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Long-term medical and psycho-social evaluation of patients undergoing orthotopic liver transplantation for alcoholic liver disease

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Abstract The major concern in transplanting patients with alcoholic liver disease (ALD) is the high rate of alcohol recidivism. Our aim was to assess the long-term outcome of liver transplantation (OLT) in a group of ALD patients in terms of post-OLT alcohol recidivism and its relationship with pre-OLT psychosocial variables and medical follow up. Fifty-one ALD patients underwent strict medical and psychosocial evaluation before and after OLT. Alcohol abuse was recorded in 60% and alcohol dependence in 40% of patients before OLT. The 5-year survival was similar to the one observed in non-ALD transplanted patients (64 vs 56%). Alcohol recidivism was observed in 33% of transplanted patients, 64% of whom were occasional and 36% were heavy drinkers. The admission of alcoholism by the patient and his/her family prior to OLT significantly predicted abstinence after OLT. A multidisciplinary approach evaluating medical and psycho-social variables before OLT and a close follow up after OLT are mandatory for ALD patients.

Key words Liver transplantation · Alcoholic liver disease · Psychosocial evaluation · Alcohol recidivism

Introduction

Despite comparable survival rates being reported in patients transplanted for ALD and for other types of liver disease [3, 4, 10–12, 14, 19, 23], many liver transplantation centers are still reluctant to consider ALD patients as candidates for OLT [17]. The major concerns are the expected high rate of alcohol recidivism [3, 12, 15, 19] and poor compliance with immunosuppressant therapy. However, highly motivated ALD patients may be identified as capable of remaining abstinent after OLT, on a psychological and psychiatric basis [14]. Such patients profess a strong attitude towards medical advice, exhibit no overt psychopathology and usually have a good social support system [10]. Moreover, most alcoholics with cirrhosis do not have significant extrahepatic complications [13], which are considered to be risk factors for a greater morbidity and mortality after OLT. In this study we assessed the long-term outcome of OLT in ALD patients appropriately selected before, and prospectively followed up after surgery in order to evaluate: (1) post-OLT relapse into alcohol consumption and (2) its relationship with pre-OLT psychosocial variables.

Materials and methods

Patients

Fifty-one patients (41 males, 10 females; mean ± SD age 48 ± 8 years) with a diagnosis of end-stage ALD (Child-Pugh B in 18 and C in 33 cases) were included in the study.

Pretransplantation assessment

Medical evaluation

The diagnosis of ALD was based on a history of excessive alcohol consumption in the absence of other causes of liver disease, with

compatible clinical and laboratory findings. Antibodies to hepatitis B, C, and D were checked in all patients. Patients with the suspicion of hepatocellular carcinoma (HCC) underwent ultrasound examination and fine-needle biopsy of the lesion, and lipiodol hepatic angiogram followed by liver CT scan. All patients underwent a full medical assessment to exclude alcohol-related extrahepatic organ damage (for example, chronic pancreatitis, cardiomyopathy, and/or ischemic cardiac disease) or neuropathies.

Psycho-social evaluation

All potential transplantation candidates with ALD underwent a specific evaluation to define their alcohol-related problems before being listed for OLT. The evaluation included the CAGE questionnaire [6]. A positive answer to at least two CAGE questions is indicative of drinking problems. Any alcohol abuse or dependence, or polydrug abuse (illicit drugs and medication) were defined according to the DSM-III-R [1]. Patients were questioned regarding the amount and duration of alcohol consumption, period of alcohol abstinence, previous alcohol rehabilitation treatments (self-help groups, Alcoholics Anonymous), family relationship and social stability (steady job, fixed home, stable marriage) and admission of alcoholism by the patient and his/her family. A mandatory 6-month period of abstinence from alcohol was required [2, 9]. Final approval for listing the patient emerged from the consultation of a multidisciplinary group (hepatologist, psychiatrist, surgeon, anesthetist, and nurse).

