be implemented both before and after transplantation.[87,88] By incorporating such measures, patients can receive essential support to sustain sobriety and mitigate complications following transplantation.

Liver Transplant Disparities in Patients With Alcohol-Associated Liver Disease

Although AUD and ALD have historically been more prevalent among men and non-Hispanic Whites, there has been an increase in the prevalence of alcohol use, high-risk drinking, and AUD among women and non-White patients over the past several decades.[2] In addition, the proportion of women with ALD and advanced fibrosis has risen from 2.6% in the early 2000s to 4.6% in 2015 to 2016.[81]

However, studies in the United States and Europe have revealed sex disparities in patients who are listed for or have received LT for ALD. For instance, an international European study of patients with ALD showed marked sex-based differences in LT-related practices, with women being more likely to be removed from the waiting list (hazard ratio [HR], 1.44) and having a lower likelihood to receive a LT (HR, 0.74) compared with men.[89] In this study, 1532 female patients were listed for LT for ALD, representing 24.8% of all listed patients, and 684 received a LT, which was 20.4% of all transplants for ALD from 2010 to 2019. Similarly, in the United States, the proportion of women with ALD who were listed for LT was lower than that of men, and of these patients, only 535 women received a LT compared with 2226 men. Moreover, other studies have demonstrated that despite having similar MELD scores, men with ALD were 95% more likely to be listed and 105% more likely to be transplanted compared with women with ALD.[90]

Additionally, racial differences were found in ALD demographics, listing, and LT practices. From a representative sample of 2708 patients with ALD in the United States from 2001 to 2016, 66.2% were White, 8.6% were Black, and 21.2% were Hispanic.[81] During the same period, 9430 patients received LT for ALD, of which 80% were White, 3.8% were Black, and 13.8% were Hispanic.[91] Furthermore, a US study regarding LT for ALD from 2014 to 2018 found that Black patients were disadvantaged as they had less access to the LT waiting list compared with other races/ethnicities.[92] This was measured by a lower listing-to-death ratio (0.13 vs 0.26 for Whites), a metric to assess the ratio of listing for LT compared with deaths from ESLD.[92,93]

Although the current pattern of LT practices may reflect the current need for organs among patients with ALD-related cirrhosis, it is crucial to monitor future changes as the population with ALD continues to evolve. These findings suggest that transplant providers should increase their attention to equitable access to LT for all eligible patients, regardless of sex or racial background.

Conclusion

AUD and ALD represent a significant global health burden that leads to high morbidity and mortality worldwide. Early detection and diagnosis of ALD pose challenges because of the lack of specific symptoms in the early stages. However, the use of validated screening tools to detect AUD, along with blood testing and imaging modalities such as ultrasound and elastography, can aid in the identification and assessment of ALD. Newer direct markers of alcohol metabolism provide valuable insights into recent alcohol consumption. In patients who develop ESLD from ALD and require LT, a multidisciplinary evaluation and comprehensive pretransplant assessments are crucial for selecting appropriate candidates. Recent studies have demonstrated promising outcomes in LT for ALD, although the risk of posttransplant relapse remains a concern. It is also important from a public health perspective to address the disparities in LT practices to ensure equitable access for all eligible ALD patients.

Disclosures

The authors have no relevant conflicts of interest to disclose.

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