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Hashing It Out Over Cannabis: Moving Towards a Standard Guideline on Substance Use for Cardiac Transplantation Eligibility that Includes Marijuana

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“When I was in England, I experimented with marijuana a time or two, and didn't like it. I didn't inhale, and I didn't try it again.”

President Bill Clinton

During the 1992 presidential campaign, then Governor Bill Clinton's infamous words sparked substantial controversy regarding the appropriateness of prior marijuana use in a presidential candidate.¹ Approximately fifteen years later, then Senator Barack Obama's openness regarding his prior marijuana use—and statements that he did inhale—drew little negative attention, reflecting a societal shift in which the stigma previously ascribed to marijuana has been blunted. Likewise, the field of medicine has evolved in its regard of the medicinal properties of marijuana in the treatment of some diseases.² In parallel, this decade has witnessed rapid decriminalized of marijuana use: 25 states the District of Columbia and Guam have now legalized medical marijuana, while 4 states (Alaska, Colorado, Oregon, and Washington) and a handful of cities have legalized recreational use.³ Although federal law considers cannabis a Schedule I substance on the books, the executive branch has frequently deferred to state and local authority with respect to enforcement.⁴ Internationally, there is significant variability in the legal status of cannabis use.

Because intoxicating and potentially addictive agents are an inherent part of nearly every society, their relationship to complex medical therapies must be thoughtfully considered and managed. Central among contemporary considerations is the overlap of marijuana use and transplantation candidacy. Heart transplant is not typical therapy; it is extraordinary therapy that requires an extraordinary level of teamwork and patient engagement to optimize the likelihood of good outcomes. In addition, it is an exceedingly limited resource in which donor organs are only available to a small fraction of patients with end-stage heart failure. Not all patients are candidates, and not all eligible patients elect to proceed with heart transplant. But if heart transplant is medically possible and a patient chooses to be listed, then that patient must engage the entire therapeutic package of pre-transplant care, surgery, immunosuppression, and follow-up. To some extent, patients need to be “all in”, or not in at all. Therefore, the path to successful transplantation becomes quite problematic for the

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patient who cannot fully engage in the process. This can occur for any number of reasons, and prime among them is substance abuse.

The International Society of Heart and Lung Transplantation recommends in the 2016 *Listing Criteria* update that “patients who remain active substance abusers (including alcohol) should not receive heart transplantation (Class III, Level of Evidence: C).”⁵ It also states that “it is reasonable to consider active tobacco smoking as a relative contraindication to transplantation. Active tobacco smoking during the previous 6 months is a risk factor for poor outcomes after transplantation (Class IIa, Level of Evidence: C).” However, this recent update punted on making any substantive recommendations regarding marijuana, stating this “is at best an issue for which no clear direction exists” such that “each center will need to develop its own specific criteria for adjudicating candidacy for marijuana users”. While medical societies have similarly deferred taking a specific stance, 8 states have passed laws specifically prohibiting denial of transplant listing based on medical marijuana use.⁶

Within this context, Dr. Neyer and colleagues, in this issue of *Circulation: Heart Failure*, conducted a web-based, 15-item, multiple-choice survey of 360 heart transplant providers from 26 countries to assess current practice patterns and attitudes regarding marijuana use and heart transplant listing.⁷ Not surprisingly, the results showed a highly heterogeneous approach. Approximately two-thirds of respondents supported listing patients who use legal medical marijuana for transplant; a third did not. Just under a third of respondents supported transplant listing for patients using legal recreational marijuana; two-thirds did not. More than two-thirds required a period of demonstrated abstinence from marijuana prior to listing; a third did not. There were no differences between the proportion of respondents supporting transplant listing after stratification by profession or region, suggesting that this heterogeneity reflects individual opinion rather than regional legal or cultural norms. Further highlighting the level of confusion surrounding this issue, among survey respondents from states with laws prohibiting patients from being denied transplant listing based on marijuana use, more than three-quarters were in potential conflict with those laws in reporting denial of all marijuana-using patients or mandating a period of abstinence.

Although the response rate was only 22% and there are other limitations to a survey of this type, what comes through the haze is clear: the variability in current marijuana policies for heart transplantation are equivalent to bad weed. Donor organs are a national resource and should thus be allocated justly and equitably. Allowing individual centers to develop their “own specific criteria for adjudicating candidacy for marijuana users” leads to substantial inconsistency and variability, as demonstrated by Dr. Neyer and colleagues. Some transplant centers may adopt more lenient criteria for a variety of reasons, ranging from a compassionate desire to give patients an opportunity for live-saving therapy to the more insidious pressure to grow transplant volume in order to keep up with today's competitive healthcare environment. Differences in state laws may also contribute to variation. For example, here in Colorado, where marijuana laws are the most permissive in the country, we have had a number of patients who were denied for transplant listing elsewhere due to active marijuana use ask to be considered for transplant at our center. Moreover, allowing variability in policy from one transplant center to another has unintended negative consequences for the greater transplant community in that it potentially leads to “shopping”

for transplant centers. Such a practice inevitably creates health care disparities in that patients with socioeconomic resources are able to move to a different center for transplant while those without resources cannot.