Posttransplantation assessment

All patients were closely followed up with routine hospital stays at 3, 6, and 12 months and then yearly after OLT at the outpatients clinic every 6 months after the 1st year following OLT for psycho-social and medical assessment.

Medical evaluation

Liver function tests (AST, ALT, ALP, GGT, total bilirubin, prothrombin time, albumin), MCV, and carbohydrate-deficient transferrin (CDT) were used as markers of alcohol abuse; antibodies to hepatitis B, C, and D were checked yearly in all patients after OLT. Liver biopsies were taken 6 and 12 months after OLT and then yearly and whenever clinically indicated on the basis of abnormal biochemical tests. The survival rates of patients transplanted for ALD were compared with those of patients transplanted for liver cirrhosis of other etiologies.

Psycho-social evaluation

All patients underwent a semi-structured interview to evaluate alcohol recidivism, defined according to Lucey as any alcohol consumption after transplantation [15]. Patients with recidivism were divided into occasional drinkers (OD) if they drank less than 200 g of alcohol a week and heavy drinkers (HD) if they drank more than 200 g of alcohol a week [24]. Patients with no recidivism were defined as abstainers (A). The relationship between the psycho-social variables evaluated during the pre-transplantation assessment and the three groups (A, OD, HD) was analyzed.

Statistical analysis

The Kaplan-Meier method was used for survival analysis; the Breslow, log-rank, and Tarone-Ware tests were used to compare survival rates between groups. The differences between psycho-social variables evaluated before OLT in the three groups of transplanted patients were determined by the chi-squared test (Pearson test) and Fisher's exact test. Liver function tests and alcohol consumption were compared in the three groups of transplanted patients by ANOVA (SPSS 8.0, Chicago, Ill., USA).

Results

Pretransplant assessment

Medical evaluation

Sixteen of the 51 ALD patients (31.3%) had been found anti-HCV + (14/16 patients were HCV-RNA +) at some stage of their alcoholic liver disease, 2 patients (3.9%) were HBsAg +, and HCC was present in 2 patients (3.9%). Chronic pancreatitis was diagnosed in 1 patient, but no diagnoses of cardiomyopathy, ischemic disease or neuropathy were recorded.

Psycho-social follow up

The CAGE questionnaire was positive in 100% of the ALD patients. Alcohol abuse was diagnosed in 60% and alcohol dependence in the remaining 40% of cases. The polydrug abuse was present in 8.8% of cases. Alcohol consumption (mean ± SD) was 103.4 ± 28.6 g alcohol/day over a (mean ± SD) period of 10.4 ± 3.0 years. The duration of alcohol abstinence before OLT (mean ± SD) was 12.9 ± 12 months. Thirty percent of ALD patients had undergone alcohol rehabilitation programs. Problems with family relationship were recorded in 20% of cases and social stability problems were observed in 12%. Alcoholism was admitted to by 32% of the ALD patients and 47% of the families.

Posttransplant assessment

Survival

The 51 ALD patients underwent OLT between November 1990 and November 1998. Seventeen patients died during follow up of causes unrelated to alcohol recidivism. The 5-year survival rate in the ALD-transplanted patients was similar to the one observed in patients transplanted for liver disease of other etiologies (64 and 56%, respectively; Fig. 1). When ALD-transplanted patients were divided according to sex, the 5-year survival rate was 58% in males and 78% in females

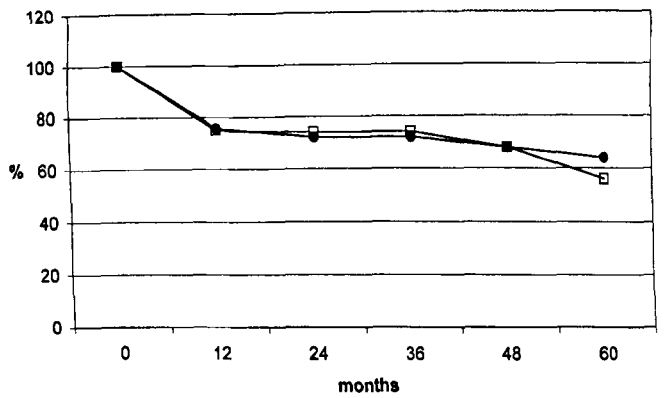

Fig. 1 Five-year survival in patients transplanted for alcoholic liver disease (*dots*) and for end-stage liver disease of other etiologies (*boxes*)

