

Early Liver Transplantation for Alcohol-Associated Liver Disease: Need for Engagement and Education of All Stakeholders

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The “6-month rule,” the policy that requires a patient with alcohol-associated liver disease (ALD) to have a stringent 6 months of monitored sobriety and treatment of alcohol use disorder to be eligible for liver transplantation (LT), was previously widespread among LT programs. In 1996, a survey of LT programs revealed that 85% enforced the rule.⁽¹⁾ The rationale for the rule was based on the ability of the liver injured by alcohol to recover with abstinence. However, the 6-month rule quickly became the minimum criteria for LT candidacy and was used as a surrogate for future risk of alcohol relapse. The rule persisted despite data demonstrating

that 6 months of enforced sobriety in a time of major illness was an unreliable predictor of alcohol relapse following LT. However, as studies^(2,3) have demonstrated a significant survival benefit to early LT (i.e., without a specific period of required sobriety) for severe alcohol-associated hepatitis, with rates of alcohol relapse comparable to LT for ALD with 6 months of sobriety, LT programs are increasingly foregoing the 6-month rule.⁽⁴⁾ In fact, many centers now offer early LT for selected patients with ALD with short intervals of sobriety and a poor prognosis for surviving 6 months. The debate regarding the acceptability of early LT for ALD has typically involved two main parties: (1) patients with ALD who need early LT and (2) the transplant providers and policy makers who have the ability to provide early LT. Amidst this controversy, have we forgotten about a key stakeholder in our community centered upon shared organs—the patient without ALD who may need a transplant in the future?

In this issue of *Hepatology Communications*, Wong et al. conducted a cross-sectional survey study of patients recruited at four clinical locations (two gastroenterology clinics, one liver transplant clinic, and one general medicine clinic) in the Canadian province of British Columbia.⁽⁵⁾ Most patients were Caucasian, male, and with liver disease; however, ALD was rare (9% of the cohort). Using a five-point Likert scale, respondents were asked their level of agreement with mandatory abstinence periods prior to LT for individuals with ALD, even in situations in which the individual would be unlikely to survive the prescribed abstinence period. They were subsequently asked if extending LT eligibility to patients without a period of abstinence would affect their trust in the LT process and affect their likelihood of registering as an organ donor. Most respondents were in agreement with abstinence periods and supported the 6-month

Abbreviations: ALD, alcohol-associated liver disease; LT, liver transplantation.

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ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO:

Brian P. Lee, M.D., M.A.S.
Department of Gastroenterology
University of California, San Francisco
San Francisco, CA
E-mail: brian.lee6@ucsf.edu

rule after receiving rationale in support of the rule. However, most respondents were neutral or agreed with relaxing the mandatory intervals of sobriety if a patient was unlikely to survive 6 months. In terms of organ donation, 42.8% of respondents felt that offering LT to patients with ALD without a fixed interval of sobriety would decrease their trust in the LT process, and 30.1% would be less likely to be an organ donor. The authors concluded that the study participants support the 6-month rule, but would be open to relaxing the criteria in patients unlikely to survive 6 months.

Since the early days of LT, concerns regarding the public opinion of LT for ALD have been raised in the LT community. Most of the donated organs in the United States and Europe derive from deceased donors, requiring consent from donors and their families. In most countries (e.g. United States, Canada), organ donation is an “opt-in” process, meaning that healthy individuals must choose to register to be an organ donor, rather than an “opt-out” process (e.g., Norway), where a prospective organ donor is presumed to consent for donation unless they have designated otherwise. As a result, public perception has the potential to affect the donor pool. If the public were to view the allocation of organ transplantation unfavorably, persons willing to “opt in” to organ donation may decline and decrease the number of available organs. The concern has been largely focused on LT for ALD, viewed as a “self-inflicted” condition and of less priority for the allocation of medical resources, particularly a scarce resource such as a donor organ. In fact, surveys have demonstrated that the public views LT for ALD unfavorably, both in the United States (Oregon) and in Europe (United Kingdom).⁽⁶⁾ However, despite concerns over public opinion, LT for ALD has emerged as the most common indication for LT.⁽⁷⁾ Long-term outcomes for LT for ALD are excellent⁽⁷⁾ and have demonstrated that while alcohol relapse following LT does occur, severe relapse and recurrent ALD are uncommon.⁽⁸⁾ In addition, organ donation rates have increased over time, thus demonstrating that the emergence of ALD as the leading indication for LT has not had a material effect on organ donation rates. The controversy and fear of public opinion in LT for ALD have been fueled again by recent challenges to the 6-month rule.

