

## Psychosocial Evaluation of Liver Transplant Candidates with Alcohol-Related Liver Disease and/or Substance Abuse

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#### Overview

Liver transplantation (LT) remains a controversial treatment for life-threatening liver disease in association with a history of alcohol use disorder (AUD). This is a curious conundrum, since the concept that addictions constitute a disease process is well-established, and the outcome after LT in selected patients with AUD is on par with that for other chronic disorders. The controversy originates, at least in part, over a concern for relapse to addictive behavior after LT. Nor are all addictions considered equally, and in this chapter we will briefly refer to addictive behaviors such as smoking, use of marijuana, non-prescribed use of prescription pain relievers, and use of illicit drugs. The contrast between the typical assessment of cigarette smoking with that of AUD is particularly striking, in light of the long-term negative consequences of smoking after transplantation. In the case of AUD, the advice of the transplant services to the LT recipient is complete abstinence. Smoking cigarettes is considered exclusionary in rare centers but not in most, and while advised to stop smoking, this is rarely a priority in posttransplant management. Recently, marijuana has joined alcohol and tobacco as a legal agent in many states in the USA. Once again, attitudes to marijuana use by transplant candidates are variable and likely in flux in transplant centers. It is against this inconsistent and unstable background that we will provide a brief review of psychosocial evaluation of patients under consideration for LT. We will initiate the discussion with a series of definitions. We will review the history of psychosocial evaluation, with particular emphasis on patients with AUD and the much discussed '6-month rule'. Next, we will turn to the present state. Finally, we will speculate about how psychosocial assessment may evolve in the future.

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#### 31.1 Introduction

Liver transplantation (LT) is the only curative treatment available for end-stage liver disease, although unfortunately the number of patients waiting for liver transplants far exceeds that of available donor livers. In order to ensure appropriate allocation of these livers to the patients who are most likely to benefit from LT, a comprehensive and in-depth evaluation of each patient who is being considered as an LT candidate is essential. The principal goal of the pre-transplant evaluation is to determine whether LT will be successful in a given candidate, which extends to an assessment of not only a patient's capacity to prosper after transplant surgery but their ability to meet the demands of the subsequent lifelong and oftentimes complex cares that are necessary after receiving a liver transplant. Although specific testing varies among transplant centers and based on patient variables, the crux of the pre-transplant evaluation therefore involves cardiopulmonary assessment, screening for underlying malignancy, infection, or occult medical disorders, and psychosocial evaluation [1].

Alcohol-related liver disease (ALD) is one of the most common indications for LT in the USA and Europe, representing almost a quarter of all LTs performed in the USA according to the OPTN/SRTR 2016 annual report [2, 3]. The use of alcohol and illicit substances is pervasive across many patient populations and has the potential to result in a myriad of economic, social, legal, and health problems. Table 31.1 shows the most recent prevalence data on alcohol and substance use among Americans aged 12 and higher [4]. The data, reported in 2014, indicate that alcohol is the most common potentially addictive substance in common use among American adults, with more than half of the adult population reporting at least social drinking. Addictive consumption of alcohol was present in 10% of users. In the USA, the *lifetime* prevalence of AUD in adults has been reported to be as high as 30% [5]. Alcohol has been well-studied in regards to its effects on the liver with excessive consumption associated with both acute and chronic liver damage.

Substance	Current use	Alcohol/substance use disorder			
Alcohol	176.6 million (52.7% <sup>a</sup> )	17 million			
Tobacco	66.9 million (25.2% <sup>a</sup> )	66.9 million (25.2% <sup>a</sup> )			
Marijuana	22.2 million	4.2 million			
Stimulant use disorder					
Cocaine		913,000			
Methamphetamines		569,000			
Other stimulants		476,000			
Hallucinogen use disorder		246,000			
Opioid use disorder					
Prescription		1.9 million			
Heroin		586,000			

Table 31.1 Prevalence of addictive behaviors in Americans aged 12 and higher in the USA

 $<sup>^{\</sup>rm a}\%$  of the population. (Reference: the National Survey on Drug Use and Health (NSDUH)—2014 (www.samhsa.gov)

Although only a small number of patients who meet the criteria for AUD will ultimately develop cirrhosis, regular alcohol intake can result in hepatic steatosis and steatohepatitis, which predispose patients to fibrosis and cirrhosis with continued use [6].

In 1964, the US Surgeon General published a landmark report bringing the dangers of smoking to the attention of the public for the first time. Since then, the prevalence of smoking cigarettes has declined from greater than 50% of adults being smokers to a prevalence of 25% today. However, as shown in Table 31.1, since all chronic use of tobacco is addictive, smoking constitutes the most common substance addiction in the USA [7]. Furthermore, the coincidence of AUD with smoking and the early resumption of cigarette smoking after LT mean that cigarette smoking is an under-recognized crisis in the field of post-transplant management [8].

The use of marijuana is a poorly researched and poorly understood phenomenon in the LT community. However, recent survey data would suggest that it is rarely a limitation on access to liver transplantation in the USA [9]. Finally, we are in the midst of an epidemic of opiate use in the USA, although the absolute numbers of users remains dwarfed by alcohol, tobacco, and marijuana. The lifetime prevalence of illicit drug use has been reported to be approximately 8% in US adults, although the lifetime prevalence of an actual illicit drug use disorder is likely closer to 2–3% [10, 11].

