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Alcoholic *Versus* Nonalcoholic Cirrhosis in a Randomized Controlled Trial of Emergency Therapy of Bleeding Varices

Marshall J. Orloff, M.D.,*,[1] Jon I. Isenberg, M.D.,† Henry O. Wheeler, M.D.,† Kevin S. Haynes, M.D.,† Horacio Jinich-Brook, M.D.,† Roderick Rapier, M.D.,† Florin Vaida, Ph.D.,‡ Robert J. Hye, M.D.,* and Susan L. Orloff, M.D.§

*Department of Surgery, †Department of Medicine/Gastroenterology, and ‡Department of Family and Preventive Medicine/Biostatistics and Bioinformatics, University of California, San Diego Medical Center, San Diego, California; and §Department of Surgery, Division of Abdominal Organ Transplantation, Oregon Health and Sciences University, Portland, Oregon

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Background. **It has been proposed that portal-systemic shunts be avoided in alcoholic cirrhotics because survival rate is allegedly lower in alcoholics than in nonalcoholics. We examined this issue in a randomized controlled trial.**

Methods. **Two hundred eleven unselected, consecutive patients with cirrhosis and bleeding esophageal varices were randomized to endoscopic sclerotherapy (EST) (*n* = 106) or emergency portacaval shunt (EPCS) (105). Treatment was initiated within 8 h. EST failure was treated by rescue portacaval shunt (PCS). Ten-year follow-up was 96%.**

Results. **Results strongly favored EPCS over EST ($P < 0.001$). Among EPCS patients, 83% were alcoholic and 17% nonalcoholic. Outcomes were (1) permanent control of bleeding 100% *versus* 100%; (2) 5-y survival 71% *versus* 78%; (3) encephalopathy 14% *versus* 19%; (4) yearly charges $38,300 *versus* $43,000.**

Conclusions. **EPCS results were similar in alcoholic and nonalcoholic cirrhotics. EPCS is an effective first line emergency treatment in all forms of cirrhosis, including alcoholic.**

Key Words: **cirrhosis; bleeding esophageal varices; emergency portacaval shunt; endoscopic sclerotherapy; alcoholic; nonalcoholic.**

INTRODUCTION

Alcoholic cirrhosis is by far the most common cause of bleeding esophageal varices (BEV) in the Western world [1–9]. By and large, use of portal-systemic shunts today has been relegated to elective rescue treatment for BEV only or mainly after endoscopic and pharmacologic therapies have failed to permanently control bleeding. Nevertheless, when portal-systemic shunts have been used for failed non-surgical therapy, it has been proposed that such procedures should be avoided in alcoholic cirrhotics because, according to retrospective, unrandomized observations of elective treatment of BEV, survival rate was significantly lower in alcoholic than in nonalcoholic cirrhotics, especially with respect to the distal splenorenal shunt [9–14]. We examined this important issue in a randomized controlled trial (RCT) in 211 unselected, consecutive patients with cirrhosis and acute BEV in whom emergency and long-term repetitive endoscopic sclerotherapy (EST) was compared with emergency direct portacaval shunt (EPCS), otherwise known as total shunt. The trial was conducted from April 18, 1988 to December 31, 2005 and was a community-wide endeavor known as the San Diego Bleeding Esophageal Varices Study. In two recent publications, we described the study in detail and reported the outcomes first with regard to control of bleeding and survival [15], and second with regard to development of portal-systemic encephalopathy (PSE) [16]. This report focuses on the influence of the etiology of cirrhosis, particularly alcoholism, on outcome, following EPCS.

PATIENTS AND METHODS

Design of Study

Our two recent publications [15, 16] described our RCT and provided full information on the protocols and methods. These include (1) design

[1] To whom correspondence and reprint requests should be addressed at University of California, San Diego Medical Center, 200 West Arbor Drive, San Diego, CA 92103-8999. E-mail: morloff@ucsd.edu.

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of study; (2) patient eligibility; (3) definitions of (a) bleeding esophageal varices (BEV), (b) unselected patients ("all comers"), (c) emergency endoscopic sclerotherapy (EST), (d) long-term endoscopic sclerotherapy (EST), (e) emergency portacaval shunt (EPCS), (f) failure of emergency primary therapy, (g) failure of long-term therapy, (h) rescue therapy, (i) informed consent; (4) randomization; (5) diagnostic work-up; (6) quantitative Child's classification; (7) initial emergency therapy during workup; (8) endoscopic sclerotherapy; (9) emergency portacaval shunt; (10) post-treatment therapy; (11) lifelong follow-up; (12) quantitation of PSE; (13) data collection. The design of our RCT required documentation of the presence or absence of alcoholism on admission and at every follow-up visit monthly for the first post-entry year and every 3 mo thereafter for 10 y or until death.

