0270-9139/84/0403-0430$02.00/0
HEPATOLOGY

Vol. 4, No. 3, pp. 430–435, 1984
Printed in U.S.A.

Prognostic Value of Child-Turcotte Criteria in Medically Treated Cirrhosis

ERIK CHRISTENSEN, POUL SCHLICHTING, LIS FAUERHOLDT, CHRISTIAN GLUUD, PER KRAGH ANDERSEN, ERIK JUHL, HEMMING POULSEN, NIELS TYGSTRUP AND THE COPENHAGEN STUDY GROUP FOR LIVER DISEASES*

Medical Department A, Division of Hepatology, Rigshospitalet; Medical Department, Division of Hepatology, Department of Pathology, Hvidovre Hospital, University of Copenhagen; Statistical Research Unit, Danish Medical and Social Science Research Councils; Medical Departments B and C, Bispebjerg Hospital; Medical Department B, Frederiksberg Hospital; Medical Departments II, III and VII, Kommunehospitalet, Copenhagen, Denmark; University Institute of Pathological Anatomy, Århus, Denmark

The Child-Turcotte criteria (CTC) (based on serum bilirubin and albumin, ascites, neurological disorder and nutrition) are established prognostic factors in patients with cirrhosis having portacaval shunt surgery. The objective of this study was to evaluate the prognostic value of CTC in conservatively treated cirrhosis. Patients (n = 245) with histologically verified cirrhosis from a control group of a controlled clinical trial were studied. Data at entry into the trial were used to classify patients according to CTC. Survival curves for up to 16 years were made, and survival rates were compared using the log-rank test. Survival decreased significantly with increasing degree of abnormality (A → B → C) of albumin ($p < 0.001$), ascites ($p < 0.001$), bilirubin ($p = 0.02$) and nutritional status ($p = 0.03$). Survival was insignificantly influenced by neurological status ($p = 0.11$) probably because none of the patients had hepatic coma at entry into the trial. The five variables in CTC were combined to a score. With increasing score, the median survival time decreased from 6.4 years (score 5) to 2 months (scores 12 or more). Furthermore, the mortality from hepatic failure, gastrointestinal bleeding or hepatocellular carcinoma increased significantly with increasing score. CTC provide valuable and easily obtainable prognostic information in cirrhosis. However, CTC are inferior to a prognostic index based on multivariate analysis of prognostic factors.

In 1964, Child and Turcotte (1) published criteria for assessment of hepatocellular functional reserve to improve selection of candidates for portosystemic shunts. The relation of the Child-Turcotte criteria (CTC) to short- and long-term survival after portosystemic shunt operation has been investigated in several studies (2–11), showing that CTC has prognostic significance. However, CTC is of limited value in predicting the therapeutic effect of portal-systemic shunt (12, 13).

This report describes the prognostic significance of CTC in conservatively treated patients with cirrhosis who were followed up to 16 years.

PATIENTS AND METHODS

The patients were included in the placebo-treated group (260 patients) of a controlled clinical trial of prednisone (10 to 15 mg daily) versus placebo in cirrhosis (14).

Patients were included in the trial provided that the diagnosis was confirmed histologically, age was under 80 years, corticosteroids had not been given before and the patient was able and willing to cooperate (14).

Fifteen patients who underwent prophylactic portacaval anastomosis (1), therapeutic portacaval anastomosis (4) or injection sclerotherapy (10) (15) were excluded; data from the remaining 245 patients were analyzed. None of these patients had advanced neurological disorder ("coma") on entry into the trial. Standard treatment was used for fluid retention, encephalopathy, infections, and episodes of bleeding were treated with blood

Received May 25, 1983; accepted November 14, 1983.

* Members of the Copenhagen Study Group for Liver Diseases are: J. T. Balslev; M. Bjørneboe; P. Christoffersen; K. Eghøje; V. Faber; S. Gjørup; B. Harvald; K. Iversen; O. Jessen; E. Juhl; H. E. Jørgensen; A. R. Krogsgaard; S. A. Nørregaard; T. Steen Olsen; H. Poulsen; F. Quaade; L. Ranek; F. Raaschou; K. Schmidt; Å. C. Thomsen; N. Tygstrup; and P. Winkel.

