

Liver transplants for alcoholic liver disease

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RJ FINGEROTE, VG BAIN, RN FEDORAK. Liver transplants for alcoholic liver disease. *Can J Gastroenterol* 1991;5(6):195-198. Alcohol related end-stage liver disease is a principal cause of liver failure. The scarcity of donor livers and the predominance of alcohol related end-stage liver disease has raised the issue of including alcoholics as candidates for liver transplantation. In rationalizing the arguments for and against the treatment of alcoholic end-stage liver disease with transplantation, factors such as recidivism, resource allocation and principles of medical practice must be considered. Public confidence in organ transplantation depends on the scientific validity and moral integrity of the policies adopted. Sound policies will prove defensible while policies based on perceptions or prejudices will, in the long run, harm the process.

Key Words: Alcohol, Alcoholism, Cirrhosis, Hepatic failure, Liver, Transplant

Transplantation du foie et hépatopathie alcoolique

RESUME: L'hépatopathie alcoolique au stade ultime est la cause principale d'insuffisance hépatique. La rareté des donneurs de foie et la prédominance des maladies du foie terminales dues à l'alcool poussent à envisager l'inclusion des alcooliques sur les listes de candidats aux transplantations hépatiques. Quand on fait le point sur la question, il est nécessaire de peser les facteurs tels que le récidivisme, la répartition des ressources et les principes de la pratique médicale. L'attitude du grand public envers les transplantations d'organes dépend de la validité scientifique et de l'intégrité morale des politiques adoptées. Ces dernières ne seront défendables que si elles se fondent sur des arguments sains. Les impressions ou préjugés pourraient s'avérer nuisibles à longue échéance.

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DURING THE PAST DECADE, LIVER transplantation has progressed from an experimental procedure to a recognized therapeutic option for patients with progressive irreversible liver disease. Transplantation indications have expanded to such an extent that, at present, it is considered the treatment of choice for chronic end-stage liver failure secondary to hepatocellular liver disease, cholestatic liver disease, selected hepatic malignancies, and inherited metabolic disorders. In addition, transplantation has become the treatment of choice for irreversible fulminant and subfulminant hepatic failure (1). Nevertheless, controversy continues to surround the question of the use of liver transplantation for the single most common cause of chronic liver disease in North America – alcohol abuse. Recent reviews have presented arguments both for and against liver transplantation in alcoholics (2, 3).

It is estimated that approximately 10% of the adult population in the United States consumes excessive amounts of alcohol, which results in over 100,000 deaths annually, 19% of which are attributed to chronic liver

failure. The cost of treating the problem of alcohol abuse amounts to over \$116 billion per year, which represents approximately 12% of annual health care expenditures. It has been suggested that alcoholics should not be candidates for liver transplantation for alcohol-related cirrhosis. Arguments which support this viewpoint focus on issues such as recidivism, disease self-infliction and resource allocation.

RECIDIVISM

Concerns regarding the likelihood of recidivism among patients with alcoholism after they have received a liver transplant have been a major deterrent to providing these patients with transplants (1). In 1988, Starzl and colleagues (4) reported a one year survival rate of 73% for patients with alcohol related end-stage liver disease, comparable to that of patients transplanted with other causes of end-stage liver disease. Recently, Kumar *et al* (5) reported that, of 73 patients who received liver transplants for alcoholic liver disease, only six of the 52 surviving recipients resumed alcohol consumption, all of whom reported consuming three or fewer drinks per week. One patient had died of allograft rejection after discharge from hospital; this patient's death was in part a result of recurrent alcohol abuse (5). In a second study from the University of Michigan, 32 alcoholics underwent liver transplantation for end-stage liver disease. After a mean follow-up of five months, one patient was noted to have used alcohol on one occasion only (6). However, since the follow-up time of these studies was short, the potential of recidivism remains a major concern.

