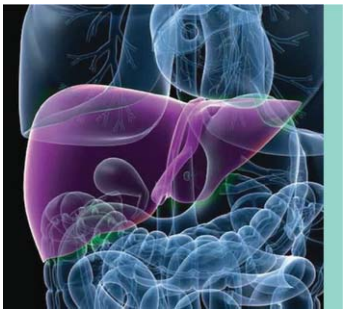

Substance Use Disorders Before and After Liver Transplantation

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Substance use disorder (SUD) is defined as a cluster of cognitive, behavioral, and physiological symptoms indicating that an individual continues to use a substance despite significant substance-related problems.[1] This definition highlights the psychological complexity of continuing a behavior despite unequivocal evidence that it is harmful. This conundrum is stark in the setting of liver transplantation (LT), especially when the substance is the source of the liver injury.

Continued use of a harmful substance is a complex balance between the internal drive to use, external pressures to use, and the individuals' subjective estimate of the immediate benefits versus the harms. Table 1 lists some of the common features of SUDs. SUDs are often long term and include personal injury, damage to family and other social relationships, and in cases of illicit substances, contravening the law. Continued use predicts noncompliance with medical directives in recipients of transplanted organs.[2] There is a paucity of prospective studies of interventions to treat SUDs in the LT population either before or after transplantation.

SUDs AND THE LT POPULATION

The substances of interest in the LT population include legal agents (alcohol, tobacco, prescribed opioids, and in some states, marijuana) and illicit agents. In some cases, such as chronic alcohol use resulting in alcoholic liver disease (ALD), the substance of abuse has a direct and recent relation to the cause of liver failure necessitating LT. In other cases, distant substance use has led to the acquisition of chronic viral hepatitis. Finally, there are forms of SUD where the link between substance use and the injury is not obvious. Tobacco addiction is an example of a widespread SUD that does not have direct hepatotoxicity and yet is highly deleterious to the LT recipient.

The impact of SUDs in the field of LT begins with selection for LT. The American Association for the Study of Liver Diseases 2013 Practice Guidelines recommend that patients with SUDs receive a psychosocial evaluation during the evaluation for LT with input from psychiatrists or addiction medicine because of the potential impact on transplant outcomes.[3] Many payer agencies require a

Abbreviations: ALD, alcoholic liver disease; LT, liver transplantation; SUD, substance use disorder.

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TABLE 1. FEATURES COMMON TO SUDs

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.

defined interval of abstinence before listing for LT. It is the prerogative of each LT program to make their own rules regarding the assessment of and response to SUDs because there are no mandatory restrictions at the federal level or by agencies such as the Organ Procurement and Transplantation Network and the United Network for Organ Sharing. There is great inconsistency both between centers and even within centers when interpreting the significance of an SUD history, especially in regard to alcohol use disorder.[4] On the other hand, the refusal to place a patient with a history of recent illicit drug use seems widespread. We lack reliable data on how US LT programs interpret current tobacco or marijuana use. Finally, prescription opioid use is even more opaque, because in many cases ''opiate substitution'' is not a recognized SUD.

EFFECT OF SUDs ON LT OUTCOMES

Alcohol is perhaps the most studied substance of abuse in the LT population. Unfortunately, data on relapse after LT are compromised by inconsistent definitions about use (i.e., ''any use,'' ''slips versus relapse,'' ''harmful drinking''), the tendency of patients to hide drinking, the difficulty of recognizing clandestine drinking, and retrospection. Despite these limitations we can confidently assert that alcohol relapse is associated with more rapid progression of fibrosis in the allograft and increased mortality after LT, albeit at 10 years.[5,6]

Tobacco use is also highly prevalent in patients with chronic liver disease, especially ALD. It is our impression that most LT programs in the United States do not require a period of abstinence from smoking as part of the transplant evaluation. Relapse after LT is common. For example, DiMartini et al.[7] showed in a prospective cohort of ALD LT recipients that persons who smoked before LT returned to heavy smoking very soon after LT. Cigarette smoking after LT leads to an increased risk for aerodigestive cancers and cardiovascular disease.[8,9] There are no prospective studies of tobacco cessation treatment programs in LT recipients.

Opioid substitution therapy is relatively common in the LT population. Patients maintained on methadone should continue because substance relapse is rare in methadone-maintained LT recipients.[10] Patients on chronic opioids also require special attention to pain and opioid management during both the perioperative period and beyond. In a retrospective study, Randall et al.[11] demonstrated graded increases in death and graft failure associated with increasing doses of prescribed opioids up to 5 years after LT. The cause of this increased mortality and morbidity is unknown. Marijuana has known effects on short-term memory, and isolated case reports of aspergillosis were associated with smoking contaminated cannabis, but otherwise studies are limited.

MANAGEMENT OF SUDs BEFORE AND AFTER LT

Aside from incorporating an addiction specialist in the care team, we have no specific recommendations regarding the management of SUDs before or after LT. The evidence for clear benefit of one treatment strategy over another in this setting is scant.[12] Many of the commonly used pharmacotherapies are not US Food and Drug Administration–approved for use in end-stage liver disease. There are also hidden barriers to treatment, including the conviction of the patient that his or her addiction has ceased or that the therapy is too cumbersome or potentially dangerous to the allograft.[13] Nonetheless, the known morbidity and mortality related to alcohol and tobacco highlights the importance of optimizing various practitioners' efforts, including those of primary care and addiction specialists.

CONCLUSIONS

SUDs and chronic liver disease are two distinct diagnoses with close interdependence and relevance in LT outcomes. Vague guidelines, imperfect payer criteria, coupled with intercenter and intracenter policy and practice variability, translate to inconsistent access and at times unnecessary exclusion for patients in need of a

lifesaving therapy. Concerted efforts are warranted to reduce tobacco and alcohol use while fostering candor and transparency with our patients regarding substance use and transplant eligibility.

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