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Liver Transplantation for Alcoholic Liver Disease: A Consideration of Reasons For and Against

David H. Van Thiel, Judith S. Gavaler, Ralph E. Tarter, Vincents J. Dindzans, Robert D. Gordon, Shunzaburo Iwatsuki, Leonard Makowka, Satoru Todo, Andreas Tzakis, and Thomas E. Starzl

Orthotopic liver transplantation is a clinical procedure that has been accepted widely as the treatment of choice for individuals with advanced chronic liver disease. As such, its application to the important clinical problem of alcoholic liver disease is inevitable. The arguments for and against liver transplantation for individuals with advanced alcoholic liver disease are presented.

ORTHOTOPIC liver transplantation has been shown to be an effective and valuable addition to the clinical therapeutic armamentarium for individuals with advanced end stage liver disease (ESLD) and those with either fulminant (FHF) or subacute hepatic failure (SHF).¹⁻³ On average, 60-75% of patients with ESLD survive orthotopic liver transplantation for 1 year or more and can expect to obtain a near complete resolution of their former hepatic disease, return to work, and have a quality of life that is acceptable to most individuals.⁴⁻⁵ For those with FHF and SHF, the prognosis and orthotopic liver transplantation is slightly less (50-65%) at 1 year than it is for those with ESLD but it is still two to 10 times more effective than any other currently available therapy.⁶⁻⁸

Many chronic alcoholics currently die of end stage liver disease (Laennec's cirrhosis) or one of its complications such as bleeding esophageal and/or gastric varices, sepsis, hepatorenal syndrome, or hepatic encephalopathy.⁹ Some also die as a direct result of alcoholic hepatitis a form of either fulminant or subacute hepatic failure.¹⁰

Alcoholics, as a group with end stage liver disease, with or without complicating alcoholic hepatitis currently comprise the single largest group of potential liver transplant candidates and probably account for more than the entire number due to all other conditions combined.¹¹ Both alcoholic cirrhosis and severe alcoholic hepatitis are potentially treatable with orthotopic liver transplantation (OLTx). More importantly, there are no alternative therapies which have the potential for similar long term sur-

vival for these individuals. What then accounts for the objection of the application of orthotopic liver transplantation to individuals with chronic alcoholism who meet all other criteria for liver transplantation?

The major arguments against the application of orthotopic liver transplantation for chronic alcoholics are as follows: (a) Alcoholism is not a disease but rather a vice, and therefore does not require medical therapy but instead should be treated by behavioral modification; (b) Alcoholism is a disease of self abuse and therefore less deserving of medical therapy than are other liver diseases not associated with self abuse; (c) There is a very high recidivism rate in alcoholics that prohibits the widespread application of orthotopic liver transplantation as a potential therapy for such individuals; (d) Orthotopic liver transplantation for alcoholics yields results that are poorer than those due to other forms of liver disease and there is a high cost associated with the procedure therefore valuable donor organs and limited financial resources should not be wasted by such transplants; (e) Alcoholics, because they have a vice or disease of self abuse, are not worthy of having a liver transplant (reasons 1, 2, and 3 above combined).

What might be reasonable answers for each of these issues that form the foundation for any consideration of a prohibition of liver transplantation for alcoholics? First, for over 30 years alcoholism has been recognized by the American Medical Association, World Health Organization, American Psychiatric Association, The American Medical Society on Alcoholism and Other Drug Dependencies, and the National Council of Alcoholism as a disease rather than a vice.¹²⁻¹⁴ The issue of alcoholism being a disease of self abuse is a bit more troublesome, but it does not distinguish alcoholism from other diseases of self abuse for which medical-surgical therapies are routinely available such as obesity, smoking, drug abuse, diabetics who fail to follow diet or exercise regimens, hypertensives or uremics who fail to monitor their intake of salt and water or individuals with anorexia or bulimia. Similarly, how do alcoholics differ in this regard from individuals who become ill because of the use of anabolic steroids for purposes of bodybuilding or to enhance their potency or those that develop fulminant hepatic failure as a result of acetaminophen therapy or abuse or the use of some other hepatotoxic substance either excessively or because of their ignorance of the potential risks of the use

From the Division of Gastroenterology, Departments of Psychiatry and Surgery, University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania.

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Reprint requests: David H. Van Thiel, 1000J Sciale Hall, Division of Gastroenterology, Pittsburgh, PA 15261.