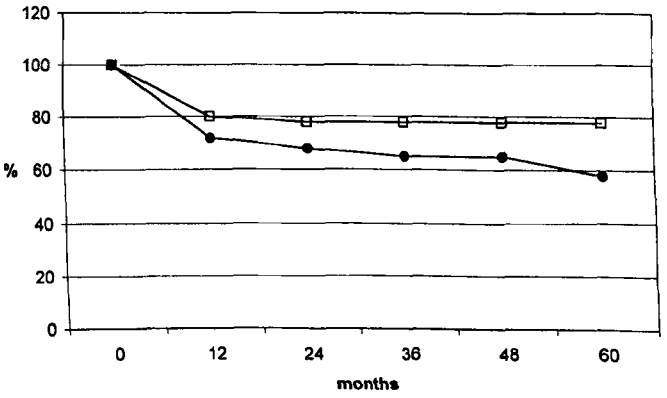

Fig. 2 Five-year survival in male (*dots*) and female (*boxes*) patients transplanted for alcoholic liver disease

(Fig. 2). The highest mortality rate was observed in the first 6 months after OLT. Long-term medical and psycho-social evaluation was performed in 34 surviving patients (26 males, 8 females). The mean follow up was 40.1 months (range 0–86 months).

Medical follow up

The immunosuppressant regimen was based on cyclosporine in 30 patients and tacrolimus in 4 patients. Azathioprine was added in 5 patients whose serum creatinine levels were higher than 2 mg/ml, prompting a reduction in cyclosporine dosage; in all patients steroids were withdrawn within 3 months of the OLT.

Liver function tests obtained every 6 months after OLT did not differ significantly between the A, OD, and HD groups, except for GGT, which was significantly higher ($P = 0.02$) at 30 months after OLT in HD than in OD or A. MCV was significantly higher 6 ($P = 0.01$), 12 ($P = 0.02$), and 18 ($P = 0.005$) months after OLT in HD than in OD and A, whereas CDT was not significantly different among the groups. Anti-HCV + was confirmed after OLT in 11/11 patients who were anti-HCV + before OLT. HBsAg + /HBV-DNA– persisted after OLT in 2/2 patients who were HBsAg + /HBV-DNA– before OLT. The only patient with HCC was free of disease 7 years after OLT.

Histological findings of acute cellular rejection were found in nine liver biopsies taken in 4/34 (11.7%) patients. All episodes of acute cellular rejection were reversed by steroids (methylprednisolone 1 g/day i.v. for 3 days) and the course was repeated in only 1 patient.

Psycho-social evaluation

The semi-structured interview was positive for a relapse into alcohol consumption in 11/34 (33%) transplanted patients, 7 defined as OD and 4 as HD. Twenty-three patients remained abstainers. Recidivism was detected 12–63 months after OLT. In 2 patients alcohol consumption was associated with social and family problems. Alcohol abuse or dependence, or polydrug abuse before OLT was not predictive of alcohol recidivism after OLT. In fact, before OLT 13/23 (56%) A, 4/7 (57%) OD, and 1/4 (25%) HD had alcohol abuse, while alcohol dependence had been recorded in the remaining 10/23A, 3/7 OD, and 3/4 HD. Two out of 23 (8.7%) A and 1/7 (14.2%) OD had polydrug abuse before OLT. No polydrug abuse had been found in A.

