Six month abstinence rule for liver transplantation in severe alcoholic liver disease patients

Aiman Obed, Steffen Stern, Anwar Jarrad, Thomas Lorf

Abstract

Alcoholic liver disease (ALD) is the second most common diagnosis among patients undergoing liver transplantation (LT). The recovery results of patients transplanted for ALD are often at least as good as those of patients transplanted for other diagnoses and better than those suffering from hepatitis C virus, cryptogenic cirrhosis, or hepatocellular carcinoma. In the case of medically non-responding patients with severe acute alcoholic hepatitis or acute-on-chronic liver failure, the refusal of LT is often based on the lack of the required alcohol abstinence period of six months. The obligatory abidance of a period of abstinence as a transplant eligibility requirement for medically non-responding patients seems unfair and inhumane, since the majority of these patients will not survive the six-month abstinence period. Data from various studies have challenged the 6-mo rule, while excellent survival results of LT have been observed in selected patients with severe alcoholic hepatitis not responding to medical therapy. Patients with severe advanced ALD should have legal access to LT. The mere lack of pre-LT abstinence should not be an obstacle for being listed.

Key words: Alcohol; Alcoholic hepatitis; Cirrhosis; Six month abstinence rule; Abstinence; Liver transplantation

TO THE EDITOR

We read the article "Acute alcoholic hepatitis, end stage alcoholic liver disease and liver transplantation: An Italian position statement" by Testino et al with particularly great interest.

In general, alcohol avoidance in patients with liver disease (especially in alcoholic liver cirrhosis) is advisable and medically beneficial,[2-4] however patients suffering from either severe acute alcoholic hepatitis (SAAH) or acute-on chronic liver failure (ACLF) and not responding to medical therapy have high 3-mo mortality rates ranging from 60%-70%, and even reaching as high as 90% within the first year.[4-7]

SAAH and ACLF are life-threatening situations demanding intensive care unit (ICU) therapy. Typically, patients in such clinical conditions are already too sick to drink, with the vast majority failing to recover by stopping their consumption of alcohol.[8-11]

Stadlbauer et al[12] revealed that patients who do not respond to medical therapy will inevitably die without a potentially lifesaving liver transplantation.

A recent study by Kumar et al[13] found that a change in MELD score at 2 wk was effective in determining the outcome. However, the study showed that an interval of 2 wk was sufficient to demonstrate an increased mortality or need for liver transplant in patients with ACLF.

Mathurin et al[8] presented a comparable conclusion regarding mortality prognosis of SAAH with an interval from 7 to 14 d after ICU admission. A lack of clinical improvement in patients with SAAH and ACLF during the first 2 wk of ICU treatment indicates a poor outcome or vital need for liver transplant.

The cornerstone for practicing evidence-based medicine is applying the best current knowledge to medical decision-making for each individual patient.

Unfortunately, with regard to the advanced end-stage ALD, current prejudices, barroom clichés, and public half-truths seem to overshadow the available evidence-based information.

The debatable 6-mo abstinence rule has not only been controversial ever since its introduction, but has also been harshly criticized and labeled as an unfair and inhumane rule with fatal consequences for ALD patients.[14,15]

The available data questions the 6-mo rule whilst confirming well-known uncertainties about its ability and usefulness in predicting (heavy) alcohol relapse after LT.[16-18]

Death or graft loss occurs in only about 4% of all ALD patients who experience a relapse of their disease. The most common causes of death in patients who continued to consume alcohol were cardiovascular events and cancer, not liver failure directly caused by alcohol consumption.[19]

Data presented by Schmeding et al[19] in 2011 clearly indicates that ALD patients have better 5 and 10-year survival rates compared with HCV-infected patients, even in the case of alcohol relapse after liver transplantation.

Recently, Deruytter et al[20] observed recidivism of alcohol after liver transplantation in 29% of ALD patients and heavy drinking after LTX in 16%. More importantly, no significant difference in survival was found between non-relapsers, occasional drinkers, and problem drinkers.

