

Alcohol and Drug Use in Liver Donors

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ISSUE

What are the issues and potential concerns about alcohol and drug use with liver donors?

DATA

Alcohol, drug, and tobacco use pose medical and psychological risks to optimal donor outcomes. Therefore the Organ Procurement and Transplantation Network (OPTN) of the US Department of Health and Human Services requires potential live liver donor's current and past history of alcohol and drug use, along with smoking, be thoroughly examined.(1) In addition, the OPTN identifies as a living donor exclusion criterion any uncontrolled diagnosable psychiatric condition requiring treatment before donation.(1) Taken together these requirements establish an active alcohol or drug use disorder would require careful assessment and treatment with remission prior to donation.

General considerations

The evaluation of a donor's mental health history is typically performed by the psychosocial assessor at the transplant program and thus is a critical component of the donor evaluation process. In the case of identified alcohol or drug use in a prospective donor, additional assessment by a mental health, addiction, or chemical dependency specialist may be necessary. Alcohol and drug use disorders have specific diagnostic criteria and are not solely based on quantity or frequency of use. Some centers perform toxicology testing on all donor candidates to screen for alcohol, tobacco and drug use. A history of an alcohol or drug use disorder does not automatically preclude living liver donation but requires careful consideration. Stable abstinence and/or engagement in addiction treatment are the cornerstones of risk reduction.

Alcohol

Alcohol is a direct hepatotoxin, therefore, it is intuitive that the use of alcohol prior to or during recovery from liver donation should be avoided. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) set guidelines for moderate alcohol use, bearing in mind moderation does not mean no risk. Heavy drinking is defined as more than 4 drinks on any day or more than 14 drinks per week for men and more than 3 drinks on any day or more than 7 drinks per week for women.(2) Only 2% of individuals who drink at or below these levels have an alcohol use disorder (AUD).(2) However, even moderate drinking can be unhealthy. Additionally, potential

donors may minimize their usage to present more favorably for donation.(3) Collateral information from family and/or clinicians caring for the individual can be useful. Biomarkers can be used to identify recent (e.g., alcohol metabolites - ethyl glucuronide and ethyl sulfate) or more sustained alcohol use (e.g., phosphatidyl ethanol). While not pathognomonic of alcohol exposure, steatosis on an MRI or liver biopsy may be an indication of excessive alcohol use (see also chapter on Liver Biopsy for Liver Donors).

At a minimum, individuals who drank or are drinking above the NIAAA moderate alcohol use quantity/frequency threshold should undergo a clinical interview to identify signs and symptoms of a diagnosable AUD. AUD are heritable disorders. Even without an active AUD, a positive family history of an AUD is important to identify and would be useful in determining future risk for those drinking above low risk levels.

An active AUD should be considered a contraindication to living liver donation due to the potential harm to the liver especially during liver regeneration. Prospective donors meeting criteria for an active AUD should be required to undergo addiction treatment and/or demonstrate an ability to remain alcohol free prior to consideration for donation. The potential donor with an AUD should also agree to remain abstinent from alcohol following donation. Ensuring ongoing addiction treatment pre- to post-donation with care coordination with addiction treatment providers would be critical to assisting in the maintenance of abstinence and monitoring of use. The stability of abstinence and risk for future relapse should be considered. For some with an AUD, stress can precipitate a relapse, and the stress of the donation surgery for some may constitute just such a trigger. For those with a remitted AUD, the clinician should determine that the patient has sustained stable abstinence. Concerns about possible relapse and the risk to health should be discussed with AUD donors. Toxicology screening can aid in the substantiation of abstinence.

While some state and national committees recommend long-term stable abstinence and low risk for relapse in potential liver donors, specific timeframes are not agreed upon.(4) Stable abstinence is typically measured in years, which may prevent timely donation. However, in general, short durations of abstinence, especially < one year indicate a high risk for relapse in those with an AUD.

In animal models, post-hepatectomy ethanol exposure was associated with enhanced susceptibility to alcohol-induced hepatic steatosis, impaired cell regeneration, and liver function impairment.(5, 6) While there is extensive research on the ill effects of alcohol in liver transplant recipients, research on living liver donors and alcohol is minimal. In the Adult-to-Adult Living Donor Liver Transplant study, 8.4% of living liver donors endorsed symptoms of an alcohol use disorder within the first two post-donation years, more than any other surveyed psychiatric syndrome.(7) These concerns led study investigators(7) as well as clinicians(8) to recommend more close monitoring of alcohol use before and after donation, especially given the time frame for liver regeneration in donors. Even for donors without an AUD and pre-donation low risk use, many centers recommend waiting approximately 6 months after donation before resuming alcohol use.

Drugs

Similar to alcohol, drug use should be screened for and potential donors meeting criteria for an active drug use disorder should be required to undergo addiction treatment and/or

demonstrate an ability to remain drug free prior to consideration for donation. Toxicology screening can aid in the substantiation of abstinence from drugs of abuse. Reassessment following addiction treatment with input from the addiction treatment provider would be essential to decision-making. As with alcohol, ongoing addiction treatment pre- to post-donation with care coordination with addiction treatment providers would be critical to assisting in the maintenance of abstinence and monitoring of use. The stability of abstinence and risk for future relapse should be considered.