The study protocol and consent forms were approved before the start of the study and at regular intervals thereafter by the UCSD Human Subjects Committee (Institutional Review Board). Figure 1 is a consort flow diagram that shows the overall design and conduct of the RCT [17, 18].

Statistical Analysis

The comparison between alcoholic and nonalcoholic cirrhosis groups used Fisher's exact test for dichotomous outcomes and Wilcoxon rank-sum test (WRT) for continuous outcomes. Survival comparisons used Gehan-WRT. The change in Child's class was compared using the exact WRT, adjusted for ties. The average change in Child's class during the first 5 y was computed based on the time spent in each category (improved, unchanged, or worse) by patients at risk. A potential limitation of the study in which there were 18 nonalcoholic patients and 87 alcoholics was the relatively small sample size of the nonalcoholic group. The power to detect large effect sizes was 80%, with Cohen's d = 0.74 or larger.

RESULTS

EPCS *Versus* EST - Outcome Data

Our recent publications described the clinical characteristics of the 211 patients, findings on upper endoscopy and liver biopsy, results of laboratory blood tests, data on rapidity of therapy, data on control of bleeding, operative and endoscopic data, data on PSE, and data on survival [15, 16]. The two groups were similar in every aspect of cirrhosis and BEV. Histologic proof of cirrhosis was ultimately obtained in all patients. Mean and median times from onset of bleeding to entry in the San Diego BEV Study were less than 20 h in both groups of patients, and from onset of bleeding to start of EST and EPCS were less than 24 h. EST achieved permanent long-term control of bleeding in only 20% of

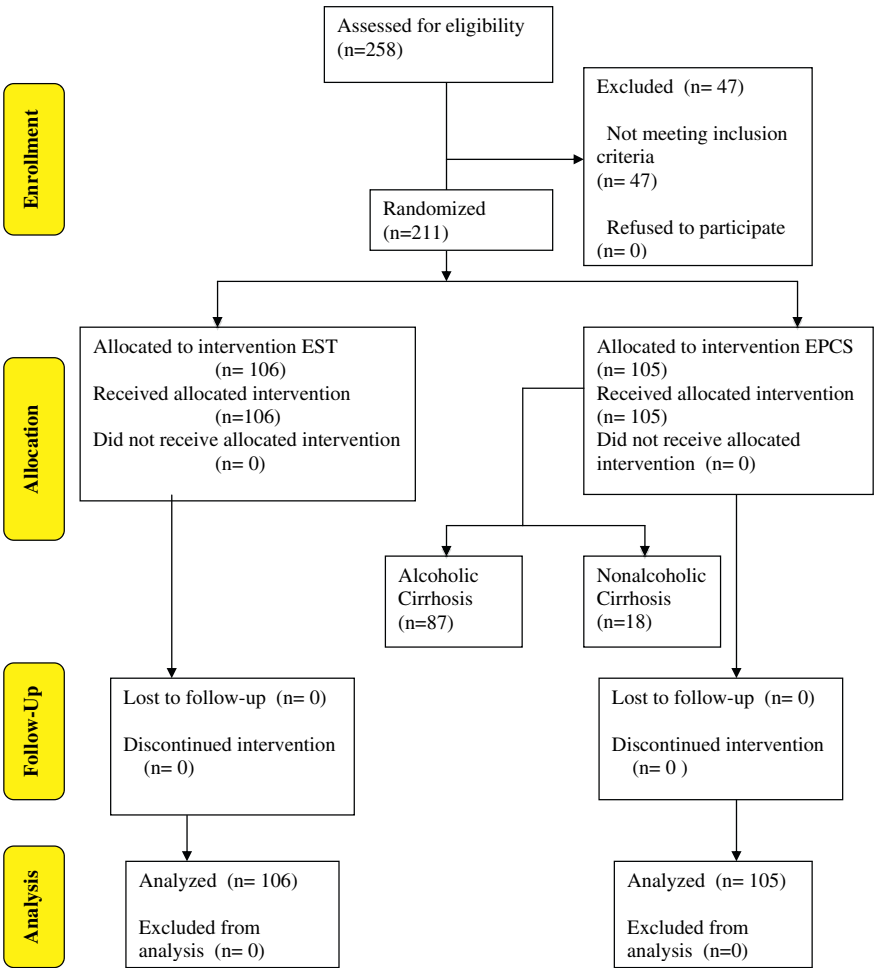

FIG. 1. Consort flow diagram showing the overall design and conduct of the prospective randomized controlled trial [17, 18]. (Color version of figure is available online.)