Liver cirrhosis: A seven year follow-up

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TSP TRAN, SV FEINMAN, B BERRIS. Liver cirrhosis: A seven year follow-up. *Can J Gastroenterol* 1991;5(1):11-14. The status of 121 patients who were found to have liver cirrhosis on liver biopsy in 1981 was assessed seven years later. The etiology of the cirrhosis was alcoholic in 52%, cryptogenic in 29.8%, hepatitis B-related in 9.1% and miscellaneous in 9.1%. In 1981, jaundice was present in 55 patients (45.8%), ascites in 52 (43%), gastrointestinal bleeding in 25 (20.7%) and encephalopathy in 10 (8.3%). During the following seven years an additional 20 patients developed ascites, 15 gastrointestinal bleeding, 32 encephalopathy and three hepatocellular carcinoma. The mortality rate was 43.8% at five years and 53.7% at seven years. The principal cause of death was liver failure (40%), followed by nonliver causes (32.3%) and gastrointestinal bleeding (13.9%). One patient died of hepatocellular carcinoma. Patients who survived seven years had fewer complications when seen in 1981 than those who died during this period ($P < 0.025$). It is concluded that, in Toronto, cirrhosis is often caused by ethanol abuse and hepatitis B infection; that it is associated with significant morbidity and mortality; and that the number of complications when the patient is first seen may be a useful indicator of prognosis. Since many cases of cirrhosis are preventable, the authors suggest that efforts directed towards prevention of cirrhosis may be more rewarding than those directed towards therapy.

Key Words: Cirrhosis, Complications, Mortality rate, Prognosis

Cirrhose du foie: Suivi à 7 ans

RESUME: L'état de 121 patients chez qui une cirrhose du foie avait été diagnostiquée d'après une biopsie hépatique en 1981 a été évalué sept ans plus tard. La cirrhose était attribuée à l'alcoolisme chez 52 %, cryptogénique chez 29,8 %, reliée à l'hépatite virale de type B chez 9,1 % et d'origines diverses chez 9,1 % des sujets. En 1981, on relevait un ictère chez 55 patients (45,8 %), une ascite chez 52 (43 %), une hémorragie digestive chez 25 (20,7 %) et une encéphalopathie chez 10 patients (8,3 %). Au cours des sept années suivantes, 20 autres patients ont développé une ascite, 15 des hémorragies digestives, 32 une encéphalopathie et 3 un carcinome hépatocellulaire. Le taux de mortalité était de 43,8 % à 5 ans et de 53,7 % à sept ans. La cause principale des décès était l'insuffisance hépatique (40 %), suivie par les causes non hépatiques (32,3 %) et

LIVER CIRRHOSIS IS A SIGNIFICANT cause of mortality and morbidity. Despite progress in the medical and surgical therapy of ascites, portal hypertension and variceal bleeding, five year survival rates are still in the range of 50% when combined etiologies are considered (1-7). The present study was an attempt to characterize and assess morbidity and mortality in a group of patients in whom liver cirrhosis had been diagnosed seven years previously.

The authors were able to trace 121 of 176 patients in whom a diagnosis of cirrhosis was made on liver biopsy in 1981. In this group the authors studied: the distribution of the varieties of cirrhosis; the prevalence of complications at the time of initial biopsy and over the ensuing seven years; the mortality rate at five and seven years after biopsy; the causes of death; and the relationship of the number of complications to prognosis.

PATIENTS AND METHODS

Between February 1, 1981 and January 31, 1982, 718 patients being investigated for the presence of liver disease had diagnostic liver biopsies in six Toronto teaching hospitals. In 176 patients, biopsies were diagnostic of cirrhosis. Patients with a diagnosis of hepatocellular carcinoma were excluded. These patients were drawn from a larger study of markers and risk factors for hepatitis B (8). Information collected included age, gender, etiology of cirrhosis, complications, presence of

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les hémorragies digestives (13,9 %). Un patient est décédé d'un carcinome hépatocellulaire. Les patients qui ont survécu sept ans avaient moins de complications quand ils ont consulté en 1981 que ceux qui sont décédés durant cette période ($P < 0,025$). On conclut qu'à Toronto la cirrhose est souvent causée par l'éthylisme et l'hépatite virale de type B; qu'elle est associée à une morbidité et à une mortalité significative; et que le nombre de complications relevées lors de la première consultation pourrait laisser présager le pronostic. Parce que de nombreux cas de cirrhose peuvent être évités, les auteurs suggèrent que les efforts investis dans la prévention pourraient s'avérer plus fructueux que ceux qui s'attachent au traitement.

