

# Aminopyrine breath test in the prognostic evaluation of patients with cirrhosis

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## Abstract

This prospective study assessed the role of aminopyrine breath test in the prognosis of patients with cirrhosis, and evaluated whether the test provided useful information not included in the Pugh score. During a period of 36 months, 125 patients with biopsy proven liver cirrhosis were included, and followed for up to 48 months (median 17 months). During follow up 43 patients died (20 of liver failure). Survival was univariately related to aminopyrine breath test ( $p < 0.02$ ), Pugh score ( $p < 0.01$ ), presence of ascites ( $p < 0.01$ ), and sex ( $p < 0.05$ ). Using Cox's regression analysis, Pugh score, aminopyrine breath test, and sex, were independent significant predictors of survival. From the Cox's model a prognostic index was computed. According to a receiver operating characteristic curve analysis, the prognostic index predicting death showed an improvement in area under the curve when compared with a prognostic index calculated excluding aminopyrine breath test, but the improvement did not reach statistical significance ( $p = 0.12$ ). A similar prognostic index was calculated to predict death from liver failure. Cox's regression analysis selected aminopyrine breath test, Pugh score, and aetiology as the best set of predictor covariates. According to a receiver operating characteristic curve analysis, a prognostic index cut off value of 2.6 had a 94% sensitivity and a 88% specificity. The prognostic index significantly improved prognostic accuracy when compared with a prognostic index calculated from Pugh score and aetiology, but excluding aminopyrine breath test ( $p = 0.05$ ). These data disclose that the aminopyrine breath test offers additional prognostic information to the Pugh score, and it may become a useful tool to better assess the prognosis of patients with cirrhosis.

As liver transplantation is now frequently offered to patients with end stage liver disease, the prognosis of patients with liver cirrhosis has aroused great interest. From a clinical point of view, the common clinical and biochemical data included in the Child-Turcotte-Pugh classification<sup>1</sup> are considered the most useful indicators of prognosis in these patients.<sup>2-4</sup> In addition, they possess the advantage of easy feasibility and low cost. A more precise definition of prognosis in cirrhosis is desirable, however, and different approaches have been attempted to improve prognostic accuracy.<sup>5-10</sup>

The aminopyrine breath test<sup>11</sup> is considered useful to evaluate patients with liver disease.<sup>12-13</sup> It is a non-invasive quantitative liver function test, which accurately predicts the outcome of

acute liver failure,<sup>14</sup> of alcoholic hepatitis,<sup>15</sup> and the risk of surgery in patients with liver disease.<sup>16</sup> Its role in the prognostic evaluation of patients with cirrhosis is uncertain. Although it is consistently found to be a predictor of survival when considered alone,<sup>17-20</sup> in two previous studies it has not been shown to significantly improve the prognostic accuracy resulting from the Pugh score.<sup>18, 20</sup>

The aim of this study is to assess the usefulness of the aminopyrine breath test in improving prognostic accuracy obtained from the Pugh score in patients with cirrhosis of the liver.

## Methods

### PATIENTS

During a period of 36 months, all patients with liver cirrhosis, admitted to the Department of Clinical Medicine, University of Padua, who fulfilled the entry criteria were entered into the study. These criteria were (i) presence of biopsy proven cirrhosis, (ii) age less than 75 years, (iii) absence of other diseases having a short prognosis per se, (iv) informed consent and willingness to cooperate in the study. One hundred and twenty five patients were selected from a group of 167 patients with chronic liver disease. Clinical and biochemical data in the 42 excluded patients are reported in Table I. Reasons for exclusion were lack of histological diagnosis in 15 patients (inability to perform the biopsy in 11, refusal in four), extrahepatic malignancies in 10 patients, hepatocellular carcinoma shown in the index or previous admission in seven patients, inability to collaborate in six patients, age over 75 years in four patients. Excluded patients did not differ in any clinical or biochemical variable from the group of 125 included patients (Table I). In these 125 patients reasons for admission were ascites and/or oedema in 69 patients, presence of oesophageal varices without previous bleeding in 20, previous digestive haemorrhage for which patients were referred for possible treatment in 12, and acute gastrointestinal bleeding in 19. Five patients were admitted for unspecific complaints.

