Follow-up of Patients after Variceal Eradication

A Comparison of Patients with Cirrhosis, Noncirrhotic Portal Fibrosis, and Extrahepatic Obstruction

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One hundred one patients, 54 with cirrhosis of liver, 31 with noncirrhotic portal fibrosis (NCPF), and 16 with extrahepatic obstruction (EHO), were followed up at monthly intervals for a mean (±SD) period of 17.9 ± 4.8 months after achieving total variceal eradication with endoscopic sclerotherapy. Recurrence of esophageal varices was seen in 19 (18.8%) patients, 12 with cirrhosis and seven with NCPF, within a mean (±SD) period of 5.7 ± 1.6 months. No patient with EHO showed recurrence. Three (2.9%) patients rebled from the recurred varices. Mean (±SD) number of sclerotherapy sessions and the amount of absolute alcohol required for eradication of recurred varices were 1.6 ± 0.8 and 3.6 ± 1.8 ml, respectively. Dysphagia and esophageal stricture were present in 15 (14.9%) patients with nearly similar frequency in patients with cirrhosis, NCPF, and EHO. Dysphagia in four patients with stricture improved without dilatation. While there were no deaths in patients with NCPF and EHO, 11 patients with cirrhosis died. There was significant ($p < 0.01$) improvement in the liver status of surviving patients with cirrhosis after variceal eradication. It can be concluded that variceal recurrence and rebleeding are not major problems after sclerotherapy. Sclerotherapy probably helps in spontaneous improvement of the liver status of surviving cirrhotics and reduces long-term morbidity and mortality of patients with NCPF and EHO.

ENDOSCOPIC SCLEROTHERAPY (EST) has now become the treatment of first choice for controlling and preventing hemorrhage from esophageal varices.[1-3] Prospective randomized clinical trials comparing long-term effects of EST with conservative medical management and portacaval shunt surgery are now becoming available.[4-10] Although almost all the studies indicate that EST decreases the incidence of variceal bleeding, they have failed to resolve whether EST affects overall survival in these patients. These studies have, however, looked at mortality and morbidity figures from the point of entry of a patient into EST treatment and not after total variceal eradication has been achieved. Also, almost all the patients included in these studies had cirrhosis of the liver. However, 20–25% of the patients with portal hypertension in developing countries suffer from noncirrhotic portal fibrosis (NCPF).[2,11] Extrahepatic obstruction (EHO) is also an important cause of portal hypertension in most parts of the world. Both NCPF and EHO patients have good liver functions[12] and theoretically should be able to lead a relatively normal life, if their problem of variceal bleeding is effectively controlled. In this article, we have critically analyzed the morbidity and mortality in three groups of portal hypertensive patients, namely, cirrhosis, NCPF, and EHO, after variceal eradication.

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Submitted for publication: November 5, 1985.

Material and Methods

Patients

Out of 137 consecutive patients admitted with variceal bleeding between February 1983 and January 1985, 101 patients (62 males and 39 females, with a mean ± SD age of 34.6 ± 14.9 years), who had achieved total eradication of varices with EST, were included in the present study and were followed up by repeated endoscopies using Olympus GIF-Q, D_3, or XP endoscopes (Olympus Optical Co., Ltd., Shinjuku-ku, Tokyo, Japan). Of the remaining 36 patients, 27 died from various causes (Fig. 1) during the course of EST and nine patients were lost to follow-up after receiving initial sclerotherapy. Fifty-four patients had cirrhosis of the liver (21 alcoholic, 33 cryptogenic or posthepatitic), 31 had NCPF, and 16 had EHO (Table 1). Patients were classified at admission according to Child's classification: 54 belonged to Child's A (9 with cirrhosis, 29 with NCPF, and 16 with EHO), 16 to Child's B (14

with cirrhosis and 2 with NCPF), and the rest, 31, to Child's C (all cirrhotics) category.

The patients were entered into the trial from the date when total eradication of varices was identified by two independent observers. Variceal eradication was achieved by injecting absolute alcohol intravariceally and using an indigenously designed Teflon® injector, as described earlier.[13,14] Each patient was closely followed and was assessed both clinically and endoscopically at regular 4-weekly intervals. Development or persistence of ascites, jaundice, hepatic encephalopathy, or dysphagia was recorded. Endoscopies were done to detect recurrence of varices, the number and pattern of new veins and any change in the status of existing gastric varices or development of new gastric varices. EST was repeated every 4 weeks till total eradication of recurred varices was achieved. The patients were maintained on oral antacids, iron, folic acid, and, if needed, diuretics and hepatic coma regimen.