TABLE 1
Comparison of traced and lost groups at the time of liver biopsy in 1981

	Traced (n=121)	Lost (n=55)	P (χ^2 or Z)
Age (years)	56.1	55.6	
Male/female	1.14/1	1.29/1	
Etiology of cirrhosis			>0.10
Alcoholic	52%	54.5%	
Cryptogenic	29.8%	21.8%	
Post hepatitis B	9.1%	14.5%	
Miscellaneous	9.1%	9.1%	
Complications			
Ascites	43%	44%	0.45
Jaundice	45.5%	49%	0.33
Gastrointestinal bleed	20.7%	27%	0.18
Encephalopathy	8.3%	14.5%	0.13
No complications	28.9%	25.5%	0.32
Hepatitis B serology			
Surface antigen positive	4%	9%	0.12
All hepatitis B virus markers	23.1%	22%	0.44
History of transfusion	28.9%	33%	0.30

markers of hepatitis B and history of transfusion.

From November 1988 to January 1989 the authors attempted to locate the 176 patients for re-study. The patient's physician was first contacted. If the physician had lost track of the patient, an attempt was made to contact the patient or the patient's family. The authors were able to locate 121 of the 176 patients and obtained information regarding the presence of additional complications such as ascites, gastrointestinal bleeding, hepatic encephalopathy and hepatocellular carcinoma between 1981 and 1988, as well as the date and cause of any deaths.

In order to determine whether the traced group was a valid sample representative of the entire group, a statistical comparison of the characteristics of the traced and lost groups was carried out. Age and gender distribution were

similar. Etiology of cirrhosis in the traced and lost groups, as well as the number of complications between survivors and deceased patients, were compared statistically using the χ^2 test. Initial complications, hepatitis B markers and history of transfusion in the traced and lost groups of patients were compared using the Z test.

RESULTS

One hundred and twenty-one patients were traced, and 55 were lost seven years after the diagnosis of cirrhosis was made on liver biopsy. Eighty-eight patients were traced through their physicians; 18 were contacted directly; and 15 were traced through their families. When the characteristics of the traced and lost groups identified in 1981 were compared, there was no statistically significant difference between them (Table 1). This suggests

that the traced group was representative of the entire group.

The etiology of cirrhosis in the traced patients was alcoholic in 63 (52%), cryptogenic in 36 (29.8%), post hepatitis B in 11 (9.1%) and miscellaneous in 11 (9.1%). The distribution of etiologies in the miscellaneous group was one congestive, three post jejuno-ileal bypass, one lupoid, five primary biliary cirrhosis and one alpha-1 anti-trypsin deficiency. In 1981 the complications were jaundice in 55 patients, ascites in 52, and encephalopathy in 10. There was a history of gastrointestinal bleeding in 25 patients. Thirty-five patients had no complications, and none had evidence of hepatocellular carcinoma. Forty patients had no complications, 41 had one, 30 had two, seven had three, and two had four. Over the next seven years an additional 20 patients developed ascites, 15 gastrointestinal bleeding, and 32 encephalopathy. Three hepatocellular carcinomas were diagnosed (Table 2).

After seven years 65 patients had died (53.8%). The five year mortality was 43.8%. If one assumed that all 55 patients who were lost to follow-up died, the seven year mortality rate would be 68.2%. The seven year mortality was 60.3% in alcoholic cirrhosis and 50% in cryptogenic cirrhosis. Three of the 11 patients with hepatitis B cirrhosis and six of the 11 patients in the miscellaneous group died. The major causes of death were liver failure (40%), nonliver causes (cardiovascular, cerebrovascular and nonhepatic malignancies) (32.3%), and gastrointestinal bleeding (13.9%). One patient died of hepatocellular carcinoma. In 12.3% of patients, the cause of death was unknown.

Statistical comparison of the number of complications per patient in 1981 between patients who survived and those who died showed that patients who survived had fewer complications than those who died ($P < 0.025$) (Figure 1).