TABLE I Clinical and biochemical data of the 42 excluded patients

Age	55 (43-64)
Sex (M/F)	35/7
Aetiology (alcoholic/non-alcoholic)	29/13
Ascites	19
Encephalopathy (grade I/II)	5/3
s-albumin (g/l)	33 (28-39)
s-bilirubin ( $\mu\text{mol/l}$ )	24 (16-45)
Prothrombin index (%)	50 (34-80)

Reference values: s-albumin: 35-50 g/l; s-bilirubin 2-17  $\mu\text{mol/l}$ ; prothrombin index: 80-100%. Data are expressed as median and interquartile range, when applicable. No significant difference from the group of 125 included patients in any variable (Mann-Whitney test, or Fisher's exact test, when applicable).

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TABLE II Clinical and biochemical data of the 125 included patients

Age	56 (45-63)
Sex (M/F)	97/28
Aetiology (alcoholic/non-alcoholic)	94/31
Ascites	75
Encephalopathy (grade I/II)	7/4
s-albumin (g/l)	33 (27-38)
s-bilirubin ( $\mu\text{mol/l}$ )	28 (14-48)
Prothrombin index (%)	54 (42-65)
Pugh score	8 (6-9)

Reference values: s-albumin: 35-50 g/l; s-bilirubin 2-17  $\mu\text{mol/l}$ ; prothrombin index: 80-100%. Data are expressed as median and interquartile range, when applicable.

Aetiology of cirrhosis was alcoholic in 94 patients, posthepatic in 24, cryptogenic in seven. No patient had primary biliary cirrhosis, haemochromatosis, or Wilson's disease.

Medication at the time of the study included cimetidine in five patients, ranitidine in 29 patients, spironolactone in 21 patients, potassium canrenoate in four patients, furosemide in 17, antibiotics in seven, and digoxin in six patients. A recent history of alcohol consumption was present in most patients with alcoholic cirrhosis (70/94). Clinical and biochemical data in the 125 patients are given in Table II.

#### STUDY PROTOCOL

At the time of inclusion in the study, the common clinical and biochemical data included in the Child-Turcotte-Pugh classification were obtained, and the Pugh score<sup>1</sup> was calculated by summing up the points obtained from the five items in the classification (Table II). The aminopyrine breath test was carried out according to Hepner and Vesell<sup>11</sup> after an oral dose of 2  $\mu\text{Ci}$  of [<sup>14</sup>C]-aminopyrine (New England Nuclear, Boston, Mass, USA), and was expressed as per cent of labelled carbon dioxide expired at two hours. Reference range for control subjects in our laboratory is 8-13%. Details of this procedure have been previously described.<sup>21</sup> No patient experienced complications or side effects related to the test.

Patients were treated according to standard medical practice, and were seen as outpatients every three months and as inpatients when necessary, and were followed for up to 48 months, with a median of 17 months (21 in censored patients). Range of time to death or censoring was 0.5-38 months and 12-48 months, respectively. Two patients were lost to follow up after three and six months, respectively. Three patients, who died of diseases not related to cirrhosis (myocardial infarction, colonic cancer, lung cancer) were censored at the time of death. All other deaths were considered liver related. Pharmacological treatment included diuretics in the presence of fluid retention, lactulose if encephalopathy was present, blood transfusion, H<sub>2</sub> blockers, glypressin, or Blakemore tubing in cases of acute gastrointestinal bleeding. Beta adrenergic blockers, endoscopic sclerotherapy, or portal systemic shunt were offered to prevent rebleeding. Because these treatments have been reported to be substantially equivalent as far as survival is concerned,<sup>22</sup> the treatment received for prevention of rebleeding was not considered in the analysis.

End point of the study was death by liver related causes. It was classified as caused by liver failure, if progressive impairment of liver function with neurological disturbances occurred, or by gastrointestinal bleeding, if it occurred within 40 days, regardless of the severity of bleeding. This definition of bleeding related death has recently been suggested by a consensus conference.<sup>22</sup> Hepatorenal syndrome, spontaneous bacterial peritonitis, and other infections were diagnosed according to established criteria. Patients who developed hepatocellular carcinoma during follow up were considered together with the other cirrhotics, and their cause of death was classified according to the clinical presentation. Secondary end point of the study was death from liver failure. To perform this analysis, patients who died of different causes were censored at the time of death.

#### DATA ANALYSIS

Statistics are given as medians and interquartile ranges.