As a component of the pre-transplant evaluation, the overarching goal of the psychosocial evaluation in the patient being considered for LT is similar to that of other components of the transplant evaluation: to predict whether a transplantation will be successful in terms of graft and patient survival and the restoration of quality of life. The patient with alcohol or substance use disorders poses unique challenges to providers, wherein the purpose of the psychosocial evaluation is to predict recurrence of addictive behaviors and other psychosocial factors which may endanger the future health of the transplant recipient.

### 31.2 Definitions

Psychosocial evaluation. Psychosocial evaluation can be loosely defined as a comprehensive assessment of a patient's psychological health, social context, self-perception, and functional capacity within the framework of their community (see Box 1). This assessment has two primary arms through which it assesses the suitability of a patient for LT; the first is to identify potential risk factors for morbidity and mortality post-operatively due to recurrent substance use, lapses in adherence to the clinical care plan, psychiatric disease, or social issues. The second is to translate these factors in high-risk individuals into recommendations for treatment interventions which may be undertaken before and/or after LT. Other suggested secondary purposes of the psychosocial evaluation include promoting fairness and equal access to care, serving as a guide for future clinical management, and addressing the psychological needs of the transplant team itself in the context of patient care [12].

#### Box 1 Components of the Psychosocial Evaluation

- 1. Substance use
  - (a) Alcohol or substance use history
  - (b) Tobacco dependence
  - (c) History of consequences related to substance use
  - (d) History of treatment (rehab, counseling, etc.)
- 2. Psychiatric health
  - (a) Known mood or psychotic disorders—stability, current treatment, etc.
  - (b) Previously unidentified mood disorders
  - (c) Personality disorders
- 3. Available resources
  - (a) Social support—quantity, quality, etc.
  - (b) Financial condition and support
  - (c) Medical insurance
  - (d) Current living situation
- 4. Adherence/non-compliance
  - (a) Ability to comply with labs, follow-up visits, recommendations
  - (b) History of medical adherence
- 5. Candidate temperament
  - (a) Maladaptive personality characteristics
  - (b) Coping mechanisms
  - (c) Motivation and adaptability
  - (d) Ability to successfully interact with the transplant team
- 6. Competence

Alcohol/substance use disorder. All substance use disorders have common elements, as shown in Box 2. The current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) defines a substance use disorder as meeting at least two of a defined set of 11 potential criteria over the preceding 12 months. These criteria are outlined as a series of questions which assess a patient's pattern of use, negative consequences of use, and elements of dependence, with the number of criteria met translating into the severity of the substance use disorder which is designated as mild, moderate, or severe [13]. The substance use disorders encompass 10 separate classes of drugs (such as alcohol, cannabis, opioids, hallucinogens, etc.) which are similarly diagnosed and stratified based on the aforementioned criteria. Although there is overlap with the preceding edition of the DSM (DSM-IV), this updated version importantly combines the historical (and often ambiguous) terms "abuse" and "dependence" into a single psychiatric disorder. The concept of alcohol and substance cravings have also been incorporated into the DSM-V, as they have become a more recognized feature of substance use disorders [14].

# Box 2 Features Common to Substance Use Disorders (SUDs) (Eccleston et al. 2017) [15]

- 1. All SUDs are chronic conditions of remission and relapse.
- 2. All SUDs are associated with an internal drive to consume the substance in question, often referred to as "craving".
- 3. SUDs often have triggers, which are situations or materials that initiate cravings.
- 4. Discontinuation of the addictive substance is often accompanied by unpleasant physical effects called withdrawal.
- 5. The use of substances is often a source of shame to the user and can lead to hiding use, reluctance to seek addiction treatment, and stigma.

**Craving.** A persistent or recurrent desire to resume an addictive activity or substance. Craving is a feature common to all forms of addiction. Cravings may persist for many years after the last exposure to the addictive substance or behavior. Cravings often arise when the subject comes in contact with specific times, places, or things, which are referred to as triggers. Interestingly, many patients with a history of AUD who are undergoing evaluation for LT deny that they experience cravings. The lack of cravings is one reason why some of these patients express a low interest in treatment or counseling for AUD [16].

Use, slips, relapse. As a disease often marked by remissions and relapses, the presence of an alcohol or substance use disorder in a patient undergoing LT naturally raises the question of a possible return to use after transplantation. Alcohol use after transplantation is not uncommon, with the prevalence reported to vary between 10 and 50% in the literature [17–21]. There are few studies available that examine relapse rates for substance use disorders other than alcohol after LT. However, a large meta-analysis including four studies reporting on illicit drug relapse found lower rates of relapse compared to alcohol (1.9% of patients/year compared to 5.6% of patients/year) [22].

A critical point in determining the burden of alcohol use after transplant lies in the concept of defining the severity of resumed consumption of alcohol. The large variation in rates for return to drinking after LT reported is in part due to inconsistency in defining 'use', 'slips', and 'relapse' [23]. Although there are currently no standardized criteria defining a relapse after transplant, it is now generally accepted that all use of alcohol after liver transplantation is not created equal. Studies have shown that all drinking behavior does not necessarily lead to uncontrolled use and negative consequences, and frequently used nomenclature now distinguishes a return to harmful and excessive drinking (relapse) from a transient lapse in sobriety which is followed by a return of abstinence (a "slip"). As long as they do not progress to a relapse, slips have not been implicated in causing significant harm and have even been hypothesized to be a healthy component of long-term sobriety [23, 24].