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of the agent? An argument based on recidivism for alcohol abuse is based upon a prejudice that is not applied to smokers or those who are obese. Moreover, the recent data available on this subject suggest that the recidivism rate for alcohol abuse and the risk for recurrent alcoholic liver disease after liver transplantation may be no greater than for any other behavior or disease process.¹⁵ Moreover, there are no data to demonstrate that the behavior (alcoholism) and recurrent alcoholic liver disease are necessarily linked. Thus, the allograft organ, because of its different genetic background, may be less susceptible or even immune to alcoholic liver disease despite recipient recidivism. Similarly, the argument that patients with alcoholic liver disease are less likely to withstand the procedure and survive the various vicissitudes of orthotopic liver transplantation as compared to those with other forms of liver diseases is not founded in fact.¹⁵ Data obtained more than a decade ago, when the current methods of liver transplantation surgery and immunosuppression regimens were not available, fail to demonstrate a poorer outcome for alcoholics as compared to others transplanted for advanced hepatocellular disease other than alcohol abuse (Figs. 1 and 2).¹⁵ In fact, the survival data for chronic alcoholics who have been transplanted are actually better than those for individuals transplanted for hepatitis B viral liver disease (Fig. 2), hepatocellular carcinoma (Fig. 3) or cholangiocarcinoma (Fig. 4), and those with fulminant hepatic failure due to any cause (Fig. 5) (Kumar et al., manuscript in preparation). The issue of alcoholism being less worthy than other potential recipients is also spurious both in principle and in specifics. For example, are alcoholics intrinsically less worthy than smokers, drug addicts, individuals with obesity or other eating disorders or those with cancer or acquired immunodeficiency syndrome (AIDS)? None of these other groups are currently denied health care for any reason, let alone the putative reason of unworthiness. Similarly the recidivism rates for smoking,

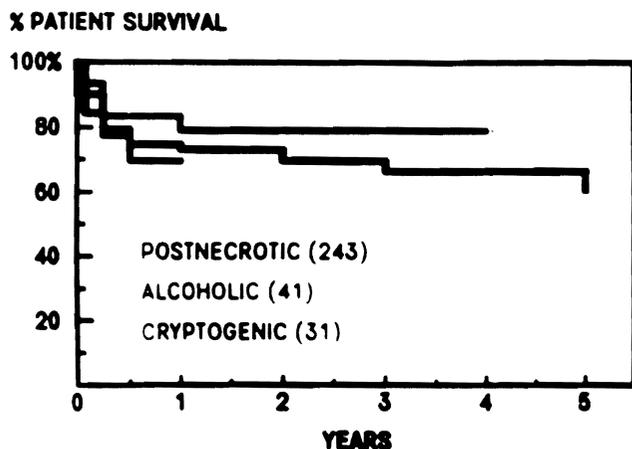


Fig. 1. Kaplan Meier survival curves for three groups of patients transplanted for cirrhosis and chronic hepatocellular failure. The group with the longest follow-up had inactive viral-induced liver disease. The group with the intermediate follow-up had cryptogenic cirrhosis. The group with the shortest follow-up was transplanted for alcohol-induced liver disease. There are no statistical differences between these three curves.

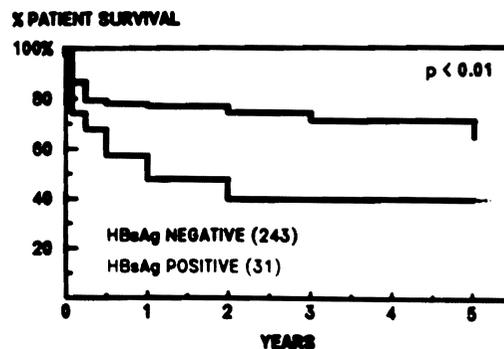


Fig. 2. Survival curves for two groups of patients with postnecrotic cirrhosis. Top curve, data for those who were HBsAg negative at the time of transplantation; bottom curve, data for those who were HBsAg positive at the time of transplantation.

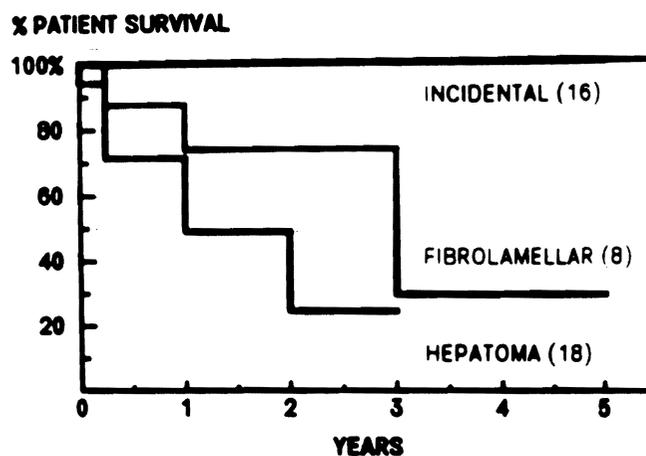


Fig. 3. Survival curves for three groups of patients transplanted for hepatocellular carcinoma. Top curve, data for the group transplanted for nonmalignant indications but who were found to have an incidental (<5 cm diameter) hepatocellular carcinoma in the resected liver; middle curve, data for those having fibrolamellar carcinomas; bottom curve, data for the group transplanted because of other types of hepatoma.