Address reprint requests to: Erik Christensen, M.D., Department of Hepatology 233, University of Copenhagen, Hvidovre Hospital, 30 Kettegaard Alle, DK-2650 Copenhagen, Denmark.

transfusion and, if necessary, with the Sengstaken-Blakemore tube, vasopressin or both.

On the basis of prospectively recorded data on admission to the trial, the patients were grouped according to each of the five variables selected by Child and Turcotte (serum bilirubin and albumin, ascites, neurological disorder and nutrition) using criteria (CTC) shown in Table 1. The classification obtained by each variable was graded as follows: A as 1; B as 2, and C as 3. In each patient, the grade for each of the five variables was combined. Serum bilirubin was not measured in 8 and albumin in 2; ascites was not recorded in 3, neurological disorder in 1 and nutritional status in 1 patient. All five variables were registered in 231 of 245 patients. The CTC score was calculated only for the 231 patients who had five variables recorded.

Survival was analyzed by the lifetable method using the log-rank test for statistical comparison of survival rates (16). Statistical comparison of variables was made using χ^2 test (discontinuous variables) or Mann-Whitney or Kruskal-Wallis nonparametric tests (continuous variables). The CTC score was compared with other prognostic variables by analyzing its significance in a Cox regression model including previously identified prognostic factors (17) using a standard computer program (BMDP 2L) (18).

TABLE 1. CTC AND THEIR DISTRIBUTION IN THE PATIENTS

Group designation (grading)	A (1)	B (2)	C (3)
Serum bilirubin (mg%)	<2.0 (75%)	2.0–3.0 (11%)	>3.0 (14%)
Serum albumin (gm%)	>3.5 (52%)	3.0–3.5 (25%)	<3.0 (23%)
Ascites	None (80%)	Easily controlled[a] (9%)	Poorly controlled[b] (11%)
Neurological disorder	None (73%)	Minimal[c] (27%)	Advanced "coma" (0%)
Nutrition	Good[d] (80%)	Fair[e] (17%)	Poor[f] (3%)

[a] Slight ascites.
[b] Moderate or marked ascites.
[c] Minimal encephalopathy.
[d] Normal or fat.
[e] Meagre.
[f] Cachectic.

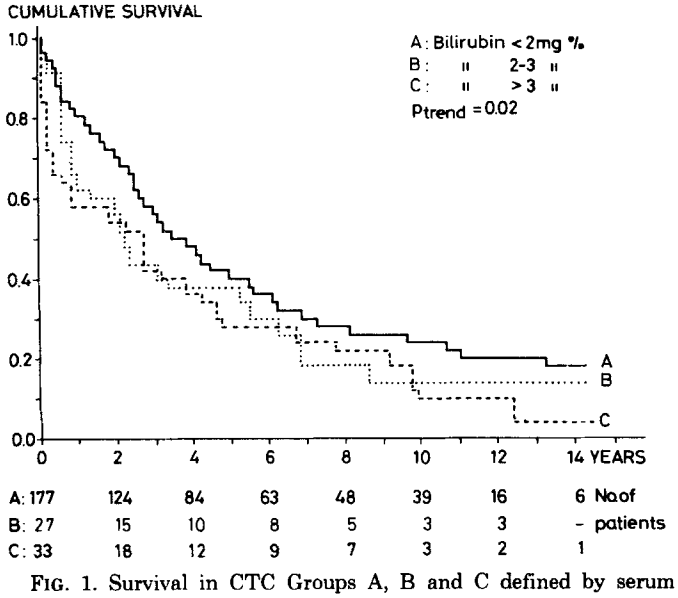

FIG. 1. Survival in CTC Groups A, B and C defined by serum bilirubin concentration.