To evaluate the prognostic value of the aminopyrine breath test and the results of the conventional investigations, a univariate analysis was performed building Kaplan-Meier plots<sup>23</sup> for each variable. To verify whether variables were univariately related to survival, curves were compared by the log-rank test,<sup>24</sup> or the *t* test for trend,<sup>25</sup> when two or three curves had to be compared, respectively.

In order to establish whether the aminopyrine breath test contributed to a better definition of the prognosis in our subjects, after the conventional data had been taken into account, a multiple regression analysis according to the Cox's proportional hazard model<sup>26</sup> was performed. In a first step the investigated variables were Pugh score, aminopyrine breath test, age, sex, aetiology, history of previous gastrointestinal bleeding, s-creatinine. In a second step, the Pugh score was substituted by the five items that define the score - namely, ascites, encephalopathy, s-albumin, s-bilirubin, and prothrombin index. Variables were first subjected to univariate analysis, then a predictor covariate was added in a stepwise fashion if the  $\chi^2$  statistics was the greatest, and its *p* value was less than 0.10. Each chosen covariate was then reconsidered and eliminated if its  $\chi^2$  value was the smallest, and its *p* value was higher than 0.15. The procedure continued stepwise until no further covariate could be added or removed according to the above mentioned criteria. To check the proportionality of risk with time in the different classes, the log minus log of cumulative hazard was plotted against time, and showed parallelism between patients with low and high values of selected predictor covariates. To evaluate the contribution provided by each parameter, the coefficient/standard error ratio was computed, and the models obtained including and excluding these variables were compared by the Wald test.<sup>27</sup>

To assess the validity of the models proposed, a split sample procedure was used. Patients were randomly divided into a training sample which

comprised approximately 60% of the patients, and a test sample which included the remainders. Validation was performed according to Schlichting *et al.*<sup>6</sup>

The clinical usefulness of the aminopyrine breath test was assessed by deriving prognostic indices<sup>27</sup> which included or excluded the test. Sensitivity and specificity of prognostic indices predicting death or death from liver failure within 18 months were computed according to standard formulae, and receiver operating characteristic curves were drawn. Areas under the curve and standard errors of areas under curve were calculated and compared according to Hanley and McNeil.<sup>28,29</sup> Because the null hypothesis predicts that no improvement in areas under curve exists after adding the aminopyrine breath test, a one sided significance test was used. All statistical analysis was performed using the BMDP statistical package.<sup>30</sup>

## Results

### FACTORS PREDICTING DEATH FROM LIVER RELATED CAUSES

During follow up 43 patients died: 20 of liver failure, 15 of gastrointestinal bleeding, three of infections, two of hepatorenal syndrome, and three of diseases not related to cirrhosis.

According to univariate analysis survival was significantly related to the aminopyrine breath test ( $p < 0.02$ ), Pugh score ( $p < 0.01$ ), s-albumin ( $p < 0.01$ ), s-bilirubin ( $p < 0.05$ ), prothrombin index ( $p < 0.01$ ), presence of ascites ( $p < 0.01$ ), presence of encephalopathy ( $p < 0.01$ ), and sex ( $p < 0.05$ ). It was not related to the aetiology of cirrhosis, or to a history of gastrointestinal bleeding.

Cox's multiple regression analysis selected Pugh score, the aminopyrine breath test, and sex as the best set of independent and significant predictors of survival. The statistical parameters of the model are given in Table III. A prognostic index predicting death (PI-d) was derived as:

$$\text{PI-d} = 0.299 \times (\text{Pugh score}) - 0.25 \times (\text{aminopyrine breath test}) - 0.955 \times (\text{sex}),$$

attributing a value of 1 for male sex and two for female sex. Median prognostic index predicting death in the whole series was 0.30 (interquartile range:  $-0.52 + 1.24$ ). The relationships between PI-d and survival are illustrated in Figure 1.

When the values of the five items included in

TABLE III Statistical parameters of Cox's models predicting death from liver-related causes or death from liver failure in 125 patients with cirrhosis

Variable	Coeff.	Coeff./SE	Improvement	
			$\chi^2$	p
<b>Death from liver-related causes</b>				
Pugh score	0.299	3.430	22.51	<0.001
ABT	-0.250	-2.505	6.53	0.01
Sex*	-0.955	-1.807	4.19	0.04
<b>Death from liver failure</b>				
ABT	-0.829	-3.557	33.67	<0.001
Pugh score	0.609	4.051	15.52	<0.001
Aetiology†	-1.203	-1.845	4.21	0.04

\*Male = 1; Female = 2.