Heart transplant policies should consistently recognize the balance of patient rights and medicinal benefits against potential harms of marijuana. Transplant providers' concerns about the overall safety of marijuana in the setting of heart transplantation are also highlighted in this study, as the majority of survey respondents felt that marijuana was physically harmful. Although the Internet would suggest that marijuana is a panacea for all that ails, the preponderance of scientific evidence would back the majority of survey respondents who expressed concerns about marijuana.⁸ There are a number of potential adverse effects of marijuana use in relation to heart transplantation, including the risk of dependence, nonadherence, weight gain, infection, coronary disease, and unregulated product preparations and dosing.⁹ Particularly relevant to the transplant population is the risk of drug-drug interactions and alterations in the liver metabolism of immunosuppressive drugs with relatively narrow therapeutic windows.¹⁰ Clearly, additional research is needed on the long-term safety of chronic cannabis use in healthy and disease states. Meanwhile, it is particularly concerning that laws have been passed in some states prohibiting denial of transplant based solely on marijuana use alone when the full risks and benefits remain unclear.

This is not to argue that marijuana is worse than tobacco or alcohol; rather, marijuana shares a number of attributes with tobacco and alcohol—and none may mix well with transplantation. Given the long-term legalization of tobacco and alcohol and the high prevalence of use, rules for transplantation are somewhat (although not completely) consistent around tobacco and alcohol use; given the relatively recent decriminalization of marijuana, perhaps it will just take time to see transplant policies coalesce around marijuana. As policies do develop, it may be helpful to consider marijuana similar to opiates during evaluation and listing for transplantation, where both have medical and recreational uses, and both have potential benefits and hazards.¹¹

While we should not require patients to jump through arbitrary hoops prior to transplantation merely to demonstrate our authority, it is important to assess whether patients can demonstrate behaviors that support good outcomes. Thus, it is reasonable to ask patients not to use substances that can impair outcomes after transplantation, or at a minimum, compel modified use in a way that could also support good post-transplant care and subsequent outcomes. Furthermore, we should not penalize honest people while rewarding those who lie, testing some people for some substances of abuse while not testing others. Finally, we should not create mixed messages between different transplant centers regarding what is required to be listed for cardiac transplantation. Therefore, a universal standard is warranted: one that clearly defines substances of abuse, asks for consistent and meaningful expectations for abstinence, provides standards for testing for all patients (not just those who admit to use), and suggests thoughtful action plans for addressing use and abuse in patients who are simultaneously suffering other medical problems and in desperate need of advanced heart failure therapies¹² (**Table**). This kind of approach, while at risk of being overly prescriptive and rigid, would go a long way in this country (and perhaps internationally) towards

clarifying expectations, supporting fair organ allocation, and realizing optimal outcomes for transplantation. While the perceptions of marijuana from the transplant community have likely shifted since candidate Clinton's notorious remarks in 1992, we are certainly not ready to openly “inhale” at this time.

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Table

Proposed universal substance use guidelines for patients being evaluated for heart transplantation.

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1. **General:** Unless medically indicated, all patients being evaluated for heart transplant must abstain from using tobacco products and illicit substances. Patients must demonstrate an ability to abstain from excess alcohol, and must abstain completely if there is a history of prior alcohol abuse/dependence or testing to suggest alcohol abuse.
 - a. Tobacco products include cigarettes, cigars, E-cigarettes (“vaping”), and chewing tobacco
 - b. Illicit substances include cocaine, heroin, amphetamines, hallucinogens, non-medically prescribed marijuana,⁴ and any other non-prescribed controlled substance.
 2. **Verification:** Toxicology should be performed at the initiation of a heart transplant evaluation and randomly thereafter for *all* patients, including:
 - a. Drug screen (urine),
 - b. Cotinine levels (blood or urine), and
 - c. Phosphatidylethanol (PEth, blood).¹³
 3. **Exceptions for Approved Substance Use:** Patients must notify the heart transplant team regarding medically prescribed controlled substances, including narcotics, benzodiazepines, and cannabis. Copies of prescriptions, medical letters, and/or provider contact information need to be provided to the heart transplant team. Patients may be required to cease use when alternative agents are felt to be more efficacious or the original reason for prescribing no longer exists.
 - a. Use of controlled substances should be reported by patients to transplant programs prospectively.
 - b. Chronic narcotic use must be prescribed by a pain management clinic or by a clinician experienced in the management of chronic pain disorders, with consideration for tapering off or using alternate options.¹¹ Such long-term narcotic use should be reviewed and approved by the heart transplantation team.
 - c. Cannabis (marijuana) may only be used if prescribed legally by a medical provider—and only if it is ingested or used topically, not smoked—with consideration for tapering off or using alternate options. Use must be reviewed and approved by the heart transplantation team.
 4. **Actions for Known Abuse:** For patients with positive screens or who endorse a history of substance abuse, a trained individual (i.e. licensed social worker, psychologist, or psychiatrist) will assess and determine if the patient has an active substance-related disorder using established mental health criteria.¹⁴ If so, prior to listing the patient must do the following:
 - a. Sign a standard contract outlining expectations.
 - b. Undergo a formal substance use assessment as directed by the trained individual.
 - c. Participate in a recommended treatment program. Ideally, this should result in demonstration of the following: insight into past substance misuse, understanding of how substance misuse has had an impact on current health, development of adequate coping skills for dealing with stressors, and presence of a social network which acknowledges the issue posed by substance misuse and supports the patient's commitment to abstinence.
 - d. Demonstrate abstinence through toxicology screening at least monthly for a minimum of 6 consecutive months. Patients with positive screens during this time period will have to re-establish at least 6 consecutive months of negative screening tests. Patients who develop positive screens while listed for transplant should be made inactive or delisted until they re-establish at least 6 consecutive months of negative screening tests.
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