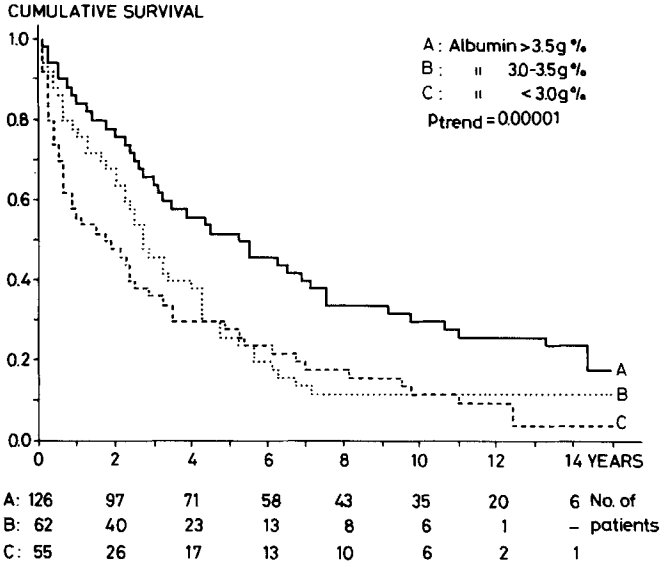

FIG. 2. Survival in CTC Groups A, B and C defined by serum albumin concentration.

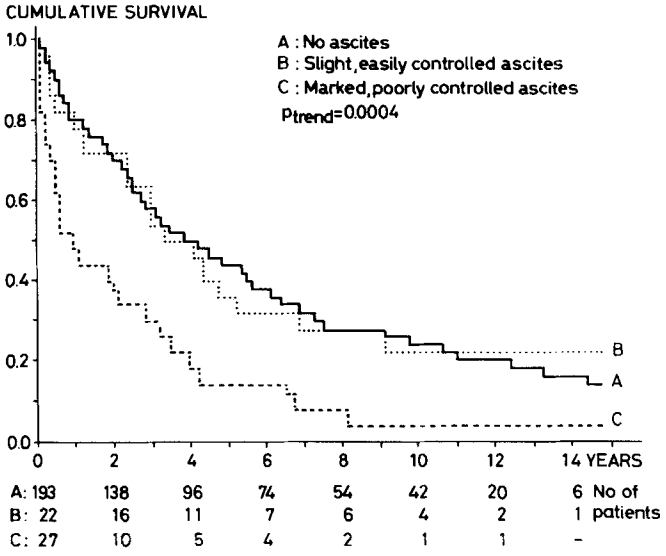

FIG. 3. Survival in CTC Groups A, B and C defined by degree of ascites.

RESULTS

The survival curves of patients in Groups A, B and C, respectively, for each of the five variables in CTC are shown in Figures 1 to 5. Figure 1 shows that patients with bilirubinemia <2 mg% had a slightly but significantly longer survival than did patients with bilirubinemia between 2 and 3 mg% or above 3 mg%. The patients

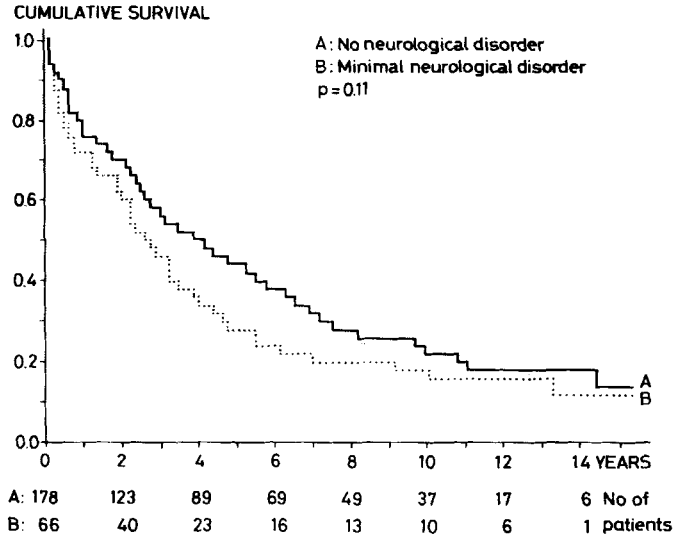

FIG. 4. Survival in CTC Groups A and B defined by neurological status.