†Alcoholic aetiology = 1; non-alcoholic aetiology = 2.

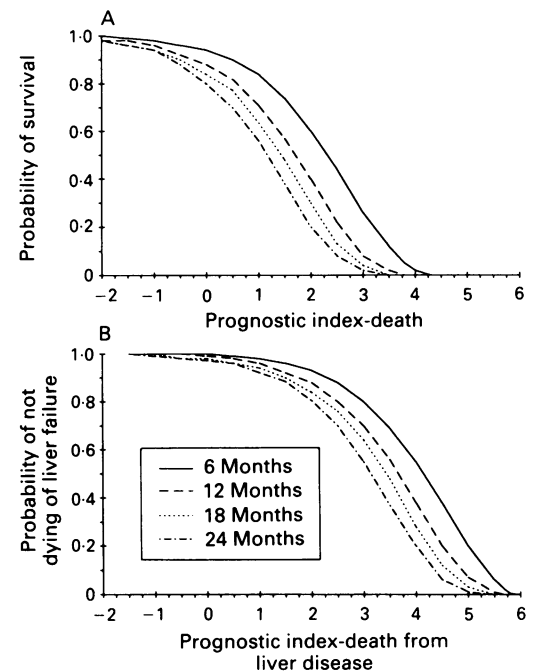


Figure 1: Relationships between the prognostic index predicting death (PI-d) and the probability of survival at different time intervals (A), and relationships between the prognostic index predicting death from liver failure (PI-lf) and the risk of death from liver failure (B).

the Pugh score were substituted to the Pugh score as candidate predictor covariates in Cox's analysis, aminopyrine breath test encephalopathy, ascites, sex, and s-bilirubin were selected by the computer procedure. Global goodness of fit was not significantly different, and aminopyrine breath test regression coefficient was nearly identical. The statistical parameters of this model are given in Table IV.

### FACTORS PREDICTING DEATH FROM LIVER FAILURE

The risk of death from liver failure was univariately related to the aminopyrine breath test ( $p < 0.01$ ), Pugh score ( $p < 0.01$ ), s-albumin ( $p < 0.01$ ), s-bilirubin ( $p < 0.01$ ), prothrombin index ( $p < 0.01$ ), presence of ascites ( $p < 0.01$ ), or encephalopathy ( $p < 0.01$ ). It was not univariately related to sex, aetiology of cirrhosis, or history of gastrointestinal bleeding.

TABLE IV Statistical parameters of Cox's models predicting death from liver-related causes or death from liver failure in 125 patients with cirrhosis, when the five variables included in the Pugh score were substituted to the score

Variable	Coeff.	Coeff./SE	Improvement	
			$\chi^2$	p
<b>Death from liver-related causes</b>				
ABT	-0.250	-2.465	16.73	<0.001
Encephalopathy*	0.725	2.300	9.22	0.002
Ascites†	-0.806	-2.133	6.31	0.01
Sex‡	-1.048	-1.969	5.97	0.02
s-bilirubin	0.007	1.991	3.23	0.07
<b>Death from liver failure</b>				
ABT	-0.945	-3.992	33.67	<0.001
Ascites†	-2.468	-2.365	13.06	<0.001
s-bilirubin	0.014	3.203	8.02	0.005

\*Without encephalopathy = 0; with encephalopathy = 1.

†Without ascites = 0; with ascites easy to control = 1; with resistant ascites = 2.

‡Male = 1; female = 2.

