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EDITORIAL

K. Höckerstedt
M. Salaspuro

Liver transplantation in alcoholic liver disease

Time for decision-making

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Liver transplantation offers the patient a fairly good chance for a new life. Today the results are much better than they were only 5 years ago, and many patients return to their previous activities and start an even more demanding life after a successful transplant procedure.

In 1992, 2353 liver transplantations were performed in Europe [7]. Among those cirrhotics for whom liver transplantation is an option is an ever-increasing number of alcoholics. In 1990, 17 % of those receiving new livers were alcoholic patients, as compared to only 5 % 6 years earlier; in fact, from 1985 to 1990, eight European countries showed this same trend. However, the percentage of transplanted patients with alcoholic disease varies considerably – from 0 % to 91 % – from country to country; moreover, large variations are often found in different centers within any one given country. Obviously, then, there is some disagreement on how to handle the alcoholic patient awaiting a new liver.

The alcoholic patient is certainly a controversial subject in this context. In many donor centers it has been argued that "if this liver goes to an alcoholic, we do not want to have anything to do with the organ harvesting – there are too many other patients dying while waiting for a liver". It is also possible that families that grant permission for organ donation might hesitate if they knew that the donor organ was going to be transplanted into a person with alcoholic liver disease. Public discussions have revealed that most people are quite unaware of the conditions under which patients with alcoholic liver disease are transplanted [9]. Too many alcoholics in a liver transplantation program might imply that these patients will be transplanted as private patients. Organs, however, should not be for sale. There is an obvious organ shortage, and, indeed, some patients do die while waiting for a new liver. In order to dissociate facts from attitudes, we believe it is time to discuss this particular subject: how shall we deal with the alcoholic patient with end-stage liver disease in transplant centers?

Alcoholic cirrhosis is by far the most common form of cirrhosis in the Western world. The disease cannot be cured by any conservative means, although many different trials of drug treatment have been tried [4]. Today only the complications may be treated with more or less satisfactory results. It has been shown that if a patient with alcoholic cirrhosis stops drinking completely and survives the 1st year, his prognosis is much better than if he continues drinking heavily [17]. In fact, for many such patients, the quality of life reaches a new plateau that can be maintained for years. Yet, it is doubtful whether merely reducing one's use of alcohol is enough to achieve the same goal [6]. For subjects in the terminal stage, abstinence does not seem to influence the course of the disease – it is simply too late [16].

Two opposite views have been expressed in discussions regarding the management of this patient category. There are transplantation groups that completely deny the alcoholic patient the possibility of a new liver, whereas others feel that transplantation should be performed whenever desired by the patient.

Let us first consider the arguments put forward against transplantation. It has been claimed that there is no reason to treat an alcoholic with liver transplantation since, by most criteria, it is no longer possible for him to live a normal life. Second-

K. Höckerstedt (✉)
Fourth Department of Surgery, University of Helsinki, Kasarmikatu 11, SF-00130, Helsinki, Finland

M. Salaspuro
Research Unit of Alcohol Diseases, University of Helsinki, Kasarmikatu 11, SF-00130 Helsinki, Finland

ly, continued drinking would only lead to destruction of the new liver graft. Moreover, patient compliance, particularly with regard to immunosuppressive drugs and outpatient controls, might be endangered. Thus, the transplanted liver could be destroyed, a liver that might have otherwise been given to a more suitable (i.e., nonalcoholic) patient. It is well known that there is an organ shortage and that patients who do not have self-inflicted diseases often die while waiting for a new liver. Why invest large sums in such an uncertain endeavor as the alcoholic patient? It is based upon these arguments that some claim transplanting livers into alcoholic patients is unjustified.

A completely opposite view has been expressed by groups that maintain that a liver should be transplanted into patients with end-stage alcoholic liver disease whenever they desire such a therapy [8, 11]. This opinion is based on results showing that alcoholics do as well as, or even better than, other cirrhotics after transplantation [11]. The survival figures are clearly better than in three other large disease groups, i.e., liver cancer, HBV hepatitis, and acute liver failure [3, 7, 10]. Alcoholic patients also return to work in the same proportion as other patient groups [11]. In 1988, a long-term study of patients transplanted because of alcoholic liver injury was reported by the Starzl group [22]. Patients studied longer than 8 years after transplantation were, in general, working and not drinking; moreover, they took part in social activities helping others with alcohol problems. Unfortunately, this report does not reveal how many of those who died within 8 years did so due to alcohol abuse. However, it has also been suggested that alcoholics, if elected for transplantation, should have a lower priority than other patients [13].

How should we then handle this situation? First of all, we have to bear in mind that numerous other self-inflicted diseases are treated by the great majority of us and by our colleagues without any further hesitation. Cigarette smoking causes lung cancer as well as heart and vascular diseases, yet we treat smokers; obese patients suffer more often from cardiovascular and orthopedic diseases than non-obese patients, but we treat them, too. We also treat patients with alcohol-induced hemorrhagic pancreatitis and drunken drivers who sustain severe traffic injuries. Drug addicts, including those with HIV infection, receive much attention and care, as do patients who have tried to commit suicide. Even sports injuries may be classified as self-inflicted, but nobody refuses to treat these patients. If we actively care for all of these patient groups, how can we then refuse to treat alcoholics with severe end-stage liver disease in the only curable way there is, i.e., liver transplantation?