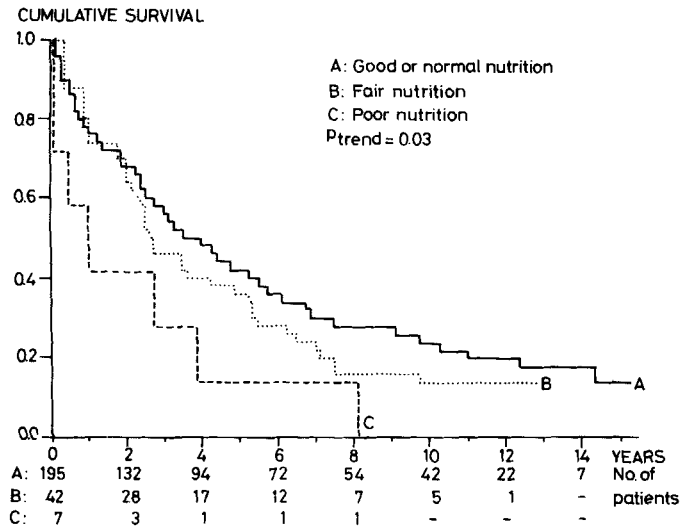

FIG. 5. Survival in CTC Groups A, B and C defined by nutritional status.

in the latter two groups had similar survival. With decreasing albumin level, there was a highly significant decrease in survival time (Figure 2). Marked ascites was associated with decreased survival compared with no or easily controlled ascites which was associated with similar survival rates (Figure 3). A tendency towards a decreased survival was seen if a slight neurological disorder (encephalopathy) was present, but this tendency was not statistically significant (Figure 4). None of the patients had advanced neurological disorders ("coma") on entry to the trial. With increasingly poor nutritional status, survival decreased (Figure 5).

Figure 6 shows the survival curves for patients grouped according to the combined CTC. A statistically significant trend of decreasing survival time with increasing total score was present. In Figure 7, a combination into three groups is shown.

Table 2 shows the distribution of other variables in groups defined by CTC score. Distribution of age, sex, duration of history, and alcoholism are similar in the three groups defined, but the higher scores were associated with other indicators of advanced disease.

This pattern is also reflected in the causes of death (Table 3). With increasing CTC score, mortality from hepatic cause increased significantly ($p_{trend} < 0.001$).

VALUE OF CTC COMPARED WITH OTHER PROGNOSTIC VARIABLES

We previously identified 12 significant prognostic variables (marked in Table 2) in 488 placebo or prednisone-treated patients (17). Of CTC, only ascites was among those variables. The other four variables in CTC were

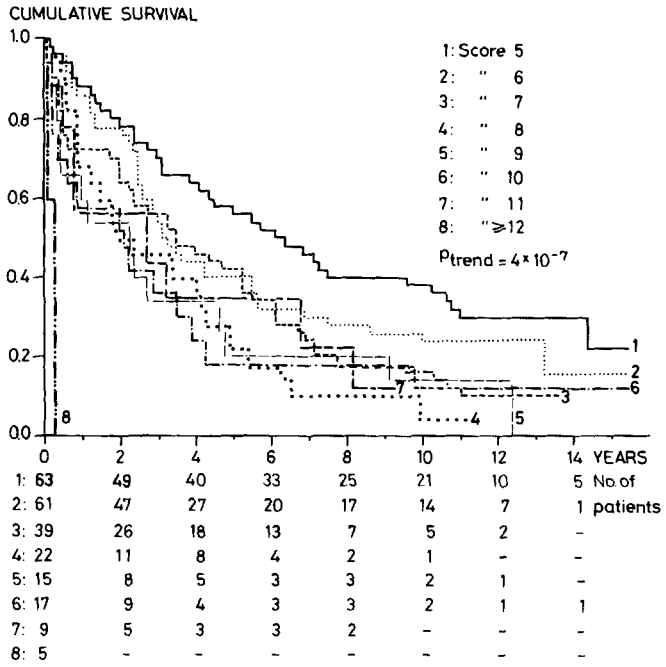

FIG. 6. Survival in nine groups defined by CTC score.