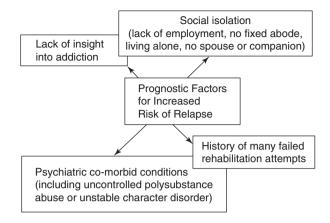
For those patients who do relapse following liver transplantation, specific patterns of ongoing alcohol use can vary widely. For instance, DiMartini and colleagues identified four distinct alcohol use trajectories based on the timing of onset, quantity consumed, and duration of alcohol use after transplant for alcoholic liver disease and suggested that these patterns may be predictive of outcome [25]. With a clearer focus on the distinction between "slips" and relapse, the implications of alcohol relapse become more striking in the literature. Recent data suggest that continuous, heavy drinking after transplant leads to allograft fibrosis and loss, which is likely accelerated compared to a native liver [20, 26]. Another proposed complication of alcohol relapse is non-adherence with vital immunosuppressive medications following LT, which can result in graft injury. However, current data regarding the presence and impact of this issue in alcohol relapsers are inconsistent [27, 28]. When patterns of alcohol use are taken into account, it is estimated that approximately 10–20% of patients relapse with sustained, harmful drinking and are therefore at risk for these graft-associated complications [21, 25, 29, 30].

## 31.3 History

The emergence of ALD as a major source of patients considered suitable for LT has occurred *pari passu* with the recognition that assessment of addictive disorders in general, and AUD in particular, is fundamental in the clinical care of patients under consideration for LT. It was not always thus. A turning point in the USA occurred in 1996 when the NIH held a workshop entitled 'Liver Transplantation for Alcoholic Liver Disease' that sought to bring together experts from the fields of addiction medicine and ALD [31]. The workshop emphasized that future advances would require a focus on AUD as much as ALD. Thus, the major needs in clinical research on LT for ALD are better documentation of the relapse rate after transplantation and the factors that predict relapse especially over an extended period (5–10 years) using reliable and objective means of documenting alcohol use. Study of relapse after transplantation may be helpful in developing better selection criteria but may also provide insights into treatment of alcoholism in patients that do not receive transplants.

The '6-month rule'. The requirement that the AUD patient demonstrate 6 months of abstinence prior to LT (commonly referred to as the "6-month rule") has become entrenched in the practice of transplant evaluation in the USA. While the 6-month interval has been justified on the grounds that it would allow patients to recover from the acute effects of alcoholic toxicity to the liver [32], in practice it has become a surrogate to predict future drinking by ALD candidates for LT. From the start of liver transplantation for ALD, experts in addiction medicine were not supportive of the 6-month rule, not least since longitudinal studies in men with ALD suggested that abstinence was secure only after 5 years [33]. Beresford offered, as an alternative, a more nuanced approach based on a careful psychosocial assessment [34]. He proposed that ALD patients undergoing evaluation for LT should be assessed by an addiction specialist, and that risk should be gauged according to the presence of

Fig. 31.1 Factors that indicate a greater risk of relapse by AUD patients undergoing evaluation for LT (Beresford et al. 1994) [34]



factors that characterize risk of relapse in patients with AUD beyond the LT setting. As shown in Fig. 31.1, he identified four domains in the candidate's psychosocial profile: social isolation/social integration; acceptance or not of their drinking problem; prior history of treatment of AUD and finally, presence of other psychological disorders. He attempted to classify these elements into a predictive score, but found that the predictive ability was limited to identifying high- and low-risk candidates. Since then, several additional protocols and prognostic tools to assess risk of alcohol relapse have been proposed. (Table 31.2). In all cases, these need to be used within a comprehensive evaluation involving experts in addiction medicine. Since then, Addolorato has advocated for the integration of an addiction specialist into the liver transplant unit to, as far as possible, remove the barriers of communication and understanding that exist between transplant and addiction medicine.

The change in attitude regarding the "6-month rule" originated in Europe, most significantly in France, where a consensus conference in 2005 came to the conclusion that a therapeutic trial of early LT in patients with alcoholic hepatitis not responsive to corticosteroid therapy was recommended "despite the brevity of the required abstinence" [35]. This important determination prepared the way for the landmark French–Belgian pilot study of rescue LT in patients with non-responsive severe alcoholic hepatitis. Similarly, consensus statements in favor of LT of selected ALD patients with shorter intervals of abstinence were produced in the UK and Italy [36–38]. A recent survey from the USA suggests that there is a change in practice in USA transplant centers also [9].

A collateral outcome of the Franco-Belgian study was the development of a model of psychosocial evaluation that sought consensus among all members of the transplant team, and empowered the professionals who were not physicians such as the nurses and social workers to express their opinions. By this means, the authors sought to ameliorate the problems posed by inconsistent evaluations and recalibrate the weight of influence of the team members to be more inclusive. Most recently, Lee et al. have shown, albeit in retrospective data, that selected patients with severe alcoholic hepatitis and a median interval of abstinence of 55 days who underwent LT in the USA had excellent short-term survival [39].