Alcohol consumption (mean ± SD) before OLT had been 96.9 ± 43 in A, 88.5 ± 15 in OD, and 125 ± 28 g alcohol/day in HD patients. The duration of alcohol consumption (mean ± SD) before OLT had been 10.1 ± 5.6 in A, 10.0 ± 2.8 in OD, and 11.2 ± 2.5 years in HD patients. The duration of abstinence (mean ± SD) before being listed for OLT had been 20.6 ± 26.3 in A, 10.4 ± 9.4 in OD, and 7.7 ± 3.0 months in HD. Six out of 23 (26%) A, 1/7 (14%) OD, and 3/4 (75%) HD had undergone some form of alcohol rehabilitation before OLT. Four out of 23 (17%) A, 3/7 (75%) OD, and none of the HD had experienced events affecting family stability such as separation or divorce before OLT. Two out of 23 (8%) A had not had a stable home before liver transplantation. Two patients had lost their jobs before OLT (social stability).

Significantly, 11/23 (47%) A and no OD or HD had admitted to alcoholism before OLT ($P = 0.002$). The family's admission of alcohol problems before OLT was significantly ($P = 0.002$) higher in HD (75%) than in OD (57%) or A (39%) patients.

Discussion

The most important limit to OLT in patients with ALD has been the rate of alcohol recidivism and possible liver injury, and non-compliance with the immunosuppressant regimen. Divergent data have been reported on the prevalence, rate of onset, and spectrum of alcohol recidivism in transplant recipients [15, 18, 20–22], possibly due to the different alcohol abuse or dependence screening programs adopted at different liver transplant centers. The outcome after OLT is also difficult to compare in such patients because different follow-up programs are used. We established very restrictive selection criteria in an attempt to predict long-term abstinence and we regularly and closely followed up all patients after OLT to avoid missing any alcoholic relapse.

The survival of patients transplanted for ALD was comparable with the rate seen in patients transplanted for other types of liver disease, thus confirming numerous reports in the literature [16]. The mortality in our series was always due to causes unrelated to alcohol recidivism, though we cannot rule out the potential influence of previous alcohol abuse on the outcome of OLT as a result of extrahepatic disease causing morbidity and death, especially soon after surgery. The effect of recidivism on medical health in transplanted patients is still under evaluation. Liver abnormalities are reported to range from mild to severe [15]. In the long-term, however, liver function was not seriously affected by any return to alcohol consumption, since only GGT was significantly higher at some stage in heavy drinkers than in occasional drinkers or abstainers.

In the setting of biochemical markers of alcohol abuse, our experience confirms that MCV is reliable, whereas CDT is apparently not, in contrast with various reports [8].

One other aspect of this study is the low rate of acute cellular rejection found in patients transplanted for ALD, confirming both a good compliance with immunosuppressant therapy and the different features of the immune system of patients with previous ALD, already described [7].

Results obtained after strict pre-OLT selection and careful post-OLT follow up demonstrated that one-third of ALD transplant recipients experienced some type of alcoholic relapse, but only two patients developed social and family problems due to alcohol recidivism. We found that among the numerous psycho-social variables before OLT, the admission of alcohol-related problems by the patient and the family may influence the likelihood of persistent abstinence after OLT, whereas the amount of alcohol consumed or the duration of alcohol consumption or dependence before OLT had no such discriminating role. Surprisingly, the period of abstinence before OLT was also not predictive of subsequent abstinence, thus confirming controversies still existing on this issue [5]. It was also clear that previous problems with family relationships or social stability before OLT had no influence on the outcome of such patients after surgery.

We consider these results acceptable, given that the relatively high rate of recidivism stems from the very rigid follow up, so that probably no cases of alcohol intake after OLT were overlooked. Of course, better results are needed in order to avoid damaging the new liver, given the shortage of donors that is still a serious problem in our country. In conclusion, a multidisciplinary approach that evaluates not only medical but also psychological suitability for OLT is mandatory to identify patients with ALD who are most likely to achieve satisfactory long-term results after surgery.

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