ELSEVIER

Alcoholic Liver Disease and Transplantation

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ALCOHOL has been and continues to be one of the most commonly abused substances in society. One of 10 persons and 1 of 3 families is the victim of alcohol-related disorders. In the United States it is the fourth most common cause of death in the 35 to 55 year age group. In Europe, 10% of all deaths are secondary to alcohol-related liver disease.

Alcohol is oxidized by alcohol dehydrogenase to acetaldehyde. Acetate enters the citric acid cycle and is utilized to make fatty acids, which may cause ballooning of hepatocytes, eventually resulting in degeneration, fatty changes, inflammatory infiltrates, fibrosis, and Mallory's hyalinization.[1–3]

When they consume the same amount of alcohol, women are at higher risk for disease than men, probably due to their decreased gastric alcohol dehydrogenase activity. In addition, the presence of hepatitis C viral infection, use of acetaminophen, and obesity are identifiable corisk factors for the progression of liver disease. More than 80 g of alcohol per day (ie, 6 to 8 drinks) for more than 8 years can be expected to lead to alcoholic liver disease.[2]

PRESENTATION

Patients may present with fatty liver, acute alcoholic hepatitis, chronic alcoholic hepatitis, or cirrhosis. Medical management and discontinuation of alcohol can improve the

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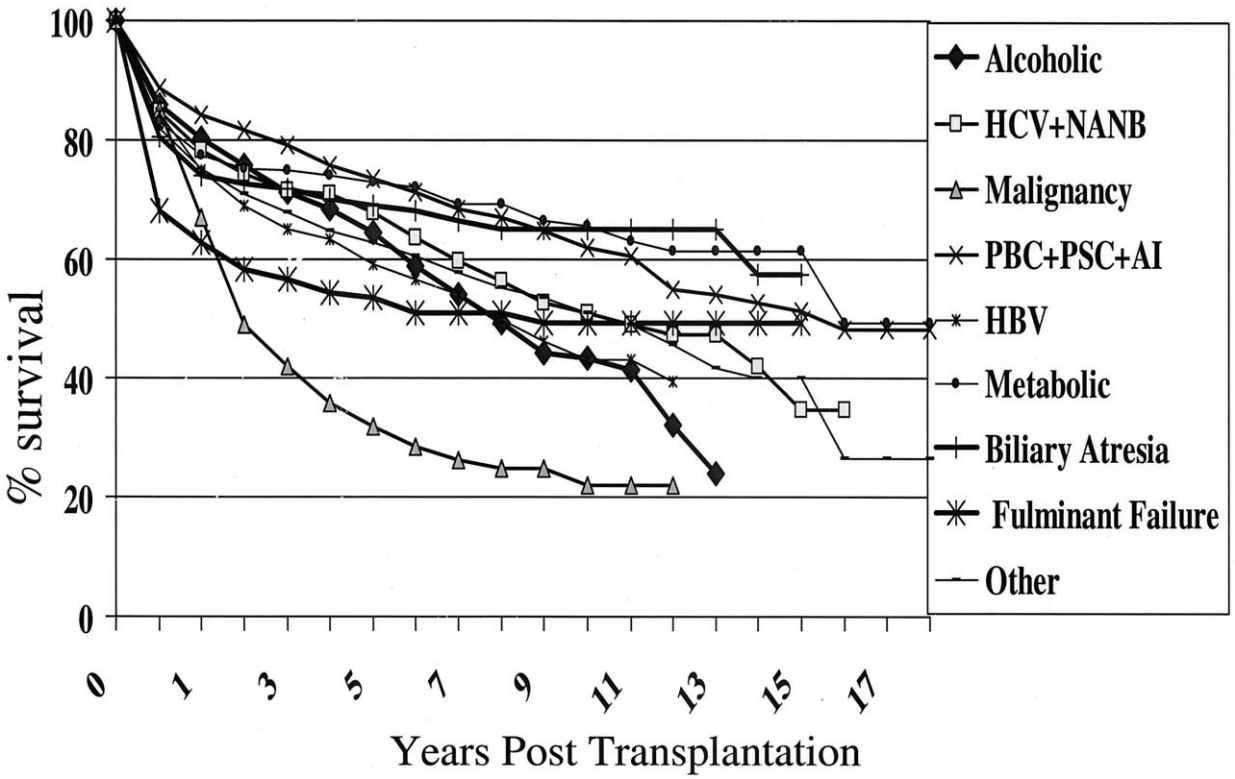