Although previous studies⁽⁹⁾ have investigated the public perception to early LT practices for ALD and

concluded that fear of negative perceptions are likely overstated, the study by Wong et al. is unique in that it surveyed a specific subpopulation of the public: All were patients, most with liver disease and a potentially direct personal stake in the allocation of organs. There can be no doubt that organ transplantation represents the pinnacle of “public-medical” partnerships. The selfless generosity of the public in providing organs for donation provides the basis for which the vast majority of lifesaving organ transplantation occurs. In turn, it is the responsibility of transplant professionals to be stewards of organ donation and adhere to the ethical principles of utility, justice, and respect for persons in the allocation process. However, caution is needed when drafting medical policy favoring public opinion over medical evidence. This is especially true in stigmatized diseases like ALD and alcohol use disorders. Even among medical providers, the transition of viewing alcohol use disorder as a disease process rather than a moral failing has been slow. The ethical principle of utility states that organ allocation should be based on expectations of a good outcome, not societal worth. Similarly, the ethical principle of justice dictates that all members of the public are morally entitled to fair access to a benefit. The 6-month rule, when applied, arbitrarily eliminates a person from fair access to transplant regardless of their prospective potential for rehabilitation from alcohol use disorder. Given that current evidence suggests that good outcomes can be achieved in selected patients with short sobriety, the 6-month rule has justifiably been increasingly abandoned.

So, how should the LT community ensure that the public trust is met if we expand access to LT for patients without a fixed interval of sobriety? First, it must be stressed that abolishing the 6-month rule does not equate to transplanting “active drinkers” and does not abolish the careful multidisciplinary selection process of determining who will derive significant survival benefit from LT, nor does it abdicate the transplant community from stewardship of the donation. (The expectation remains that despite a short duration of sobriety, patients undergoing early LT are committed to lifelong abstinence after early LT.) Indeed, in the literature demonstrating good outcomes of early LT for severe alcohol-associated hepatitis, most patients were not deemed candidates for early LT.^(2,3) Second, it is important to disseminate the best available scientific evidence to defend

the rationale for policy change. Although Wong et al. provided the survey respondent rationale for the 6-month rule, it provided no evidence to describe the flaws of the 6-month rule, thus offering a biased view of fixed sobriety intervals. We hypothesize that a more nuanced education regarding the lack of predictive value of the 6-month rule on harmful drinking after LT would have decreased positive attitudes toward the 6-month rule. Third, the LT community must be transparent in the LT selection process and be accountable for post-LT outcomes. In addition, with widespread availability of accurate alcohol biomarkers such as ethyl glucuronide and phosphatidylethanol, LT programs now have enhanced tools for detecting relapse before and after LT. Estimations of post-LT relapse are widely variable, and biomarkers will allow for improved detection and a better understanding of post-LT alcohol use. Regardless of sobriety length at the time of LT, LT professionals need to acknowledge that alcohol use disorder is a relapsing disease and implement protocols for monitoring and addressing alcohol relapse.

In conclusion, the debate regarding the acceptability of early LT for ALD remains controversial, and many centers continue to enforce the 6-month rule for patients with ALD.⁽⁴⁾ As debate continues, the study by Wong et al. serves as an important reminder that we not forget the importance of engaging all stakeholders in our discussion. Any policy change for ALD has the ability to shape the supply and allocation of shared organs for our entire community. Increased research and scientific evidence to inform the selection processes and interventions to predict and reduce alcohol relapse, accurate dissemination of these data, and increased awareness for providers and the public alike will

provide a framework to achieve the consensus needed for responsible policy change.

John P. Rice, M.D.¹

Brian P. Lee, M.D., M.A.S. ²

¹School of Medicine and Public Health
Gastroenterology and Hepatology
University of Wisconsin
Madison, WI

²Department of Gastroenterology
University of California, San Francisco
San Francisco, CA

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