An opioid use disorder or history of such a disorder may raise concerns about post-donation relapse if opioid analgesics are used. For these donors, stable abstinence and a post-operative pain management plan are needed including rapid transition off opioids and a care provider to hold/dispense pain medications. Transplant teams carefully consider these cases due to the potential for harm to the donor if they relapse. The consideration of donors on medication assisted therapy such as methadone, naltrexone, or buprenorphine is controversial. The stress of the surgery and the need for pain management may destabilize the donor's addiction recovery. Methadone should be restarted immediately after partial hepatectomy but perhaps at a lower dose due to reduced liver volume. Naltrexone, an opioid antagonist, would need to be discontinued prior to the surgery to allow opioid pain management. Buprenorphine, a partial opioid agonist, could also be maintained like methadone with consideration of need for higher doses of opioid analgesia to overcome the partial blockade. Factors to consider include the donor's stability in their addiction recovery as well as the choice and duration of post-operative analgesia. Clinical care should be closely coordinated with the donor's addiction treatment team.

Also controversial are potential donors with chronic pain syndromes treated with opioid analgesics for pain management and improved quality of life. These patients require careful consideration and evaluation by a mental health professional to identify co-morbid psychopathology that may complicate donation or post-operative pain management. The pain location, intensity and response to opioids should be considered. Such donors, like those with an addiction, can have a reduced threshold for pain and a high tolerance for opioid analgesics. The pain management plan should take this tolerance into consideration while minimizing additional exposure to opioids. The donor team should consult with the opioid prescribing physician and review state registries for controlled substances to gather clinical information and create a mutually agreed upon post-operative pain management plan. The team should consider whether pre-existing chronic pain could be exacerbated by the donation surgery (e.g., chronic back pain) and/or result in the need for a higher chronic dose of opioids post-donation. In the Adult To Adult Living Donor Liver Transplant study, post-donation abdominal or back pain on average was rated relatively low, and donors reported low levels of pain interfering with functioning.(9) However a higher level of abdominal/back pain pre-donation was associated with higher levels of post-donation pain.(9) For all of these groups, the use of a care provider to hold/dispense at home pain medications may be useful. Coordination with the opioid prescriber is essential prior to donation.

Cannabis

Marijuana is the most commonly used psychotropic drug in the US, after alcohol. It's widespread availability, different forms of use (e.g., edibles, vaping, smoking) and legalization for recreational and medicinal use in a growing number of states make marijuana a controversial topic for practitioners.(10)

While it is appropriate to assess marijuana use in all liver donors, many centers do not have specific exclusion criteria and may manage on a case-by-case basis. Similar to users of other drugs, potential donors with a cannabis use disorder may be required to undergo addiction counseling and demonstrate an ability to discontinue use prior to donation. If required to discontinue marijuana use prior to donation, toxicology screening can be used to confirm abstinence. Potential donors using medicinal marijuana require a careful history for reasons of medicinal use (e.g., chronic pain, anxiety, nausea, insomnia) as these symptoms may be exacerbated by donation. The Institutes of Medicine report identified potential associations between respiratory diseases and smoked marijuana use,(11) which may be a consideration for surgical clearance. However, a report of kidney donors followed out to one-year post-donation did not find marijuana use impacted medical outcomes, including pulmonary and infectious outcomes, compared to non-marijuana users.(12) While inhaled versions of marijuana are associated with health risks, the risks associated with other forms of marijuana such as edibles, are not well known.

Tobacco

Due to the effects of cigarette smoking on wound healing, vasoconstriction, and the increased potential for infections, the discontinuation of cigarette/tobacco use and perhaps even nicotine prior to and following donation is recommended.(13, 14) In *kidney donors* tobacco use was associated with a 1.4 time greater likelihood of perioperative complications.(15) In general smokers who quit approximately 4 weeks or more before surgery have a lower risk of complications and better results 6 months afterwards. Every tobacco-free week after 4 weeks improves health outcomes by 19%, due to improved blood flow throughout the body to essential organs.(16) In a small observational study 70% of liver donors who stopped smoking prior to donation gained weight; one donor was disqualified due to weight gain.(17) This suggests counseling on weight management is important alongside tobacco cessation advice.

Cotinine levels can determine when nicotine is no longer present in the body and may be used to determine tobacco/nicotine cessation. Cotinine levels can be detected in the bloodstream up to 10 days and may be detectable up to three weeks in urine.

RECOMMENDATIONS

1. Donors should be thoroughly screened by a multidisciplinary team for past or active alcohol and drug use disorders through all phases.
2. Alcohol or drug use disorders pose both medical and psychosocial risks to optimal donor outcomes.
3. Active alcohol or drug abuse is considered a contraindication to living liver donation and such donors should undergo addiction treatment prior to being considered for donation.
4. It is recommended donors demonstrate a period of abstinence from alcohol and drugs before and after donation. For donors with an alcohol or drug use disorder the longer a donor has been abstinent the less likely they are to relapse bearing in mind stable abstinence is measured in years. Less than one year of abstinence from an alcohol or drug use disorder indicates a high risk for future relapse and can be supported by ongoing addiction treatment and toxicology monitoring.

5. There are no set guidelines or recommendations for the selection or management of patients with active or past alcohol or drug use disorder. Each center should address each patient on a case-by-case basis with the risks to the donor carefully considered.

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