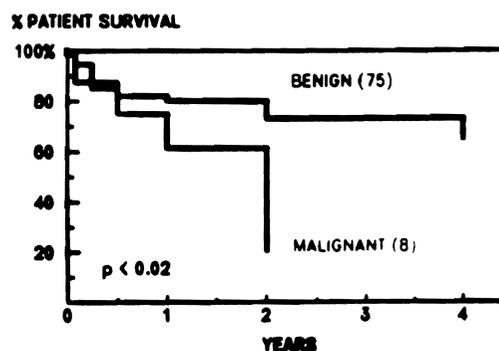


Fig. 4. Survival curve for patients transplanted with a cholangiocarcinoma complicating primary sclerosing cholangitis (lower curve) and those with primary sclerosing cholangitis without a cholangiocarcinoma.

drug addiction, and obesity are equal to, if not greater than, those for alcoholism.

Since the arguments against the application of transplantation for alcoholic liver disease are not particularly valid or at least not substantial, what then are the most recent results of liver transplantation when it has been applied to the problem of advanced alcoholic liver disease? Little or no published data exist addressing this issue.

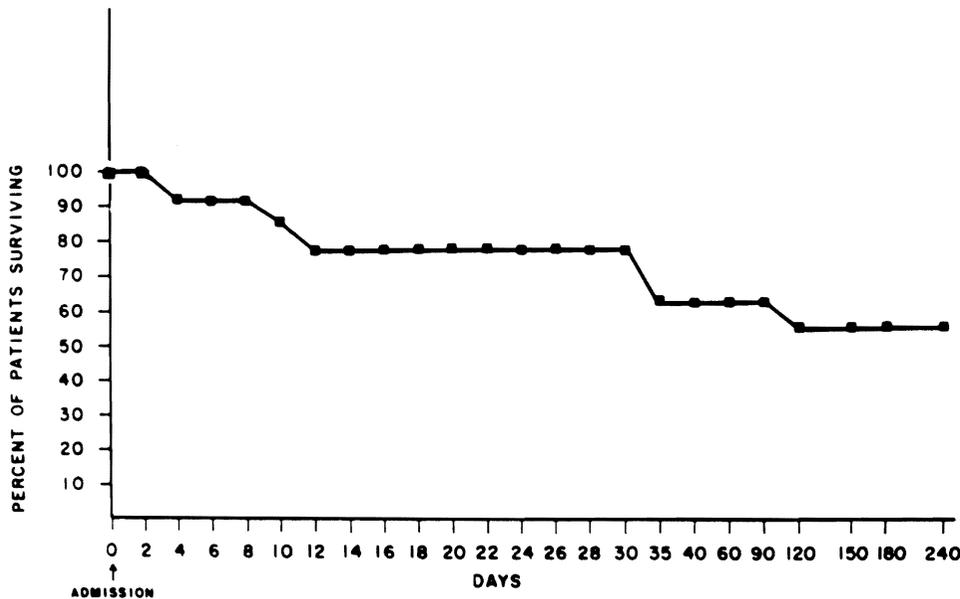


Fig. 5. Survival curve for adults (age > 16 years) transplanted for fulminant hepatic failure.

Nonetheless a considerable worldwide experience with the application of orthotopic liver transplantation for alcoholic liver disease does exist. For example, at a single institution, the University of Pittsburgh, more than 80 liver transplants have been performed for this particular specific indication (Kumar et al., manuscript in preparation) and the majority of these cases have been reported.¹⁵ The long-term survival of these patients is not known for certain, but the short-term survival is known (Fig. 1). As shown in Fig. 1, the survival of individuals transplanted because of advanced alcoholic liver disease has been no different than that of individuals transplanted for other forms of advanced hepatocellular disease at the end of 1 year. More importantly the survival of alcoholics has been better than that experienced by individuals transplanted for hepatitis B virus related liver disease and those with clinically evident hepatic cancer (Figs. 2-4), indications for liver transplantation that are accepted widely if not generally.^{1-5, 16, 17}

More importantly, when these individuals, their spouses, and physicians have been contacted, the recidivism rate of alcoholics transplanted because of chronic hepatic failure has been impressively small, at least so far (Ref. 15 and Kumar et al., manuscript in preparation). It should be noted however, that most lapses in sobriety occur early with the vast majority occurring within 6 months.^{16, 17} Based upon these data, liver transplantation and its attendant stresses would appear to be a rather long-term "sobering" experience. Even more importantly, the percentage of such patients who have returned to full-time employment or their former occupation compares favorably with the experience with other groups of patients transplanted for reasons often more generally accepted.^{18, 19} Taken together, the survival obtained, the relative prolonged sobriety achieved, and the success at returning alcoholics to gainful employment as full mem-

bers of a working society makes liver transplantation appear not only as a reasonable form of medical therapy but one that should be performed in preference to other competitive therapies as none of the others has the potential of producing an outcome with results as good in terms of possible longevity of survival, sobriety, and quality of life.

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