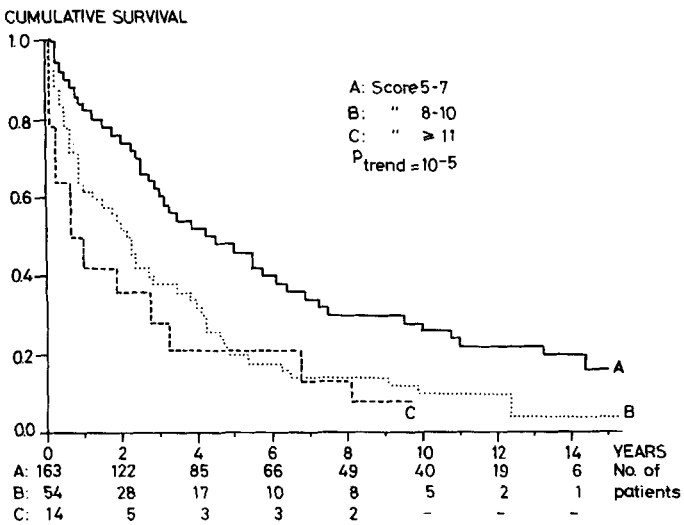

FIG. 7. Survival in three groups defined by CTC score.

TABLE 2. VARIABLES IN SUBGROUPS DEFINED BY CTC SCORE

Variable	CTC score			p Value
	≤7	8–10	≥11	
General	N:163	N:54	N:14	
Median age (years)[a]	60	59.5	59.5	0.91
Males (%)[a]	60	61	36	0.19
Median duration of history (months)	6	6	5	0.96
Clinical				
[Ascites (%)[a]	2	52	100]	
[Neurological disorder (%)	5	15	36]	
[Nutritional status affected (%)	12	33	57]	
Steadily progressive course (%)	36	75	85	<0.0001
Alcoholism (%)	42	44	29	0.56
Incapacitation (%)	25	51	79	<0.0001
Spider nevi (%)	21	54	64	<0.0001
Peripheral edema (%)	17	54	79	<0.0001
Esophageal varices on radiography (%)	6	10	36	0.0008
Median systolic/diastolic blood pressure (mm of mercury)	140/85	140/85	123/75	0.005/0.009
Median body weight (kg)	66.5	64.9	64.1	0.34
Biochemical				
[Median bilirubin (mg%) (<1.0)	0.9	2.4	3.9]	
[Median albumin (gm%) (>4.4)	3.84	2.80	2.37]	
Median aspartate amino transferase (mmoles/liter/hr) (<1.7)	2.8	4.6	3.2	0.002
Median alkaline phosphatase (King Armstrong Units) (<10.0)	12.6	15.2	16.3	0.03
Median acetylcholine esterase (μmoles/min/ml) (2.0–6.1)[a]	3.00	1.40	1.58	<0.0001
Median prothrombin index (% of normal) (>70)[a]	73	51.5	42.5	<0.0001
Median γ-globulin (gm%) (<1.1)	1.60	2.20	2.80	<0.0001
Median sulfobromophthalein retention (% after 45 min) (<5)	18.5	30.0	40.7	<0.0001
Antinuclear factor (%)[a]	32	45	50	0.28
Histological				
Parenchymal nodules ≥ normal lobules (%)[a]	18	11	9	0.88
Large piece-meal necroses (>5 hepatocytes) (%)[a]	15	20	36	0.14
Efferent veins in parenchymal nodules (%)[a]	42	32	45	0.47
Moderate or marked liver connective tissue inflammation (%)[a]	62	58	45	0.53
Small focal liver cell necroses (%)[a]	75	80	82	0.70
Eosinophil leucocytes in liver parenchyma (%)[a]	20	15	27	0.57
Predominantly broad connective tissue septa (%)	38	61	91	<0.0001
Nonseptal fibrosis > 500 μm (%)	15	30	45	0.007
Blurred septal-parenchymal junction (%)	39	49	82	0.01
Pericellular fibrosis (%)	21	26	67	0.02
Dilated sinusoids (%)	8	13	36	0.01
Increased amount of connective tissue in sinusoids (%)	13	18	56	0.01
Chronic aggressive hepatitis (%)	21	24	0	0.20

[a] Previously identified prognostic variable in a Cox regression analysis (17).

eliminated as insignificant in the multivariate model (17).