Fig 1. Long-term survival post-liver transplantation for alcoholic versus other conditions (n = 4000), with permission.[24]

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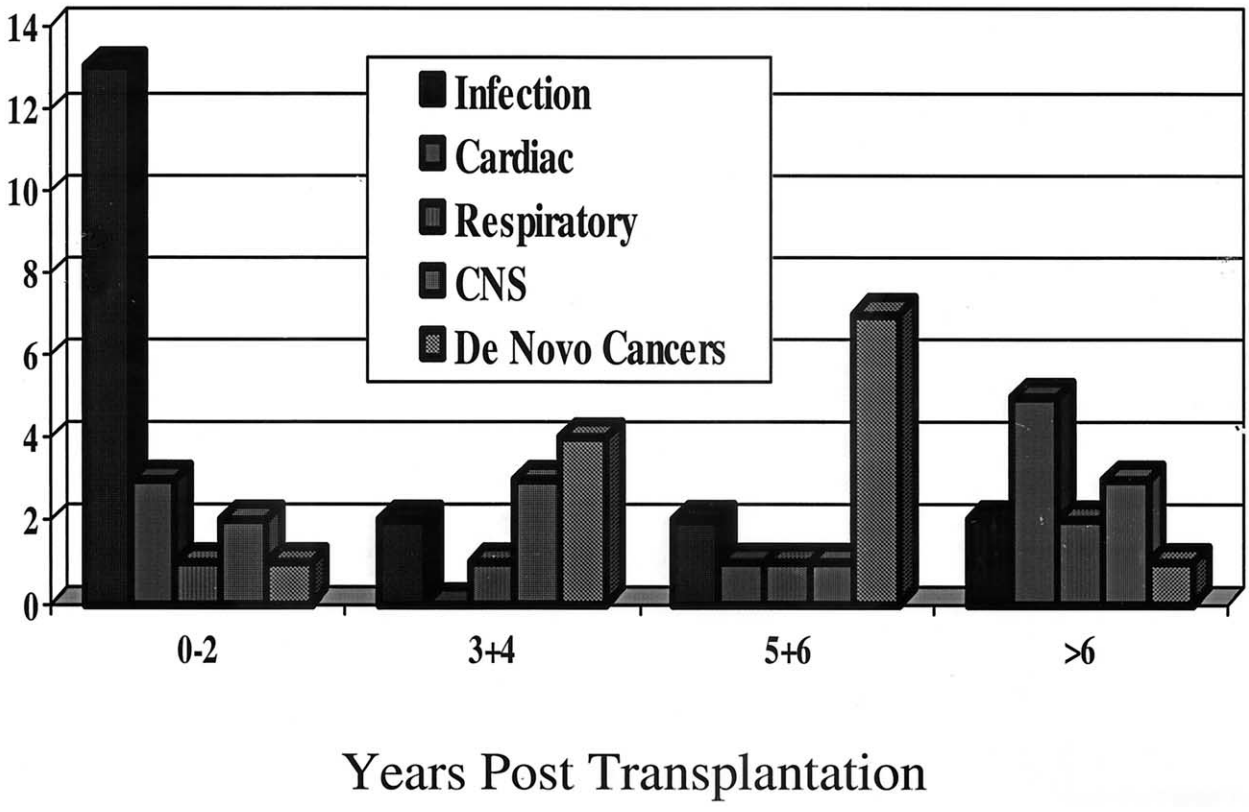

Fig 2. Causes of death for post-liver transplantation for alcoholic liver disease, with permission.[25]

situation in the early stages of the disease when it is confined to fatty changes, to acute or even to chronic hepatitis, but cirrhotic changes are irreversible and often progressive.[4–6] Discriminant function (DF) has been used as a guideline for prognosis of the illness when the patient present initially. A DF score <32 is often reversible; >32 carries a poor prognosis. (DF = [prothrombin time in seconds minus control prothrombin time × 4.6 + total serum bilirubin (mg/dL)).] Medical management can occasionally be successful in patients with early cirrhosis, al-