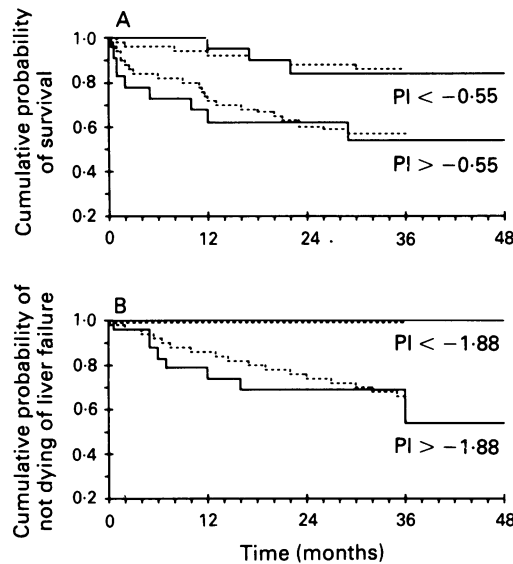


Figure 2: Validation of Cox's models. (A) cumulative probability of survival in the patients of the test set divided according to the values of prognostic index predicting death (solid lines), and probability of survival calculated from the training set according to the Cox's model (dotted lines). (B) cumulative probability of not dying of liver failure in the patients of the test set divided according to the levels of prognostic index predicting death from liver failure (solid lines), and probability of not dying of liver failure calculated from the training set according to the Cox's model (dotted lines).

Applying Cox's regression analysis, the aminopyrine breath test, the Pugh score, and aetiology were the best set of covariates significantly predicting the death from liver failure. The statistical parameters of this model are given in Table III. From the model a prognostic index predicting death from liver failure (PI-1f) was computed as:

$$PI-1f = 0.609 \times (\text{Pugh score}) - 0.829 \times (\text{aminopyrine breath test}) - 1.203 \times (\text{aetiology}),$$

attributing a value of 1 for alcoholic aetiology, and 2 for non-alcoholic aetiology. Median prognostic index predicting death from liver failure in the whole series was 0.41 (interquartile range: -1.64 + 2.16). The relationships between PI-1f and risk of death from liver failure is illustrated in Figure 1.

When Cox's regression analysis was performed including the variables which constitute the Pugh score, selected predictor covariates were the aminopyrine breath test, ascites, and s-bilirubin. Overall goodness of fit was not significantly different from that of the model containing Pugh score. The aminopyrine breath test regression coefficient was similar. Statistical parameters of this model are given in Table IV.

VALIDITY OF THE MODELS

This was assessed using a split sample technique. Prognostic index predicting death and prognostic index predicting death from liver failure were recalculated in a training set of approximately 60% of randomly selected patients. Individual prognostic indices were calculated for the test set comprising the remainders. Regression coefficients in the training set were very similar to those of the complete set of 125 patients. The test set was divided into two

groups based upon prognostic indexes above or below the median value, and mean estimated survival function for the patients in the two classes were computed. These were compared with the observed outcome in the same patients calculated according to Kaplan-Meier plots. No significant difference between observed and expected mortality, or mortality from liver failure, was found in patients with different levels of prognostic indexes (Fig 2).

CLINICAL USEFULNESS OF PROGNOSTIC INDEXES

To evaluate the clinical usefulness of the addition of the aminopyrine breath test to the common data in the prediction of death, prognostic index predicting death (which comprises Pugh score, the aminopyrine breath test and sex) was compared with a prognostic index computed only from Pugh score and sex. Sensitivity and specificity in predicting death within 18 months were calculated in eight equal intervals of prognostic indexes, and receiver operating characteristic curves were drawn. The best discriminant point of prognostic index predicting death was