In a later study from the same unit reporting on 45 patients undergoing transplantation for alcohol related end-stage liver disease, five patients returned to alcohol use. Survival data did not differ from results for liver transplant in nonalcoholic patients. Follow-up was greater than 12 months in 28 patients (7). Psychological well-being of alcoholic liver transplant patients following transplantation has been examined and is similar to that of nonalcoholic recipients (8).

Neither of these studies used pre-operative sobriety as a selection criterion. In this regard, Starzl *et al* (4) suggested that "the imposition of an arbitrary period of abstinence before transplantation would seem medically unsound or even inhumane." Reports from other transplant centres are necessary before the importance of a period of abstinence can be determined.

Certainly, returning to heavy drinking could ruin a transplanted liver over a number of years. More likely, relapse into heavy drinking would interfere with the daily ingestion of multiple medications essential for immunosuppression and survival. As well, alcohol may interfere with both the absorption and metabolism of medications necessary post transplantation. Alcohol is an inducer of the P-450 system and as cyclosporine is metabolized by the P-450 system alteration in immunosuppression may result. As a group, therefore, the patients with alcoholic cirrhosis may have a lower survival rate after receiving a transplant than do controls. Nevertheless, these possibilities do not provide solid reasons for excluding those with alcohol related end-stage liver disease from consideration for transplantation.

GENETICS OR LIFESTYLE?

A second argument that has been advanced against liver transplantation for those who are alcoholics is that, since liver failure secondary to alcohol abuse is a self-inflicted disease, society should not assume the burden of care for alcoholics with liver failure. Support for this point of view is tenuous because there is little doubt that alcohol abuse has a genetic component. A specific gene has been identified in the brain tissue recovered during post mortem examinations in 69% of a series of 35 known alcoholics, compared with 20% of a series of 35 non-alcoholics from the general population (9). There is also a higher concordance of alcohol abuse in monozygotic twins compared to that in fraternal twins (10). Studies have demonstrated that, even when raised apart from their alcoholic parents, sons of alcoholics have

a higher rate of alcohol abuse (11). Alcohol abuse may be found in people suffering from depression or personality disorders, both of which have strong genetic predispositions. Thus, it is debatable whether alcohol abuse is a lifestyle decision or the result of a genetic predisposition.

Even if alcoholism was a 'lifestyle disease', would that truly remove from society the burden of providing optimal medical care to patients with alcohol related liver failure? Society accepts the burden of treating diabetes mellitus in obese patients whose diabetes might be controlled by dietary restriction alone. Similarly, cigarette smokers are not denied the privilege of admission to an intensive care unit, or of a heart transplant should they develop ischemic cardiomyopathy, or of surgery should they develop lung cancer. Arguably, both overeating and cigarette smoking are decisions of lifestyle in much the same way as alcohol abuse. Denial of health care benefits to the obese patient and the cigarette smoker is not a social practice; thus, it would seem anomalous to deny full health care benefits to those who suffer from alcoholism.

RESOURCE ALLOCATION

Liver transplantation uses a non-renewable and extremely scarce resource – a donor liver. Although patients with alcohol related end-stage liver disease represent approximately 50% of patients with end-stage liver disease, patients with alcohol related liver disease currently account for less than 10% of those receiving transplants (2). In the future, as large liver transplant programmes deplete the pool of patients with nonalcohol related causes of liver failure who require transplantation, they may transplant more patients with alcohol related liver failure in order to maintain the therapeutic momentum of the programs. Obviously, if patients with alcohol related end-stage liver disease were accepted for liver transplantation on an equal basis with patients whose disease is not related to alcoholism, an enormous number of additional candidates might further exacerbate the problems stemming from

scarcity of donor livers. Although the allocation of organs in short supply does present vexing ethical problems, this fact cannot be allowed to become the basis for a moralistic public policy which advocates selective punishment of a certain group of patients whose disease may, in fact, be genetically triggered.

PRINCIPLES OF PRACTICE

Nevertheless, in the face of limited health care resources, it is critical to establish principles to guide allocation of transplant organs. Dossetor (12), established three dimensions under which ethical issues relating to the allocation of cadaveric organs could be discussed: micro-allocation, macro-allocation and mega-allocation.