Statistics

Results of various observations were reported as mean ± standard deviation of the mean. Statistical significance of different parameters was determined by Student's t-test and chi square analyses. The clinical course of the patients with cirrhosis of the liver was analyzed in two ways: (1) comparison of the pre- and postsclerotherapy liver status using Child's classification (the statistical analyses were done using the chi square test for matched pairs in polychotomy[15]), and (2) comparison of the morbidity and mortality during the follow-up period of patients with NCPF and EHO.

Results

Variceal Recurrence

Mean (±SD) period of follow-up was 17.9 ± 4.8 (range: 6 to 27) months (Table 1). Nineteen (18.8%) patients were detected to have a recurrence during this period; 12 (22.2%) with cirrhosis of the liver and seven (22.5%) with NCPF. None of the patients with portal hypertension due to EHO had shown recurrence of varices. There was no significant difference in the pattern of recurrence between patients with cirrhosis of liver and NCPF (Table 1). Ten of these patients belonged to Child's A, three to Child's B, and six to Child's C category of liver disease. Fourteen (74%) patients had grade 4 and the remaining had grade 3 varices at the time of initial admission (prior to first EST). The mean (±SD) time of reappearance of veins was 5.71 ± 1.6 months (range: 3 to 10 months) after eradication. Distinct variceal columns were seen in all the patients. These recurred veins generally looked thin, short, and superficial.

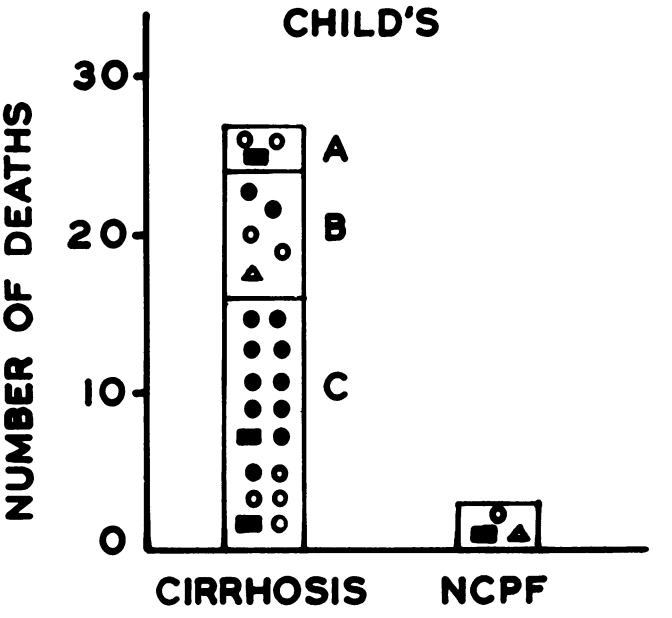

FIG. 1. The causes of death in 27 patients who died before variceal eradication could be achieved in them; symbolized as (○) death due to esophageal variceal bleeding, (■) due to bleeding from gastric varices, (●) due to hepatic coma, (△) due to pulmonary complications.

Gastric Varices

Nine (8.9%) patients had gastric varices before initial sclerotherapy. Five of these patients were among the 19 patients who had esophageal variceal recurrence. In all except three patients, gastric varices disappeared after esophageal variceal eradication and did not recur in any. In these three patients, the size of the gastric varices remained unaltered.

Resclerotherapy

Thirty-one EST sessions were required by the 19 patients with recurrence of varices. The mean (±SD)

TABLE 1. *Observations on Patients with Recurrence of Varices**

Parameter	Cirrhosis (N = 54)	NCPF (N = 31)	EHO (N = 16)	Total (N = 101)
Patients with variceal recurrence	12 (22.2)†	7 (22.5)	0	19 (18.8)
Follow-up (months)	18.6 ± 4.2	17.5 ± 5.7	16.9 ± 4.2	17.9 ± 4.8
Time of recurrence (months)	5.45 ± 1.7	6.0 ± 1.4	—	5.7 ± 1.6
Number of varices	1.5 ± 0.6	1.2 ± 0.5	—	1.3 ± 0.54
Number of EST sessions	1.6 ± 0.6	1.6 ± 0.9	—	1.6 ± 0.8
Amount of alcohol (ml)	4.0 ± 1.7	3.4 ± 2.1	—	3.6 ± 1.8

* Values of various parameters are shown as mean ± SD.

† Values in parentheses denote percentages.