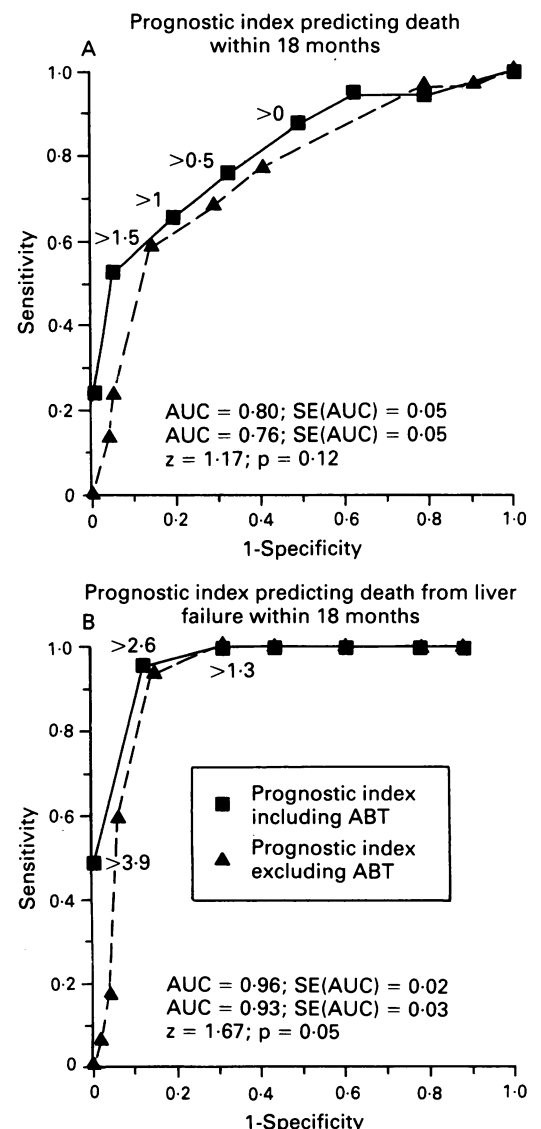


Figure 3: Receiver operating characteristic curves of the prediction of death (upper panel) or of death from liver failure (lower panel) according to prognostic indices computed including ABT (solid lines) or excluding ABT (dashed lines).

0.5; which had a 75% sensitivity and a 67% specificity in predicting death within 18 months. The receiver operating characteristic curve calculated from prognostic index predicting death was always nearer to the upper left corner than that calculated without the aminopyrine breath test (Fig 3). Areas under curve calculated from prognostic index predicting death (0.80; SE (AUC)=0.05) was larger than that calculated from a prognostic index excluding the aminopyrine breath test (0.76; SE (AUC)=0.05), but the difference did not reach statistical significance ( $z=1.17$ ;  $p=0.12$ ; one-sided test).

A similar analysis was performed to assess the clinical usefulness of prognostic index predicting death from liver failure. Prognostic index predicting death from liver failure (obtained from the aminopyrine breath test, the Pugh score, and aetiology) was compared with a prognostic index calculated excluding aminopyrine breath test, and receiver operating characteristic curves were drawn. The best discriminant point for prognostic index predicting death from liver failure was 2.6, which had a sensitivity of 94% and a specificity of 88% in predicting death from liver failure within 18 months (Fig 3). The receiver operating characteristic curve drawn according to prognostic index predicting death from liver failure always depicted a better performance than that of the prognostic index obtained excluding aminopyrine breath test. Areas under curve was also significantly larger (AUC=0.96 *v* 0.93; SE (AUC)=0.02 *v* 0.03;  $z=1.67$ ;  $p=0.05$ , one-sided test).

### Discussion

In the current study we have provided evidence that aminopyrine breath test is a strong predictor of survival in patients with cirrhosis, and that it adds information not available from the common clinical and biochemical data included in the Pugh score in the assessment of the risk of death from liver failure.

The aminopyrine breath test has already been shown to be useful in conditions of acute liver damage, such as alcoholic hepatitis,<sup>15</sup> or fulminant hepatic failure.<sup>14</sup> In numerous series of patients with cirrhosis it was also reported to have a strong predictor effect when considered alone.<sup>17-20</sup> Only two studies<sup>18,20</sup> have examined the possibility that the aminopyrine breath test could improve prognostic ability derived from the Pugh score in patients with cirrhosis, and both failed to show significant effects. Villeneuve *et al.*,<sup>18</sup> analysing a group of 187 patients with cirrhosis followed for a mean of 28 months, observed that it was not possible to include the aminopyrine breath test in the set of selected covariates in Cox's model predicting death, which comprised most of the data used to define the Pugh score. They concluded that the aminopyrine breath test had no additional prognostic usefulness, once the data included in the Pugh score were considered. Adler *et al.*<sup>20</sup> recently developed a stepwise logistic regression to identify cirrhotic patients who were going to die within one year. They observed that the association of the aminopyrine breath test and the presence of ascites was the best set of covariates

predicting death, superior to the other common clinical and biochemical data. When the prognostic index derived from the aminopyrine breath test and ascites was compared with the Pugh score, however, the difference in effectiveness was weakly in favour of the aminopyrine breath test and ascites, and it did not reach statistical significance.