At the micro-allocation level, issues as they exist between the patient and his or her physician are addressed. In the case of liver transplantation, such issues include decisions about whether the patient wishes to undergo liver transplantation and whether the physician feels the procedure is appropriate for the patient, from both a physiological and psychological point of view. Extrahepatic dysfunctions associated with alcohol related liver disease, such as cardiomyopathy or chronic organic brain syndrome may contraindicate liver transplantation.

At the macro-allocation level, issues relate to statistics, programs or economics. A transplantation program committee might consider a patient with alcohol related liver disease an inappropriate transplant candidate due to a lack of economic resources, concern regarding a poor result of surgery, or limitations on the total number of transplants to be done.

At the mega-allocation level, issues addressed are of a more political nature; these decisions are not linked solely to the cause of the patient's liver disease. Vigorous opposition to liver transplantation might come from a "puritanic element who would not want to see public resources used for a procedure on individuals not socially approved of — who, in fact, have brought on their troubles by their own sinful actions" (14), or a government might decide to

discontinue completely funding of transplantations in the face of rising health costs.

Traditionally, need has been the guiding criteria in determining who should undergo liver transplantation. This may be appropriate when enough resources exist that everyone who requires these resources may receive them; however, in considering the limited number of transplantable livers available, other allocative mechanisms need to be considered (12). These include allocation of the basis of: the best medical outcome; random selection based on chance; first come, first served; ability to pay; social worth; the 'squeaky wheel' factor in which family or public pressure is used to influence medical decisions; medical-legal considerations; and public policy. Most of these allocation factors do not concentrate on the physician's or the patient's values. For instance, program and institutional values are most strongly represented in decisions based upon medicopolitical considerations.

Social worth and the ability to pay as allocation principles completely ignore such factors as causality and medical indications for procedures. Although physical need clearly has to be established in order to make an invasive procedure such as liver transplantation medically appropriate, the indications for surgery may also be dependent upon the nonmedical factors previously outlined. When used in the past as criteria for the allocation of health care resources, social worth has led to a situation in which resources were allocated to those members of society who most closely resemble members of the allocation committee. Citing social worth as a factor in transplant allocation, George D Lundberg commented (13):

"If I had one liver to transplant and 50,000 possible recipients, I wouldn't let the fact that a great creative genius might drink again deter me from giving him or her a needed new liver to allow another 30 years of creativity."

Thus, allocation on the basis of social worth opens the door for arbitrary value judgements about such factors as intelligence quotient, nationality, race

and religion (14). With these allocation factors in mind, one must appraise again the issue of liver transplantation in the case of patients with alcohol related liver disease.

CONCLUSIONS

The Hippocratic Principle would suggest that the health care professional is obliged to treat the patient in the manner which would most benefit the patient. Clearly, for a patient dying from alcoholic liver failure, the one procedure most likely to provide a lasting benefit is liver transplantation. Success rates reported for cases of liver transplantation in alcoholic liver disease are similar to those reported for transplantation necessitated as a result of other causes of chronic liver failure. Therefore, risk of transplantation failure is not a valid reason to deny a liver transplant to a patient with alcohol related end-stage liver disease. Refusing an alcoholic patient a liver transplant because of a concern regarding recidivism may reflect a lack of confidence in the capability of modern medicine to rehabilitate those with chronic alcoholism, or it may reflect a selectively moral approach to allocation procedures. Failure to consider alcoholics equally for liver transplantation will open the door to other judgements of individual worth: Is a prostitute with fulminant hepatitis B worthy of this same resource? What about a young patient with Wilson's disease in dying need precipitated by his or her own decision to stop penicillamine?

As has been suggested by Verhey (15): *"When scarcity makes allocation necessary, sanctity requires random selection and forbids the God-like judgement that one life is worth more than another. Random selection alone will sustain a relationship of truthfulness and trust between physician and patient. We may not deny scarcity, we may not deny sanctity; the best we can do is to act with integrity."*

A policy adopting Verhey's approach would favour allocation which avoided value-laden and thus dangerously prejudiced selection criteria.