Table 1. Rate of De Novo Malignancy Post-Liver Transplantation

	Alcoholic LTx Patients Group I (n = 185)				Nonalcoholic LTx Patients Group II (n = 649)			
Organ/System	Observed	Expected SEER	SIR	95% Confidence Interval	Observed	Expected SEER	SIR	95% Confidence Interval
Gastrointestinal (esophagus, stomach, colon and rectum)	1	1.3	0.77	0.02–4.29	7	4.33	1.62	0.65–3.34
Genitourinary (kidney, ureter, prostate, bladder)	5	2.23	2.24	0.72–5.22	6	6.46	0.93	0.34–2.03
Oropharyngeal (oral cavity, pharynx, and larynx)	7	0.28	25.45*	10.23–52.43	1	0.79	1.25	0.03–7.01
Pulmonary (lung and bronchus)	5	1.34	3.72*	1.21–8.68	4	4.35	0.92	0.25–2.34
Female gynecological (breast, ovarian, uterine, and cervical)	1	1.08	0.92	0.02–5.02	3	5.8	0.52	0.11–1.52
Other								
Unknown primary	1				1			
Melanoma	1				1			
Skin cancer (squamous cell and basal cell)†	(15)				(16)			
Miscellaneous	1				8			
Total	21 + (15!)				31 + (16!)			

* P = <.05.
† SEER rates not available (with permission[25]).

though this is controversial. Agents that have been used include steroids, propylthiouracil, insulin and glucogen, amlodipine, parenteral nutrition, androgenic steroids, colchicine, amino acids, transfusions, and vitamins B_1, B_{12}, and folate.[7,8]

The definitive therapy for advanced and decompensated alcoholic cirrhosis is hepatic replacement. This is one of the leading indications for liver transplantation in adults in the United States. However, a major controversy is related to the belief that the disease is caused by individual addictive behavior, with the concern for recidivism and noncompliance leading to graft loss. In addition, a negative societal opinion of liver transplantation for this indication raises the concern that organ donations might be adversely affected.[9–12]

Once decompensation has occurred, a thorough evaluation is performed, including psychiatric and social as well as medical and surgical evaluations. A 6-month period of abstinence should be considered mandatory for liver transplantation candidates. Exceptions are occasionally made in unusual cases, where the liver disease is life threatening and there is no time to undergo rehabilitation and a 6-month period of abstinence.[13] However, given the shortage of organs, many centers are refusing to pursue liver transplantation in this situation.

OUTCOME AFTER LIVER TRANSPLANTATION

There are several reports suggesting that short-term (3–5 year) survival in patients transplanted for alcohol liver disease are either the same or better when compared with patients transplanted for other conditions.[14–23] At our center, we examined a relatively large population of patients over an extended period of time. From a population of 4000 liver transplantation (LTx) patients, a cohort of 567 patients underwent liver transplantation for alcoholic liver disease. In the first 5 to 7 years, survival of alcoholic patients was comparable with nonalcoholic transplantation recipients. However, thereafter, the deterioration in survival was greater in this group such that the actuarial survival was only about 25%[24] (Fig 1). An analysis of a cohort of alcoholic patients ($n = 185$) revealed the causes of patient death to be age-related diseases, namely, cerebral vascular accidents, myocardial infarctions, respiratory failure, infection, and *de novo* cancers (Fig 2). Although 20% ($n = 32$) had a documented history of recidivism, only one death was directly related to alcohol abuse alone, with an additional three deaths from noncompliance and recidivism.[25] When *de novo* cancers were analyzed in further detail in alcoholic ($n = 185$) and nonalcoholic ($n = 649$) groups and were compared with the general population using surveillance epidemiological end result (SEER) data matched for age, gender, and length of follow-up, the incidence of oropharyngeal and lung cancers were found to be 25 and 4 times higher, respectively, than the SEER rates. In contrast, cancers in nonalcoholic liver transplant recipients were not increased (Table 1). The rate of recidivism did not appear to correlate with the length of sobriety prior to liver transplantation or the impact of rehabilitation in a group of patients who were sober for more than 2 years.[2525] Recently, harman and nonharman (naturally occurring neurotransmitters) alcogens have been suggested to be useful predictors of alcohol abuse and relapse.[26]

CONCLUSION

Liver transplantation for alcoholic liver disease requires careful patient selection and mandates the involvement of psychiatrists, social workers, substance-abuse specialists, and an experienced rehabilitation team. While short-term outcomes are better than those after other indications for liver transplantation, long-term survival beyond 5 years is significantly lower, a finding that seems to be related to smoking, cardiovascular disease, and *de novo* cancers.

Based on these findings, careful post-liver transplantation screening programs to detect *de novo* cancers at early stages are mandatory in order to improve long-term survival in patients with alcoholic liver disease who require transplantation.

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