TABLE 2. *Comparison of the Liver Status of Cirrhotics—Pre- and Postvariceal Eradication*

Child's Grade	Presclerotherapy	After Variceal Eradication*	p
A	9	33	
B	14	11	$p < 0.01$
C	31	10	

* Evaluation done at the end of the follow-up period or at death.

number of EST sessions required per patient to totally obliterate the new varices and the mean (±SD) amount of alcohol required for this purpose is shown in Table 1. Four (21%) patients had a second recurrence within 3 to 5 months, which again could be tackled by one to two courses of EST.

Rebleeding

Rebleeding from varices occurred in three patients, two with cirrhosis and one with NCPF. Bleeding was from recurrence of esophageal varices below the post-sclerotherapy stricture in two patients, one with cirrhosis and another with NCPF. One patient with cirrhosis bled from gastric varices that were present before initial sclerotherapy and persisted after esophageal variceal eradication. Four other Child's C cirrhotics, in end stage hepatic failure, bled during the course of their terminal illness. Emergency endoscopy could not be performed in them to identify the site of bleeding because of deep coma.

Esophageal Stricture

Fifteen (14.9%) patients—six (11.7%) with cirrhosis, seven (22.5%) with NCPF, and two (12.5%) with EHO—had esophageal stricture with dysphagia at the time of entry into the trial. All of them were initially followed for a period of 2–3 months without dilatation and were treated with antacids and, if needed, metaclopramide (10 mg tds). Dysphagia improved spontaneously in four (27%) of them within this period. Eleven patients, however, required a mean (±SD) of 2.33 ± 0.87 dilatations to relieve their symptoms.

Clinical Course

Since in this study we have included follow-up of only those patients who had successfully completed variceal eradication, patients who died before total variceal obliteration was achieved have been excluded (Fig. 1).

All patients with NCPF, except two who belonged to Child's B class, and all the patients with EHO were in Child's A category in the presclerotherapy period. The two NCPF patients returned to Child's A category within a few days of variceal bleeding.

Applying the chi square test for matched pairs in polychotomy for assessing the liver status in the cirrhotic patients in the pre- and postsclerotherapy period, a significant ($p < 0.01$) increase was found in the number of patients who improved after EST, going from C to B as well as A and also from B to A category of Child's liver disease (Table 2).

Of the 10 patients with cirrhosis who continued in Child's C category, six suffered from chronic intermittent portasystemic encephalopathy. Three other patients continued moderate drinking and persisted with ascites and jaundice. One patient remained with refractory ascites. Patients belonging to NCPF and EHO groups continued in Child's A class with good liver functions all through.

There were 11 (10.9%) deaths after total variceal eradication was achieved, all in the cirrhotic group. Eight patients belonging to Child's C category succumbed to hepatic encephalopathy. Four of these patients developed upper gastrointestinal hemorrhage during the course of the terminal disease. Two other patients died of rebleeding from varices. One patient, an epileptic female with Child's A cirrhosis, committed suicide by taking an overdose of phenobarbitone. There were no deaths in the NCPF and EHO groups.

Discussion

One of the strong criticisms of the efficacy of endoscopic sclerotherapy has been a high incidence of rebleeding.[16] This could occur after initial successful eradication of esophageal varices due to recurrence of esophageal varices, development or enlargement of existing gastric varices, or incidental erosive mucosal lesions of the upper gastrointestinal tract. Theoretically, if careful attention is paid to manage each of these possible etiological factors, it should be possible to minimize the chances of rebleeding. The results of our study support this contention. While recurrence of esophageal varices was seen in 18.8% of patients, rebleeding was encountered only in three (2.9%). Reports from Cape Town and King's College Hospital, London, have mentioned recurrence of varices in about two-thirds of patients with a high incidence of rebleeding.[8,16] Our lower rebleeding rates could possibly be because of our policy of monthly re-endoscopy, which would detect variceal recurrence much earlier than others who have followed up their patients at 3–12 monthly intervals.[5,8,16] Since, in all these studies, rebleeding was due to recurrence of esophageal varices, it can be argued that these bleeding episodes could have been prevented had endoscopy and repeat EST been done at an early date, as was done in our study.

As in two of our patients, one is sometimes faced with the problem of recurrence of varices below the level of esophageal stricture. Besides the apprehension of rupturing the varices during dilatation, recurred veins in these

patients are likely to be missed at endoscopy and may result in massive bleeding. Management of bleeding from such recurred varices below an esophageal stricture is often difficult.