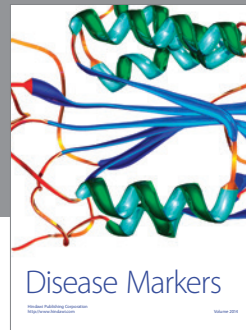
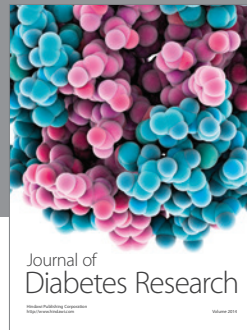
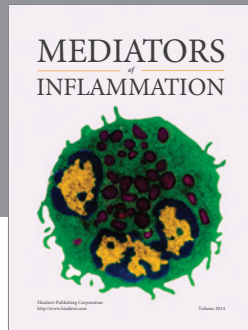
In summary, in assessing the role of liver transplantation in alcoholic liver disease, the issue of the etiology of liver

failure cannot and must not be used in determining whether transplantation is an appropriate form of therapy. Patients must be judged exclusively on the basis of their willingness to undergo the procedure and their suitability for the procedure as determined by hard statistical analysis of data generated by properly conducted trials.

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REFERENCES

1. Scharschmidt BF. Human liver transplantation: Analysis of data on 540 patients from four centers. *Hepatology* 1984;4:95S-101S.
 2. Moss AH, Siegler M. Should alcoholics compete equally for liver transplantation? *JAMA* 1991;265:1295-8.
 3. Cohen C, Benjamin M, AUTHOR, et al. Alcoholics and liver transplantation. *JAMA* 1991;265:1299-301.
 4. Starzl TE, Van Thiel D, Tzakis AG, et al. Orthotopic liver transplantation for alcoholic cirrhosis. *JAMA* 1988;260:2542-4.
 5. Kumar S, Stauber RE, Gavaler JS, et al. Orthotopic liver transplantation for alcoholic liver disease. *Hepatology* 1990;11:159-64.
 6. Lucey MR, Merion JM, Henley KS, et al. Selection of patients with alcoholic liver disease for orthotopic liver transplantation. *Hepatology* 1989;10:572.
 7. Lucey MR, Merion RM, Henley KS, et al. Liver transplantation in alcoholic liver disease – the University of Michigan experience. *Gastroenterology* 1991;100:A767.
 8. Beresford TP, Wilson D, Blow FC, et al. Psychological health in alcoholic and nonalcoholic liver transplant recipients. *Gastroenterology* 1991;100:A220.
 9. Blum K, Noble EP, Sheridan PJ, et al. Allelic association of human dopamine D₂ receptor gene in alcoholism. *JAMA* 1990;263:2055-60.
 10. Hrubec Z, Omenn GS. Evidence of genetic predisposition to alcoholic cirrhosis and psychosis: Twin concordances for alcoholism and its biological end points by zygosity among male veterans. *Alcoholism: Clin Exp Res* 1981;5:207-15.
 11. Goodwin DW, Schulsinger F, Moller N, et al. Drinking problems in adopted and nonadopted sons of alcoholics. *Arch Gen Psychiatry* 1974;31:164-9.
 12. Dosssetor JB. Ethical considerations: Ethical issues in organ allocation. *Transplant Proc* 1988;20:1053-8.
 13. Lundberg GD. License to plunder or to paint. *JAMA* 1983;250:2966-7.
 14. Atterbury CE. The alcoholic in the lifeboat: Should drinkers be candidates for liver transplantation? *Clin Gastroenterol* 1986;8:1-4.
 15. Verhey A. Sanctity and scarcity: The making of tragedy. In: Lammers SE, Verhey A, eds. *On Moral Medicine*. Grand Rapids: William B Eerdmans 1987:653-7.
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