 Table 31.2
 Prognostic tools to assess risk of alcohol relapse and/or psychological risk profile

Authors	Instrument	Key factors	Comments	Reference
Beresford et al.	University of Michigan alcoholism prognosis score	Four domains; see Fig. 31.1	Based on review of the non-transplant literature regarding AUD Stratifies high and low risk.	[34]
Rodrigue et al.	Alcohol relapse risk assessment	Nine predictive factors: tobacco dependence, continued alcohol use after liver disease diagnosis, low motivation for alcohol treatment, poor stress management skills, no rehabilitation relationship, limited social support, lack of nonmedical behavioral consequences, and continued engagement in social activities with alcohol present	Retrospective, single center Stratifies high and low risk	[59]
De Gottardi et al.	The high-risk alcoholism relapse (HBAR)	Three predictive factors: duration of heavy drinking, usual number of daily drinks, number of prior inpatient alcohol- related treatment experiences.	Designed to predict "heavy drinking." Not specific to transplant	[30]
Maldonado et al.	The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT)	Comprehensive interview instrument to identify subjects who might be at risk for negative psychosocial outcomes post-transplant	Designed for all solid organ transplants. Requires skill and is time-consuming Provides a risk score	[60]
Twillman et al.	The Transplant Evaluation Rating Scale (TERS)	Classifies patients on a 3-point semi-structured scale in ten aspects of psychosocial functioning thought to be important in adjusting to transplantation	Designed for solid organ transplant Provides a summary score to indicate current level of functioning and a weighted score for each variable	[61]
Olbrisch et al.	The Psychosocial Assessment of Candidates for Transplantation (PACT)	Classifies patients on a 5-point semi-structured scale of eight items that assess various aspects of psychosocial health	Designed for solid organ transplant Provides a summary score and the rater's overall impression—offers more flexibility in using clinical judgment	[62]

## 31.4 Current State

Current guidelines from professional societies recommend that patients with ALD and/or substance use disorders undergo psychosocial evaluation prior to liver transplantation. For instance, practice guidelines from the American Association for the Study of Liver Disease (AASLD) and American Society of Transplantation (AST) specify that patients should be evaluated for and meet reasonable expectations for adherence to medical directives, mental health, and adequate social support [1]. In addition, the International Liver Transplant Society more explicitly recommends that patients with ALD be at a minimum assessed by mental health specialists and an alcohol specialist prior to listing for transplantation [40].

Common practices at transplant centers, in reality, vary from one another while adhering to these fundamental recommendations [41]. The psychosocial evaluation of the LT candidate is multifaceted and complex, requiring a multidisciplinary team with members of the transplant team tasked with this evaluation including social workers, nurse or physician specialists, psychologists, psychiatrists, and/or addiction specialists, depending on the center. In our transplant center at the University of Wisconsin, each patient presented to the LT selection committee who has ALD or concerns for a substance use disorder is assessed not only by our transplant social workers, who evaluate all LT candidates, but also by an addiction medicine specialist. Information is acquired not only through direct interview with the patient, but often through other sources such as family, friends, medical records, and previous providers with the patient's consent. This is often crucial in LT candidates as associated factors such as substance use, encephalopathy, or critical illness may result in the patient themselves being an unreliable historian [12].

Transplant social workers and addiction specialists are vital components of the transplant evaluation committee, especially with respect to patients with ALD and/ or substance use issues. Social workers not only assess aspects of the pre-transplant evaluation common to all candidates such as insurance coverage, patient expectations, and advanced directives, but conduct a full psychosocial assessment that often addresses complex social situations and mental or emotional health deficiencies that are frequently a result of or related to the patient's underlying substance use disorder. In doing so, social workers explore the impact of psychosocial factors on transplant readiness and identify potential barriers to the transplant as well as areas for intervention before and after the transplant. For instance, social workers are often key in assessing the quality and quantity of a candidate's social support system, which has been identified time and time again as a crucial factor in determining post-LT alcohol relapse as well as medical and psychiatric outcomes [42]. Our center, as do many others, requires the availability of both a primary and secondary support person to be closely involved in the patient's medical care. In candidates with a substance use history, addiction specialists provide an assessment from the standpoint of identification of the nature and extent of the substance use as well as providing a quantification of the risk for potential relapse after LT. This often requires an extensive review of prior medical records, family interviews, and legal records to obtain collateral information in order to fully define the candidate's

substance use history. In addition, the addiction specialist makes recommendations to the transplant team regarding appropriate substance use interventions (counseling, rehab, etc.) that may be beneficial prior to LT.

Multiple instruments have been developed for the purpose of evaluating the psychosocial factors relevant to transplantation and are widely used in pre-transplant evaluations, such as The Psychological Assessment of Candidates for Transplantation (PACT) and The Transplantation Evaluation Rating Scale (TERS) [43] (see Table 31.2). Beresford made one of the first efforts at codifying the prognostic assessment for long-term sobriety in LT candidates. The four elements he identified are shown in Fig. 31.1. All the subsequent instruments have tended to use similar indices of good or poor prognosis for AUD. In our center, we utilize "The Stanford Integrated Psychosocial Assessment for Transplant" or "SIPAT", as it has been designed for all forms of SUD in the setting of transplantation. This validated, comprehensive screening tool evaluates 18 psychosocial risk factors and assigns patients an objective score, thereby allowing standardization of the psychosocial assessment. Prospective studies have shown that high SIPAT scores are significantly correlated with poor medical and psychosocial outcomes post-transplantation [44]. One limitation of SIPAT is that it is long and involved, and tends to be cumbersome to administer. We use the SIPAT score to provide a relative quantitative scale. However, we do not have an absolute threshold for acceptance. Rather, it helps our social worker and addiction specialist to stratify the candidate as high or low risk for resumption of the addiction in question.