Considering only placebo-treated patients, we included CTC score in a new Cox regression analysis (17, 18) together with 12 previously identified prognostic variables and performed a stepwise elimination of insignificant variables (backward elimination). CTC score was not significant at any step of the analysis and was eliminated (after ascites) in the last step. Since this analysis was based on fewer patients (the placebo group only) not all of the 12 originally identified prognostic variables remained significant.

Thus, the prognostic value of CTC is incomplete; other variables have additional prognostic information (17).

INFLUENCE OF PREDNISONE TREATMENT

In prednisone-treated patients, the prognostic value of CTC was similar to that observed in placebo-treated

TABLE 3. CAUSES OF DEATH IN SUBGROUPS DEFINED BY CTC SCORE

	CTC score			Total
	≤7	8–10	≥11	
No. of patients	163	54	14	231
No. of deaths (% of patients)	126 (77%)	50 (93%)	13 (93%)	189
Main cause of death				
Hepatic (% of deaths)	54 (43%)	36 (72%)	11 (85%)	101
Hepatic failure	27	16	6	49
Hepatic failure and GI bleeding	11	14	3	28
GI bleeding	9	6	2	17
Hepatocellular carcinoma	6	0	0	6
Splenectomy	1	0	0	1
Nonhepatic (% of deaths)	72 (57%)	14 (28%)	2 (15%)	88
Infection	10	4	0	14
Cardiovascular disease	32	7	2	41
Extrahepatic malignancy	20	1	0	21
Other nonhepatic cause	10	2	0	12

patients except for the following: during prednisone treatment, prognosis was slightly better in patients with albumin of 3.0 to 3.5 gm% ($p = 0.03$), without ascites ($p = 0.03$), but slightly worse in patients with marked ascites ($p = 0.06$) compared to placebo treatment.

DISCUSSION

CTC were not the result of systematic analysis of all potentially useful prognostic variables but emerged from general clinical experience in assessing hepatocellular functional reserve in patients considered for portosystemic shunt operation. Nevertheless, CTC have proved to be important prognostic factors in patients who undergo portosystemic shunt operation (2–11). Unfortunately, CTC have not proved useful in deciding if patients should be recommended for portal-systemic shunt or medical treatment (13). The explanation may be that CTC—as shown in this report—have a similar prognostic value in conservatively treated patients.

CTC Categories B and C are indicators of advanced liver disease and were designed for patients being considered for portal-systemic shunt operation. Among such patients, there is an almost equal distribution of patients in Categories A, B and C (11). In contrast, the present study includes few patients in Category C because criteria of inclusion (see "Patients and Methods") were not fulfilled by some of the more severely ill patients (19) of which many would be in Category C. Furthermore, we studied the data at admission to the trial corresponding rather closely to the time of diagnosis, while most reports on patients having portal-systemic shunt operations performed analyze data at the time patients are considered for portal-systemic shunting. Thus, selection of patients and early assessment of CTC explain why Categories A and B are more frequent in our patients. Nevertheless, in our patients, CTC had a significant prognostic influence which is similar to that reported for shunted patients (2–11).

Of the individual criteria, serum albumin had the most marked prognostic influence followed by degree of ascites; serum bilirubin and nutritional status had less prognostic influence. Neurological status had no significant prognostic influence, probably because none of the patients had coma at the entry into the trial.

Combination of the five variables to a score markedly increased the prognostic information. As emphasized by Conn, there is no general agreement as to how the criteria should be combined (11). Many reports use addition of the numbers 1, 2 or 3 (for A, B or C) for each of the five components to a total score between 5 and 15. This scoring, which implies equal weighing of the five variables, may not be optimal but it has the advantage of simplicity. The definition of Groups A, B and C for the combined criteria varies considerably (11). One may prefer to use the raw score between 5 and 15 giving a more finely graded measurement of the prognosis. As seen from Figure 6 survival decreases with increasing score. The effect of patients with coma on the score is missing in our data and may be limited because patients with coma are likely to have a high score contribution (2 or 3) from other components, and prognosis is already extremely poor for scores of 12 and above (Figure 6). Since the groups with the highest scores include few patients, the prognostic results for these scores are less precise. Accordingly, we condensed the groups to a smaller number. After condensation into three groups, there was still a considerable difference in the survival curves (Figure 7).