At variance with previous reports, the aminopyrine breath test was an important prognostic index in our series. In fact, mortality from liver related causes was best predicted by a prognostic index which contained the Pugh score, the aminopyrine breath test, and sex, and the aminopyrine breath test significantly improved the efficiency of the regression, as assessed by the Wald test.<sup>27</sup>

From a practical point of view, however, one might wonder whether the improvement in the goodness of fit of the regression produced an improvement in the accuracy of the discrimination of patients who will eventually die from those who will survive. The receiver operating characteristic curve analysis showed that sensitivity and specificity of the prognostic index predicting death, containing the aminopyrine breath test, the Pugh score, and sex, were always better than those of a prognostic index derived only from Pugh score and sex. The difference in efficiency did not reach statistical significance, however, probably because of the insufficient sample size, and the relative magnitude of the standard errors. A further observation is that this type of analysis cannot take into account the different times to death, at variance with the Cox's regression model. Therefore a part of information is lost in the receiver operating characteristic curve analysis.

As the previous analysis was not able to show the clinical usefulness of the aminopyrine breath test in predicting liver related death, a secondary analysis was carried out considering only deaths from liver failure, which are expected to be more strictly linked to liver function derangement. This regression equation fitted the data better than that of overall mortality, as shown by the global  $\chi^2$  values. In this regression the aminopyrine breath test and the Pugh score were still the main prognostic indicators. The third indicator, much less important according to the coefficient/standard error ratio, was aetiology, while in Cox's model predicting overall mortality it was sex. Because alcoholic aetiology and male sex were strictly associated in our series ( $\chi^2=5.15$ ;  $p<0.025$ ), it is likely that the difference in the third parameter of the regression is expression of the same phenomenon.<sup>27</sup>

In this setting the aminopyrine breath test was the first covariate to enter the regression – that is, the more strictly associated to the risk of death from liver failure – and the weight of the aminopyrine breath test in the overall regression was only marginally less than that of the Pugh score, as assessed by the coefficient/standard error ratio. The prognostic index predicting death from liver failure (obtained from the aminopyrine breath test, the Pugh score, and aetiology) was reasonably stable, when recalculated on 60% of the data, and proved valid in the assessment of the remaining patients. The

receiver operating characteristic curve analysis showed that a prognostic index predicting death from liver failure value of 2.6 had a sensitivity of 94% and a specificity of 88% in predicting death from liver failure within 18 months. The area under curve of the receiver operating characteristic curve calculated from the complete set of covariates was significantly larger than that of a prognostic index which excluded the aminopyrine breath test. This also implies that from a practical point of view the addition of the aminopyrine breath test to the common data improved efficiency in predicting death from liver failure.

The results of the present study are at variance with those of Villeneuve *et al.*,<sup>18</sup> who performed a study very similar to ours. The reason for this difference is not evident. It may be caused by, at least in part, to the different populations studied, as our study mostly comprised patients with alcoholic cirrhosis, and none with primary biliary cirrhosis, while in the Canadian study only 55% had alcoholic cirrhosis, and 10% had primary biliary cirrhosis. As it was shown that the aminopyrine breath test is poorly associated to the severity of cholestatic conditions,<sup>31</sup> the presence of cases with primary biliary cirrhosis in the Canadian study may have contributed to decrease the overall efficiency of the aminopyrine breath test in the whole series. Furthermore, a much larger proportion of patients with alcoholic cirrhosis had a history of recent alcohol consumption in our series, and this may have improved prognostic efficiency, as the aminopyrine breath test was found particularly effective in evaluating the severity of acute alcoholic damage.<sup>15</sup>

The pathophysiological mechanisms through which the aminopyrine breath test appeared to be superior to the Pugh score are entirely speculative, but may include the following: (i) there may be substantial variations in the scoring according to Pugh, because two variables are qualitative<sup>2</sup>; (ii) s-albumin, s-bilirubin, and prothrombin index may change irrespectively of liver function impairment because of different pathophysiological mechanisms<sup>13</sup>; (iii) removal rate of aminopyrine represents an estimate of the ability of the liver in removing the drug, and should be more strictly related to the severity of liver disease than the measurement of a concentration in blood of a substance metabolised by the liver.<sup>32</sup>

In conclusion, the aminopyrine breath test significantly improved the prognostic ability of the Pugh score in the prognosis of death from liver failure in patients with cirrhosis. Should these data be confirmed in other studies in different settings, the aminopyrine breath test could prove to be a useful clinical tool to routinely evaluate the prognosis of patients with cirrhosis in addition to common clinical and biochemical data, because it is non-invasive, safe, and has an acceptable cost.

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