Concurrent psychiatric disorders are common in patients with end-stage liver disease, with studies reporting significant depressive symptoms in up to 57-63% of patients and anxiety symptoms in up to 50% of patients awaiting LT [45, 46]. The prevalence of comorbid psychiatric illness in those with ALD may be even higher when compared to those with liver disease from other etiologies [47]. Identification of these disorders in the pre-LT period is one of the aims of the psychosocial evaluation and is important for many reasons. Patients with chronic illnesses and comorbid depression/anxiety are more likely to be medically non-compliant [48]. In addition, untreated mood disorders have been associated with poor quality of life, poor recovery, and overall mortality following LT [48, 49]. Personality disorders are also important to recognize in the candidate with alcohol or substance use given their high prevalence rate in this population; antisocial personality disorder is the most common in those with ALD and may predict relapse after LT [45]. Maladaptive personality characteristics and coping abilities are also important aspects to consider during evaluation [46]. Psychiatric assessment varies among transplant centers but may include screening questionnaires, coping inventories, personality assessments, and/or neuropsychological batteries depending on specific concerns for a particular candidate [46]. More in-depth psychiatric evaluation may also be required based on issues brought to light during the initial psychosocial assessment, and to that effect a licensed mental health practitioner is attached to the LT evaluation team in many institutions. Whether any of these psychiatric comorbidities should be considered a contraindication to LT has been the subject of some debate; currently there are no psychiatric disorders that are considered absolute contraindications [1].

However, their presence should provoke careful consideration regarding stability of the psychiatric disease and available social support as well as the potential effect on nonadherence and ability to cooperate with the transplant team.

## 31.5 Limitations of the Psychosocial Evaluation

There are limitations of the psychosocial evaluation of the candidate for LT, some of which are confined to the patient with ALD or substance use while others apply to the LT candidate in general. In the population with AUD, as stated earlier, determining a patient's potential risk for relapse after LT remains a primary goal of the psychosocial evaluation, which is dependent on the history from the subject and the subject's family. However, patients with AUD or other forms of SUD not infrequently perceive that candor comes at the risk of jeopardizing their chances of getting a transplant [50]. Therefore, rationalization or concealment of alcohol use is common in patients with AUD undergoing liver transplant evaluation [34]. Failure by the patient to fully disclose during the psychosocial evaluation the extent of alcohol use, or inform the transplant team of a return to alcohol use in the interval before transplantation, are therefore concerning problems, but not uncommon. One retrospective study of disclosure in this population found that 21% of the patients in their cohort who had been cleared from a psychosocial standpoint were ultimately found to have non-disclosed driving-under-the-influence (DUI) convictions in their history, with 61% of those DUIs occurring during periods of claimed sobriety [51]. Similarly, a prospective study of psychotherapy for patients with AUD under consideration for LT, in which candor concerning alcohol use was encouraged by keeping drinking questionnaires in confidence, except in medical emergencies, found that 23 of 99 subjects (25% of sample) drank after randomization but before transplant [52]. The best protection against the failure to recognize the severity of a patient's AUD is to establish a close trusting clinical bond between the patient and the transplant team. The use of biomarkers of alcohol use may help or hinder this effort [53]. When biomarkers are used to improve communication, they are likely to help, whereas when they are seen by the patient as a form of entrapment, they are likely to be counterproductive.

Our ability to critically assess the pre-transplant psychosocial evaluation is also limited, in part due to variation in practices between different transplant institutions and even within the same institution [41]. There have been many efforts to improve and standardize the process with screening tools such as those shown in Table 31.2, but these instruments are not used universally. Efforts to study the decision-making process of the LT selection committee itself have been undertaken in order to identify opportunities for improvement. A multicenter study of four US transplant centers involved observation of selection committee meetings followed by analysis based on qualitative sociologic methods. The authors found that although committee function was overall similar, structure varied considerably by center. Notably, they also found that although recent or active substance abuse was routinely agreed upon as sufficient for declining to list a patient for LT, discussions of other

psychosocial barriers to LT such as psychiatric disease, lack of social support, non-compliance, or inadequate insurance often resulted in protracted and sometimes even contentious committee discussion. As expected, committee members confirmed that these psychosocial issues were among the most difficult topics to navigate [41]. Therefore, although we do not question the necessity of the psychosocial evaluation prior to LT, it is our opinion that we should in humility recognize the limitations of the process and maintain a skeptical eye on the overall reliability and validity of the psychosocial evaluation itself within the framework of the LT selection process.

Understanding the process of the psychosocial evaluation, and indeed LT candidate selection in general, is important not only for the sake of technical improvement but also for the purposes of transparency for patients, their families, and the public. Unfortunately, from a patient's perspective, this process often remains shrouded in mystery, particularly for the less tangible components of the evaluation, such as psychosocial eligibility. There are little data available regarding the transparency of the psychosocial evaluation prior to LT. However, one study assessing the content of LT centers' posted internet content regarding eligibility found that only a third discussed substance use while even fewer discussed their policy regarding alcohol use in patients with ALD. Overall, detailed accounts of psychosocial eligibility requirements were rare [54].