When discussing the arguments put forward against transplantation, one must include the possibility that the alcoholic patient may, in fact, continue drinking excessively even after transplantation. Thus far, there have been no reports of the appearance of alcoholic cirrhosis in a transplanted liver, but the follow-up time is too short in most reports for any conclusions. On the other hand, alcohol-induced histological changes in the liver have been observed 2 years after transplantation in a patient who continued drinking [5].

The majority of centers performing liver transplantation for alcoholic disease have adopted a policy of demanding some kind of patient collaboration. Complete abstinence is the most common requirement [18], although its definition is lacking in most reports. An abstinence period of 6 months before transplantation was initially recommended by the Consensus Conference on Liver Transplantation in 1983 [12]. This advice is still followed in many centers, but the exact policy of every institution is not known. The 6-month demand has not been tested in any proper studies, and we do not know how long such a period eventually should be. Individual differences in the severity and course of alcoholic disease certainly exist. In cases of acute liver failure, the stipulation of abstinence cannot be followed.

The length of the abstinence period has recently been tested in the United States, where a patient charged a doctor for having demanded a 2-year-long abstinence period before evaluation for transplantation could be performed. The court decided that the requirement of 2 years' preoperative sobriety is longer than the likely natural course of the patient's fatal disease and, thus, that it cannot be justified [1]. Such a procedure has not yet been reported in Europe. It should, however, be emphasized that following a longer period of abstinence, the liver function in most cases improves in many patients, making liver transplantation unnecessary [14].

A requirement of some period of abstinence is supported by recent data by Bird et al. [5]. They found that 12 preoperatively abstinent patients transplanted for chronic end-stage liver disease were not drinking postoperatively, whereas three other patients transplanted without preoperative abstinence had returned to drinking. In the study by Kumar et al. [11], the majority had stayed sober longer than 6 months pretransplantation. Six out of 52 patients (12%) surviving transplantation for alcoholic liver disease resumed alcohol consumption after surgery. By comparison, 20% of the patients transplanted for nonalcoholic diseases were drinking after transplantation [11]; at follow-up, the s-γ-glutamyl transferase (s-γ-GT), an indicator of alcohol consumption, was normal in a greater percentage of alcoholics than nonalcoholics. Also, the percentage of patients working after transplantation was no different from that seen in patients transplanted for nonalcoholic disease [11]. Beresford et al. [3], on the

other hand, found no relevance in the duration of sobriety to the relapse of 15 transplanted patients. In the only long-term study (up to 14 years follow-up) published thus far, only 2 out of 21 patients died due to rejection [22]. This indicates that the great majority of patients seem to have followed their doctors' prescriptions in taking the immunosuppressive drugs, indicating a good compliance. When estimating the results in most of these studies, we have to remember that the follow-up times are quite short, usually of less than 3 years' duration.

The number of liver transplantations might increase considerably if transplantation in alcohol-induced liver disease were to increase without any common suggestions of therapeutical standards. The costs of liver transplant programs might even double. However, when evaluating the costs of transplantation because of alcoholic liver disease, people forget that unless transplanted, these patients will remain consumers of expensive hospital care, just like other cirrhotics. In the terminal phase they may undergo multiple treatments for complications like bleeding, ascites, trauma, delirium, and coma. Treatment for these costly complications is often performed in the intensive care unit. The price of one single variceal bleeding treatment may be as high as 25% of the cost for a transplantation [15].

When a subject with alcoholic disease is evaluated for liver transplantation, every effort should be made to evaluate the degree of alcohol dependence and to estimate the outcome after transplantation. The degree of alcohol dependence may correlate to the future use of alcohol by a transplanted patient, and it could be assessed, for instance, by using the Severity of Alcohol Dependence Questionnaire (SADQ) [23]. This questionnaire correlates with indices of withdrawal symptom severity, as assessed by a physician for patients attending a detoxification unit. However, its capability of predicting alcoholism treatment outcome has not been assessed. Also, the correct diagnosis should be verified. Is the cirrhosis really induced by alcohol abuse or are other factors involved, such as drug abuse, another liver disease, or even α-1-antitrypsin deficiency? The diagnosis should be based on both liver histology and laboratory findings (reversed s-ASAT/s-ALAT ratio, a considerably increased s-γ-GT), a normal α-1-antitrypsin level, a normal s-α-fetoprotein, a normal transferrin saturation and ferritin level, no autoantibodies, and the like [19, 20]. It is clear that severe extrahepatic disease precludes grafting in many patients with alcohol cirrhosis [14]. Alcohol-induced cerebral disease, cardiomyopathy, neuropathy, pancreatic disease, and malnutrition, as well as psychic disturbances, are common in these subjects [14, 25]. Pretransplant evaluation of the patient's dependence on alcohol should include some psychosocial investigation, such as the DSM-III-R criteria [2, 10]. In our transplant center, the alcoholic patient undergoes testing by a neurologist, a psychologist, a psychiatrist, and a physician well experienced in alcoholic liver disease. The role of treatment programs in keeping the patient abstinent has been found to be useful by most authors [26], although opposite views have also been expressed [22].