Little is known about the fate of gastric varices after eradication of esophageal varices. While some investigators have reported that they disappear once esophageal varices are obliterated,[17] others maintain that gastric varices can bleed after ablation of esophageal varices, whether due to an increase in the size of existing gastric varices or to the appearance of new gastric varices is not clearly known. In the present study, gastric varices disappeared in two-thirds of the patients after esophageal variceal eradication. In none of the 19 patients who had recurrence of esophageal varices did gastric varices appear. The possibility of gastric varices appearing at a later date, when esophageal varices have already become large, cannot, however, be excluded. Terblanche et al.[7] have reported two patients who presented with bleeding from gastric varices after being lost to initial follow-up.

The incidence of other bleeding lesions associated with portal hypertension is very low in developing countries like India.[11] This could possibly be due to a relatively low incidence of alcoholism and alcoholic cirrhosis in India as compared with the Western countries. In the present series also, alcoholic cirrhosis comprised only 20.8% of total patients with portal hypertension. We still advised regular antacids to our patients and asked them to avoid all steroidal and nonsteroidal drugs and alcohol and were successful in preventing bleeding from erosive mucosal lesions. Unlike earlier reports, recent studies from the West have indicated a low frequency of associated lesions.[18]

The frequency and profile of variceal recurrence was nearly similar between patients with NCPF and cirrhosis (Table 1). Varices had recurred in none of the patients with EHO. It is possible that recurrence occurs much later in this group of patients because of the presence of a larger number of extrahepatic collateral channels in them. In the only other report, Johnson et al.[19] found that patients with EHO remained free from rebleeding for a mean of 2.5 years, as compared with 10 months in cirrhotics. Severity of the underlying disease also was not found to influence variceal recurrence in our series.

There are conflicting reports about the efficacy of EST in improving the survival rates in cirrhotic patients.[10] While three controlled trials have shown better survival in the injected group of patients than in controls,[4–6] others have demonstrated little difference in the long-term survival between the two groups.[7–10] Confusion has been due to inconsistencies in patient selection, the points at which patients were entered in the trial, and the way in which the controls were treated.[20] While our results cannot indicate whether EST improved the overall survival in cirrhotic patients, as we have not included any conservatively treated controls and also have excluded deaths before variceal eradication was achieved, our data, however, clearly show that the liver status of surviving cirrhotic patients had improved with variceal obliteration (Table 2). There was a significant reduction in the number of patients belonging to Child's C class of liver disease after EST. Prognostic value of Child–Turcotte's criteria in medically treated cirrhosis has been reaffirmed recently.[21] Our observations are supported by preliminary observations by Macdougall et al.,[5] who have reported recovery in liver functions after EST. Although the exact mechanism underlying improvement in the liver status is not clear, it is likely to be due to spontaneous recovery, once EST reduces the onslaughts of bleeding.

Patients with noncirrhotic portal fibrosis and extrahepatic obstruction are known to have good liver functions.[11,12,22] While jaundice, ascites, and hepatic encephalopathy are quite uncommon, the only fatal complication seen in these patients is variceal bleeding.[22,23] Portacaval or lienorenal shunt surgery is accompanied with a fair degree of morbidity and mortality in patients with these two diseases.[11,24] The fact that 100% survival without significant morbidity could be accomplished by EST in these patients has great therapeutic potential. It is in these patients with NCPF and EHO that prophylactic EST can be contemplated in the future, once the technique of EST improves with reduced complications and mortality. Except for patients with massive splenomegaly and hypersplenism, EST may prove to be the most effective and useful treatment for this group of patients.

The long-term morbidity of EST was limited to dysphagia, which was present in 14.9% of patients. There was no significant difference in the incidence of dysphagia among the three groups of portal hypertensive patients. It has been earlier shown by us that esophageal ulcers occurring after EST are generally benign and should not be considered as a complication leading to stricture formation.[25]

Esophageal motility disorders leading to dysphagia without esophageal stricture formation have been reported by some workers.[26] We did not encounter this phenomenon. Dysphagia was, however, seen to improve spontaneously in four (27%) of our patients with the passage of time along with a reduction in esophageal narrowing. This could possibly be due to reorganization and slow resorption of the fibrous tissue of the stricture. A tendency to restricture formation and recurrence of dysphagia after initial successful dilatation of the stricture was not observed in any patient.

On the basis of our results, it can be concluded that recurrence of varices and rebleeding are not a major problem once variceal eradication has been accomplished. EST probably helps in improvement of the liver status of

surviving cirrhotics and overall survival of noncirrhotics and EHO patients. Keeping in mind the costs and overall complications of shunt surgery,[7] EST appears to be a safer, simpler, and a cost-effective treatment for the long-term management of portal hypertension.

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