## 31.6 Future Directions

Perhaps the most critical point in gauging the psychosocial evaluation is to consider whether the outcome ultimately matches the purpose, which is to predict a successful LT. It is difficult to quantify this objective, as there are no available data regarding how often a thorough psychosocial assessment reveals barriers that either preclude a candidate from receiving LT or allow pre-LT interventions to occur which thereby improve LT candidacy. Pre-transplant psychosocial scores as determined by evaluation committees have been found to predict mortality and posttransplant complications [55], and social support specifically has been identified as an important predictor of post-LT survival [56]. Studies of the ability of the psychosocial assessment to predict post-LT outcomes also frequently focus on secondary outcomes such as quality of life (QOL), adherence, mental health, rejection, and other variables. A large systematic review evaluating the prognostic value of pre-LT variables other than substance abuse on clinical outcomes suggested that they do in fact inform post-operative care for individual patients. For instance, they found that low conscientiousness was associated with greater non-adherence, and although pre-LT cognitive performance did not predict survival, it may predict poorer QOL after LT [57]. In addition, Goetzmann and colleagues found that pre-LT variables explain up to 40% of variance in post-LT psychosocial outcome variables [58].

Although we have much to learn regarding the interplay of psychosocial variables in the setting of liver transplantation, it is clear that the psychosocial evaluation is paramount in the LT selection process for patients with ALD and/or

substance use disorders. Continued efforts are especially needed to further elucidate risk factors for alcohol and substance use relapse, standardize the decision-making process across transplant centers, and improve the transparency of psychosocial eligibility criteria.

## **Key Points**

- 1. The principal goal of the pre-transplant psychosocial evaluation is to determine a patient's capacity to prosper after transplant surgery including their ability to meet the demands of the lifelong and oftentimes complex cares that are necessary after receiving a liver transplant.
- In patients with alcohol or substance use disorders, the purpose of the psychosocial evaluation is to predict recurrence of addictive behaviors and other psychosocial factors which may endanger the future health of the transplant recipient.
- 3. All substance use disorders have common elements, including chronicity with remission and relapse, craving, withdrawal symptoms when the substance is stopped, and the fact that a history of SUD is often a source of shame to the user and can lead to hiding use, reluctance to seek addiction treatment, and stigma.
- 4. The psychosocial evaluation of the LT candidate is multifaceted and complex, requiring a multidisciplinary team with members of the transplant team tasked with this evaluation including social workers, nurse or physician specialists, psychologists, psychiatrists, and/or addiction specialists.
- 5. Quantitative instruments, such as the SIPAT score, help the transplant team to stratify the candidate as high or low risk for resumption of the addiction in question.

## References

- 1. Martin P, DiMartini A, Feng S, Brown R, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Hepatology. 2014;59(3):1144–65.
- 2. Burra P, Senzolo M, Adam R, Delvart V, Karam V, Germani G, et al. Liver transplantation for alcoholic liver disease in Europe: a study from the ELTR (European Liver Transplant Registry). Am J Transplant. 2010;10(1):138–48.
- 3. Kim WR, Lake JR, Smith JM, Schladt DP, Skeans MA, Harper AM, et al. OPTN/SRTR 2016 annual data report: liver. Am J Transplant. 2018;18(Supp 1):172–253.
- Center for Behavioral Health Statistics and Quality. Behavioral health trends in the United States: results from the 2014 National Survey on Drug Use and Health (HHS Publication No. SMA 15–4927, NSDUH Series H-50). 2015. http://www.samhsa.gov/data/.
- Grant BF, Goldstein RB, Saha TD, Chou P, Jung J, Zhang H, et al. Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiat. 2015;72(8):757.

- 6. Lucey MR, Weinrieb RM. Alcohol and substance abuse. Semin Liver Dis. 2009;29(1):066–73.
- 7. Anon: the health consequences of smoking—50 years of progress: a report of the surgeon general. https://www.surgeongeneral.gov/library/reports/50-years-of-progress/fact-sheet.html.
- 8. DiMartini A, Javed L, Russell S, Dew MA, Fitzgerald MG, Jain A, et al. Tobacco use following liver transplantation for alcoholic liver disease: an underestimated problem. Liver Transpl. 2005;11(6):69–83.
- 9. Zhu J, Chen PY, Frankel M, Selby RR, Fong TL. Contemporary policies regarding alcohol and marijuana use among liver transplant programs in the United States. Transplantation. 2018;102(3):433–9.
- Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age of onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62:593