We suggest that people from liver transplant centers in Europe get together to discuss this problem. The decision to transplant should be made on medical and ethical grounds, not on moral grounds [21, 24]. It is now time to draw up guidelines indicating under what conditions liver transplantation might be considered a reasonable option for patients with alcoholic liver disease. We owe it to the patients, to the general public, to the donor families and donor hospitals, and to ourselves.

References

1. Allen v Mansour (1986) 86-73429 District court for the eastern district of Michigan, Southern Division, USA
2. American Psychiatric Association (1987) Diagnostic and statistical manual, 3rd edn, revised. Washington, DC
3. Beresford TP, Turcotte JG, Merion R (1990) A rational approach to liver transplantation for the alcoholic patient. Psychosomatics 31: 241–253
4. Bird GL, Williams R (1990) Treatment of advanced alcoholic liver disease. Alcohol 25: 197–206
5. Bird GL, O'Grady JG, Harvey FAH, Calne RY, Williams R (1990) Liver transplantation in patients with alcoholic cirrhosis: selection criteria and rates of survival and relapse. BMJ 301: 15–17
6. Borowsky SA, Strome S, Lott E (1981) Continued drinking and survival in alcoholic cirrhotics. Gastroenterology 80: 1405–1409
7. European Liver Transplant Registry (1991) Hôpital Paul Brousse, Villejuif, France
8. Flavin DK, Niven RG, Kelsey JE (1988) Alcoholism and orthotopic liver transplantation. JAMA 259: 1546–1547
9. Gertsch P (1992) Transplantation hépatique chez le cirrhotique alcoholique: arguments pour. Schweiz Med Wochenschr 122: 631–633
10. Iwatsuki S, Starzl TE, Todo S (1990) Experience in 1000 liver transplants under cyclosporin-steroid therapy: a survival report. Transplant Proc 22: 1576–1578
11. Kumar S, Stauber RE, Gavaler JS, Basista MH, Dindzans VJ, Schade RB, Rabinovitz M, Tarter R, Gordon R, Starzl TE, Thiel DH van (1990) Orthotopic liver transplantation for alcoholic liver disease. Hepatology 11: 159–164
12. Liver transplantation consensus conference (1983) JAMA 250: 2961–2964

13. Moss AH, Siegler M (1991) Should alcoholics compete equally for liver transplantation? JAMA 265: 1295–1298
14. Neuberger JM (1989) Transplantation for alcoholic liver disease. Contraindicated by alcohol dependence or extrahepatic disease. BMJ 299: 693–694
15. O'Donnell TF Jr, Gembarowocz RM, Gallow AD (1980) The economic impact of acute variceal bleeding: cost-effectiveness implications for medical and surgical therapy. Surgery 88: 693–697
16. Pande NV, Resnick RH, Yee W, Eckardt VP, Shurberg JL (1978) Cirrhotic portal hypertension: morbidity of continued alcoholism. Gastroenterology 74: 64–69
17. Powell WJ, Klatskin G (1968) Duration of survival of patients with Laennec's cirrhosis. Am J Med 98: 695–716
18. Rohner A (1992) Le transplantation hépatique dans la cirrhose alcoholique est-elle légitime? Schweiz Med Wochenschr 122: 628–630
19. Salaspuro M (1987) Use of enzymes for the diagnosis of alcohol-related organ damage. Enzyme 37: 87–107
20. Salaspuro M (1989) Characteristics of laboratory markers in alcohol-related organ damage. Scand J Gastroenterol 24: 769–780
21. Schenker S, Perkins HS, Sorrell MF (1990) Should patients with end-stage alcoholic liver disease have a new liver? Hepatology 11: 314–319
22. Starzl TE, Thiel D van, Tzakis AG, Iwatsuki S, Todo S, Marsh JW, Koneru B (1988) Orthotopic liver transplantation for alcoholic cirrhosis. JAMA 260: 2542–2544
23. Stockwell T, Murphy D, Hodgson R (1983) The severity of alcohol dependence questionnaire: its use, reliability and validity. Br J Addict 78: 145–155
24. Thiel DH van, Gavaler JS, Tarter RE, Dindzans VJ, Gordon RD, Iwatsuki S, Makowka L, Todo S, Tzakis AG, Starzl TE (1989) Liver transplantation for alcoholic liver disease: a consideration of reasons for and against. Alcoholism 13: 181–184
25. Urbano-Marquez A, Estruch R, Navarro-Lopez F, Grau JM, Mont L, Rubin E (1989) The effects of alcoholism on skeletal and cardiac muscle. N Engl J Med 320: 409–416
26. Zimberg S (1989) Individual management of psychotherapy: psychoactive substance use disorders (alcohol). In: American Psychiatric Association (ed) Treatments of psychiatric disorders. Washington, DC, pp 1093–1103