The prognostic influence of CTC was also reflected in causes of death. The mortality from hepatic cause increases significantly with increasing score.

A number of clinical, biochemical and histological variables besides CTC differed in patients with different CTC score (Table 2) implying correlation with CTC. Some of these variables (marked in Table 2) have previously proved prognostic (17). Some of the latter (acetylcholinesterase and prothrombin index) closely correlate with CTC score (Table 2) and may explain why the CTC score did not contribute significantly in the Cox regression analysis. However, variables which do not significantly correlate with CTC score have been identified as important prognostic variables [e.g., age, sex and more histologic variables (Table 2)]. These variables have additional prognostic information. Thus, CTC do not comprise the optimal combination of prognostic factors. Nevertheless, because CTC are simple and easily applicable in clinical practice, they may be useful for quick assessment of prognosis.

Acknowledgments: We thank the Department of Data Processing at Rigshospitalet for generous computer access and secretary Inger-Lise Petersen for valuable assistance.

REFERENCES

1. Child CG, Turcotte JG. Surgery and portal hypertension. In: Child CG, ed. The liver and portal hypertension. Philadelphia: W. B. Saunders Co., 1964: 50.
2. Wantz GE, Payne MA. Experience with portacaval shunt for portal hypertension. N Engl J Med 1961: 265:721–728.
3. Foster JH, Ellison LH, Donovan TJ, et al. Quantity and quality of survival after portosystemic shunts. Am J Surg 1971; 121:490–501.
4. Campbell DP, Parker DE, Anagnostopoulos CE. Survival prediction in portacaval shunts: a computerized statistical analysis. Am J Surg 1973; 126:748–751.
5. Turcotte JG, Lambert MJ. Variceal hemorrhage, hepatic cirrhosis, and portacaval shunts. Surgery 1973; 73:810–817.
6. Cameron JL, Zuidema GD, Smith GW, et al. Mesocaval shunts for the control of bleeding esophageal varices. Surgery 1979; 85:257–262.
7. Dowling JB. Ten years experience with mesocaval grafts. Surg Gynecol Obstet 1979; 149:518–522.
8. Smith RB, Warren WD, Salan AA, et al. Dacron interposition shunts for portal hypertension. Ann Surg 1980; 192:9–17.
9. Cello JP, Deveney KE, Trunkey DD, et al. Factors influencing survival after therapeutic shunts. Am J Surg 1981; 141:257–265.
10. Conn HO, Resnick RH, Grace ND, et al. Distal splenorenal shunt vs. portal-systemic shunt: current status of a controlled trial. Hepatology 1981; 1:151–160.
11. Conn HO. A peek at the Child-Turcotte classification. Hepatology 1981; 1:673–676.
12. Resnick RH, Chalmers TC, Ishihara AM, et al. A controlled study of the prophylactic portacaval shunt. Ann Intern Med 1969; 70:675–688.
13. Resnick RH, Iber FL, Ishihara AM, et al. A controlled study of the therapeutic portacaval shunt. Gastroenterology 1974; 67:843–857.
14. Copenhagen Study Group for Liver Diseases. Sex, ascites and alcoholism in survival of patients with cirrhosis. Effect of prednisone. N Engl J Med 1974; 291:271–273.
15. Christensen E, Fauerholdt L, Schlichting P, et al. Aspects of the natural history of gastrointestinal bleeding in cirrhosis and the effect of prednisone. Gastroenterology 1981; 81:944–952.
16. Peto R, Pike MC, Armitage P, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. Br J Cancer 1977; 35:1–39.
17. Schlichting P, Christensen E, Andersen PK et al. Prognostic factors in cirrhosis identified by Cox's regression model. Hepatology 1983; 3:889–895.
18. Dixon WJ. BMDP statistical software. University of California Press, Berkeley, Los Angeles, 1981.
19. Juhl E, Hilden M, Tygstrup N, et al. Effect of selection in controlled clinical trials. A supplement to the CSL predisone trial in cirrhosis. Scand J Gastroenterol 1971; Suppl 9:171–175.