  –602.
- 11. Merikangas KR, McClair VL. Epidemiology of substance use disorders. Hum Genet. 2012;131(6):779–89.
- 12. Olbrisch ME, Benedict SM, Ashe K, Levenson JL. Psychological assessment and care of organ transplant patients. J Consult Clin Psychol. 2002;70(3):771–83.
- 13. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, (DSM-5). 5th ed. Washington, DC: American Psychiatric Publishing; 2013.
- 14. Murphy CM, Stojek MK, Few LR, Rothbaum AO, Mackillop J. Craving as an alcohol use disorder symptom in DSM-5: an empirical examination in a treatment-seeking sample. Exp Clin Psychopharmacol. 2014;22(1):43–9.
- 15. Eccleston JL, Lucey MR. Substance use disorders before and after liver transplantation. Clin Liver Dis. 2017;10(4):100–2.
- Weinrieb RM, Van Horn DH, McLennan AT, Volpicelli JR, Calarco JS, Lucey MR. Drinking behavior and motivation for treatment among alcohol-dependent liver transplant candidates. J Addict Dis. 2001;20(2):105–19.
- 17. Everson G, Bharadhwaj G, House R, Talamantes M, Bilir B, Shrestha R, et al. Long-term follow-up of patients with alcoholic liver disease who underwent hepatic transplantation. Liver Transpl Surg. 1997;3:263–74.
- 18. Faure S, Herrero A, Jung B, Duny Y, Daures JP, Mura T, et al. Excessive alcohol consumption after liver transplantation impacts on long-term survival, whatever the primary indication. J Hepatol. 2012;57:306–12.
- 19. Tome S, Lucey MR. Timing of liver transplantation in alcoholic cirrhosis. J Hepatol. 2003;39(3):302–7.
- Rice JP, Eickhoff J, Agni R, Ghufran A, Brahmbhatt R, Lucey MR. Abusive drinking after liver transplantation is associated with allograft loss and advanced allograft fibrosis. Liver Transpl. 2013;19:1377–86.
- 21. Bjornsson E, Olsson J, Rydell A, Fredriksson K, Eriksson C, Sjoberg C, et al. Long-term follow-up of patients with alcoholic liver disease after liver transplantation in Sweden: impact of structured management on recidivism. Scand J Gastroenterol. 2005;40(2):206–16.
- 22. Dew MA, DiMartini AF, Steel J, DeVito Dabbs AJ, Myaskovsky L, Unruh M, et al. Metaanalysis of risk for relapse to substance use after transplantation of the liver or other solid organs. Liver Transpl. 2008;14:159–72.
- 23. Fuller RK. Definition and diagnosis of relapse to drinking. Liver Transpl Surg. 1997;3(3): 258–62.
- Lucey MR. Liver transplantation for alcoholic liver disease: past, present, and future. Liver Transpl. 2007;13(2):190–2.
- 25. DiMartini A, Dew MA, Day N, Fitzgerald MG, Jones BL, de Vera M, et al. Trajectories of alcohol consumption following liver transplantation. Am J Transplant. 2010;10(10):2305–12.
- 26. Erard-Poinsot D, Guillaud O, Hervieu V, Thimonier E, Vallin M, Chambon-Augoyard C, et al. Severe alcoholic relapse after liver transplantation: what consequences on the graft? A study based on liver biopsies analysis. Liver Transpl. 2016;22:773–84.
- Berlakovich GA. Challenges in transplantation for alcoholic liver disease. World J Gastroenterol. 2014;20(25):8033–9.

- 28. Pageaux GP, Bismuth M, Perney P, Costes V, Jaber S, Possoz P, et al. Alcohol relapse after liver transplantation for alcoholic liver disease. J Hepatol. 2003;38(5):629–34.
- Dumortier J, Dharancy S, Cannesson A, Lassailly G, Rolland B, Pruvot FR, et al. Recurrent alcoholic cirrhosis in severe alcoholic relapse after liver transplantation: a frequent and serious complication. Amer J Gastroenterol. 2015;110:1160–6.
- De Gottardi A, Spahr L, Gelez P, Morard I, Mentha G, Guillaud O, et al. A simple score for predicting alcohol relapse after liver transplantation: results from 387 patients over 15 years. Arch Intern Med. 2007;167(11):1183–8.
- 31. Hoofnagle JH, Kresina T, Fuller RK, Lake JR, Lucey MR, Sorrell MF, et al. Liver transplantation for alcoholic liver disease: executive statement and recommendations. Summary of a National Institutes of Health workshop held December 6-7, 1996, Bethesda, Maryland. Liver Transpl Surg. 1997;3(3):347–50.
- 32. Lucey MR, Brown KA, Everson GT, Fung JJ, Gish R, Keeffe EB, et al. Minimal criteria for placement of adults on the liver transplant waiting list: a report of a national conference organized by the American Society of Transplant Physicians and the American Association for the Study of Liver Diseases. Liver Transpl. 1997;3:628–37.
- 33. Vaillant GE. A 60-year follow-up of alcoholic men. Addiction. 2003;98(8):1043-51.
- 34. Beresford TP. Psychological assessment of alcoholic candidates for liver transplantation. In: Lucey MR, Merion RM, Beresford TP, editors. Liver Transplantation and the Alcoholic Patient. Medical, surgical and psychosocial issues. Cambridge University Press; 1994. p. 29–49.
- Consensus conference: indications for liver transplantation, January 19 and 20, 2005,
   Lyon-Palais Des Congress. Text of Recommendations (Long Version). Liver Transpl. 2006:12;998–1011.
- 36. Bathgate AJ. UK Liver Transplant Units. Recommendations for alcohol-related liver disease. Lancet. 2006;367:2045–6.
- 37. Webb K, Shepherd L, Day E, Masterton G, Neuberger J. Transplantation for alcoholic liver disease: report of a consensus meeting. Liver Transpl. 2006 Feb;12(2):301–5.
- 38. Testino G, Burra P, Bonino F, Piani F, Sumberaz A, Peressutti R, et al. Acute alcoholic hepatitis, end stage alcoholic liver disease and liver transplantation: an Italian position statement. World J Gastroenterol. 2014;20:14642–51.
- 39. Lee BP, Mehta N, Platt L, Gurakar A, Rice JP, Lucey MR, et al. Outcomes of early liver transplantation for patients with severe alcoholic hepatitis. Gastroenterology. 2018;155(2):422–30.
- 40. Addolorato G, Bataller R, Burra P, DiMartini A, Graziadei I, Lucey MR, et al. Liver transplantation for alcoholic liver disease. Transplantation. 2016;100:981–7.
- 41. Volk ML, Biggins SW, Huang MA, Argo CK, Fontana RJ, Anspach RR. Decision making in liver transplant selection committees: a multicenter study. Ann Intern Med. 2011; 155(8):503–8.
- 42. Telles-Correia D, Mega I. Candidates for liver transplantation with alcoholic liver disease: psychosocial aspects. World J Gastroenterol. 2015;21(39):11027–33.
- 43. Jowsey SG, Taylor ML, Schneekloth TD, Clark MM. Psychosocial challenges in transplantation. J Psychiatr Pract. 2001;7(6):404–14.
- 44. Maldonado JR, Sher Y, Lolak S, Swendsen H, Skibola D, Neri E, et al. The Stanford Integrated Psychosocial Assessment for Transplantation: a prospective study of medical and psychosocial outcomes. Psychosom Med. 2015;77(9):1018–30.
- Krahn LE, DiMartini A. Psychiatric and psychosocial aspects of liver transplantation. Liver Transpl. 2005;11(10):1157–68.
- Grover S, Sarkar S. Liver transplant—psychiatric and psychosocial aspects. J Clin Exp Hepatol. 2012;2:382–92.
- 47. Jinjuvadia R, Jinjuvadia C, Puangsricharoen P, Chalasani N, Crabb DW, Liangpunsakul S, et al. Concomitant psychiatric and nonalcohol-related substance use disorders among hospitalized with alcoholic liver disease in the United States. Alcohol Clin Exp Res. 2018;42(2):397–402.
- 48. Miller LR, Paulson D, Eshelman A, Bugenski M, Brown KA, Moonka D, et al. Mental health affects the quality of life and recovery after liver transplantation. Liver Transpl. 2013;19:1272–8.