DISCUSSION

Alcoholic cirrhosis was present in 52% of the present study group and was the most common type of cirrhosis. Alcoholic cirrhosis is also the most com-

Figure 1) Comparison of number of initial complications (ascites, jaundice, gastrointestinal bleeding and encephalopathy) in the survivors and the deceased (n=121). χ^2 value for distribution of number of complications for both groups: $\chi^2=12.94$; $df=4$; $P<0.025$

TABLE 2
Complications in 1981 and new complications developing between 1981 and 1988

Complications	1981	1988
Ascites	52 (43%)	20
Gastrointestinal bleeding	25 (20.3%)	15
Encephalopathy	10 (8.3%)	32
Hepatocellular carcinoma	0	3

mon type of cirrhosis seen in Europe. In studies from Britain and Scandinavia (3-5), alcoholic cirrhosis accounted for 50 to 54% of cirrhotics. In Japan, however, alcoholic cirrhosis appears to be a less frequent cause of cirrhosis than in Canada and Europe, and accounted for 33% and 39% of cirrhotics in two series (6,7). Cryptogenic cirrhosis accounted for 29.8% and hepatitis B-related cirrhosis accounted for 9.1% of the cirrhotics in the present series. In Japan, cryptogenic cirrhosis was present in 41% and 39.5% in two series, and hepatitis B-related cirrhosis was present in 21% and 24% (6,7). These findings may be accounted for by the higher prevalence of viral hepatitis B in Japan. The development of more sensitive serological markers for hepatitis B, such as the polymerase chain reaction and the new serological test for hepatitis C, will likely reshape the data in the cryptogenic group of cirrhotics. It is possible that the cirrhosis in a significant number of patients in this group may be due to previously unrecognized hepatitis B or C.

When the present patients were first studied in 1981, 71.1% had complica-

tions of cirrhosis. Jaundice and ascites were most common, followed by gastrointestinal bleeding and encephalopathy. The frequency of complications was very similar in two studies reported from Britain (1,5). Over the next seven years there were numerous additional complications, noted in Table 2.

Established cirrhosis has a high mortality rate. In the present patients it was 43.8% at five years and 53.7% at seven years. If it is assumed that all of the patients lost to follow-up had died, the seven year mortality rate would be increased to 68.2%. In other studies the five year mortality ranges between 30 and 50% (9-11). The mortality rate is very similar in alcoholic (60.3%) and cryptogenic cirrhosis (50%). The numbers in hepatitis B and in the miscellaneous group of cirrhotics were too small to draw valid conclusions. In other studies the mortality rate appeared to be unrelated to etiology and was very similar in alcoholic, cryptogenic and hepatitis B-related cirrhosis (7-9).

The major causes of death attributable to liver disease in the present

patients were liver failure in 40%, gastrointestinal bleeding in 13.9% and hepatocellular carcinoma in one patient. In 12.3% the cause was unknown, and 32.3% died from non-hepatic causes. Similar findings have been reported from Scandinavia (10), but in Japan there was a much higher mortality due to hepatocellular carcinoma (7). In the present study only one patient died of hepatocellular carcinoma over seven years. The mortality rate from hepatocellular carcinoma following cirrhosis varies greatly. It was only 4% in the United States (11) and as high as 44% in Japan; however, this was over a 26 year follow-up (7). Hepatocellular carcinoma is much more prevalent in countries such as Japan, where there is a high prevalence of hepatitis B. It is clear that the incidence of hepatocellular carcinoma is increasing, both in the Far East (7) and in the West (12-14), possibly because of prolonged survival in cirrhotic patients, as well as improved means of detection and awareness of causal relationships.

There have been a number of studies which have attempted to identify prognostic indicators in cirrhosis. This is now of some importance, since it may help to identify patients who will benefit from a variety of treatment modalities, particularly liver transplantation. Clinical, biochemical and morphological factors have been assessed often in combination (15), and until recently Child's criteria have been used most frequently (16). The present authors have shown that when the frequency of initial complications in patients who survived was compared to the frequency in those who had died seven years later, there were significantly fewer complications in the survivors. Thus, assessment of the number of complications when patients are first seen may be a useful bedside indicator of prognosis, the predictive value of which should be validated prospectively in an independent series of patients.

In conclusion, the authors have shown that in Toronto, cirrhosis is often ethanol related, cryptogenic or due to chronic hepatitis B infection; that complications are frequent; and that mortality is still high. They have

also shown that the number of complications when the patient is first seen may be a useful clinical indicator of prognosis and may help to identify candidates for liver transplantation. Since a significant number of cases of cirrhosis are preventable, the authors suggest that efforts directed towards prevention of cirrhosis may be more rewarding than those directed towards therapy.

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