Simultaneously, medical law experts are repetitively reminded, albeit from a different point of view than those in practical medicine, that constitutional law prohibits discrimination against subgroups and life differentiations as being either worthy or unworthy of life. They stress that the exclusion of non-sober ALD patients from being listed discriminated them and violated said constitutional law.[21]

Considering that patients who experience acute liver failure after ecstasy consumption[22] or are suffering from acute hepatitis B infections due to careless sexual practices[23] have full access to the waiting list raises the question as to why patients with SAAH or ACLF should be treated any differently.

The United Network for Organ Sharing (UNOS) has still adopted the 6-mo rule, although it does advise that "exceptional" cases be referred to regional review boards for consideration.

The American Association for the Study of Liver Disease contemporary guidelines also advise 6 mo of zero alcohol consumption before LT, but they highlighted that this rule as it stands is not a defining factor as to whether or not a patient is accepted as a candidate for a liver transplant.[24]

In the end, alcoholism has to be accepted as a disease that, in some cases, has a genetic background.[25,26] The lack of pre-transplant abstinence should not be considered as a justification for denying the legal right to have access to the liver transplantation waiting list for patients with advanced ALD.[27]

Transplantation for alcoholic liver disease is prejudiced, with its worthiness often being questioned due to the common misconception of ALD being regarded as a type of self-inflicted harm.[28-30]

The segregation of patients with severe alcoholic cirrhosis who are considered to be proper candidates for LT after complete evaluation must be avoided.[31]

Furthermore, the necessity of LT for ALD patients is generally misperceived and not taken seriously by general physicians or the general public. However, there are no moral or ethical arguments that could justify the exclusion of very ill patients with ALD from potentially lifesaving LT.[32,33]. On the contrary, it would be considered a death sentence for these patients. The number of patients who have already passed away before they were even presented to a transplant...
Treatment with artificial liver support devices has value in correcting major pathophysiological disturbances, and might be of individual help as a bridging procedure in patients with ACLF and SAAH until transplantation.

In the end, the 6-mo rule is insufficient in predicting relapse risk after liver transplantation. Liver transplantation may be lifesaving in cases of advanced ALD or alcoholic hepatitis, but inflexible sobriety rules eliminate patients with a low risk of relapse from transplant consideration.

Lastly, it must be noted that the United Nations’ Universal Declaration of Human Rights acknowledges that all human beings are born free and equal in terms of dignity and rights. Everyone has the right to life, liberty, security, and a standard of living adequate for the health and well-being of themselves and their family.

National transplant policy boards, patient support groups, and legislation clearly need to act and collaborate transparently and closely in regards to national constitutional law in order to educate the public and clarify that liver transplantation for advanced ALD is not a matter of medical scientific discussion, but rather a societal dilemma that has the potential to improve the life expectancy of many desperate patients.

We agree with all suggestions made by Testino et al,[1], particularly with regard to efforts made to improve the screening of de novo tumors after liver transplantation and the prevention of cardiovascular complications, which are indeed required within the follow-up care in order to achieve further improvement for long-term outcome.

In summary, we conclude that the selection and allocation criteria for advanced end-stage ALD, especially the abstinence rule, should be appropriately revised to avoid further preventable patient death. In cases of SAAH and ACLF that do not respond to medical therapy 2 wk after admission, liver transplantation should be compulsory, regardless of achieved abstinence time.

REFERENCES

13. Kumar R, Krishnamoorthy TL, Tan HK, Lui HF, Chow WC. Change in model for end-stage liver disease score at two weeks, as an indicator of mortality or liver transplantation at 60 days in acute-on-chronic liver failure. Gastroenterol Rep (Oxf) 2014; Epub ahead of print [PMID: 25351261 DOI: 10.1093/gastro/gou075]
17. Bird GL, O’Grady JD, Harvey FA, Calne RY, Williams R. Liver transplantation in patients with alcoholic cirrhosis: selection