- 49. Dew MA, Rosenberger EM, Myaskovsky L, DiMartini AF, DeVito Dabbs AJ, Posluszny DM, et al. Depression and anxiety as risk factors for morbidity and mortality after organ transplantation: a systematic review and meta-analysis. Transplantation. 2015;100(5):988–1003.
- 50. Weinrieb RM, Van Horn DH, McLellan AT, Lucey MR. Interpreting the significance of drinking by alcohol-dependent liver transplant patients: fostering candor is the key to recovery. Liver Transpl. 2000;6(6):769–76.
- 51. Bajaj JS, Saeian K, Hafeezullah M, Franco J, Thompson A, Anderson R. Failure to fully disclose during pretransplant psychological evaluation in alcoholic liver disease: a driving under the influence corroboration study. Liver Transpl. 2008;14:1632–6.
- 52. Weinrieb RM, Van Horn DH, Lynch KG, Lucey MR. A randomized, controlled study of treatment for alcohol dependence in patients awaiting liver transplantation. Liver Transpl. 2011;17:539–47.
- 53. Cabezas J, Lucey MR, Bateller R. Biomarkers for monitoring alcohol use. Clin Liver Dis. 2016;8(3):59–63.
- 54. Eccleston JL, Tamez DA, German MN, Remington P, Lucey MR. Behind closed doors: the transparency surrounding eligibility criteria for liver transplantation. Hepatology. 2018;68(Supp 1):1146.
- 55. Benson AA, Rowe M, Eid A, Bluth K, Merhav H, Khalaileh A, et al. Pre-liver transplant psychosocial evaluation predicts post-transplantation outcomes. Psychol Health Med. 2018;23(7):788–96.
- 56. Telles-Correia D, Barbosa A, Mega I, Barroso E, Monteiro E. Psychiatric and psychosocial predictors of medical outcome after liver transplantation: a prospective, single-center study. Transplant Proc. 2011;43(1):155–7.
- 57. Fineberg SK, West A, Na PJ, Oldham M, Schilsky M, Hawkins KA, et al. Utility of pretransplant psychological measures to predict posttransplant outcomes in liver transplant patients: a systematic review. Gen Hosp Psychiatry. 2016;40:4–11.
- 58. Goetzmann L, Klaghofer R, Wagner-Huber R, Halter J, Boehler A, Muellhaupt B, et al. Psychosocial vulnerability predicts psychosocial outcome after an organ transplant: results of a prospective study with lung, liver, and bone marrow patients. J Psychosom Res. 2007;62(1):93–100.
- 59. Rodrigue JR, Hanto DW, Curry MP. The alcohol relapse risk assessment: a scoring system to predict the risk of relapse to any alcohol use after liver transplant. Prog Transplant. 2013;23:310–8.
- 60. Maldonado JR, Dubois HC, David EE, Sher Y, Lolak S, Dyal J, et al. The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT): a new tool for the psychosocial evaluation of pre-transplant candidates. Psychosomatics. 2012;53:123–32.
- 61. Twillman RK, Manetto C, Wellisch DK, Wolcott DL. The transplant evaluation rating scale: a revision of the psychosocial levels system for evaluating organ transplant candidates. Psychosomatics. 1993;34(2):144–53.
- 62. Olbrisch ME, Levenson JL, Hamer R. The PACT: a rating scale for the study of clinical decision-making in psychosocial screening of organ transplant candidates. Clin Transpl. 1989;3:164–9.