

Prognostic Factors for Survival in Patients with Liver Cirrhosis

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1. Introduction

Liver cirrhosis is the final stage of various chronic liver diseases. The concept is essentially morphological, defined as a diffuse alteration of hepatic architecture by the presence of necrosis, fibrosis and regenerative nodules. These disorders conduct to intrahepatic vascular changes and to the reduction of functional mass. Finally, the consequences are the development of portal hypertension and the occurrence of liver failure. (Ampurdanés S, 2002)

For many decades, alcohol was considered the leading cause of cirrhosis. But actually, viral hepatitis by viruses B (HBV) and C (HCV) are recognized as the most important sources. (Mandayam S) Another common cause is Nonalcoholic Fatty Liver Disease (NAFLD), followed by autoimmune diseases with or without cholestasis, among others.

1.1 Natural history of liver cirrhosis and its complications

The studies that provide more data on the natural history of cirrhosis are related to the evolution of chronic hepatitis by HBV and HCV. These are based on prospective, retrospective and cross studies, but are conditioned by factors that make difficult to establish absolute evidence on the natural history of the disease. (Serra MA., 2006)

Of those patients with HCV, 50% usually develop chronic liver disease including cirrhosis and liver cancer. It is estimated that 15% of chronically infected persons develop liver cirrhosis within 20 years. (Wiese M, 2005) However, there are individual differences. Currently it is known that 33% of patients develop cirrhosis in less than 20 years, while another 31% will need many more years in order to develop the same damage. (Serra MA 2006)

Usually it is a silent disease. Most patients are asymptomatic or have nonspecific symptoms until decompensation occurs. They can start with symptoms related to complications of liver failure or portal hypertension.

Ascites is the most common complication and of earlier onset. Once patients with cirrhosis develop ascites the prognosis worsens. It is estimated that approximately 50% of them could die within two years if they do not have a transplant. So, this is a major criterion for liver transplant evaluation in the United States and Europe. (Settle 2004, Sagnelli 2005)

Along with ascites, there may be other serious complication such as spontaneous bacterial peritonitis. In these cases, the probability of survival one year after this complication appears is only 40%. This is a strong reason for evaluating these patients as candidates for transplantation. (Corrao 1997) Similarly, other complications may appear such as hepatic encephalopathy and hepatic-renal syndrome. Both also worsen the prognosis. (Mandaya 2004)

Variceal hemorrhage occurs in 30 to 40% of patients with liver cirrhosis. In the past two decades, even with the improvement achieved in the treatment and in the prognosis after bleeding, mortality at six weeks is still high. It is estimated between 15 and 30% in patients with stage C of Child-Pugh. (Hands 2008)

After a first episode of hepatic encephalopathy the survival of cirrhotic patients is 42% in the first year, and 23% in the following three years. (Mendez-Sanchez 2005)

Hepatocellular carcinoma is another major complication and can occur at any stage of cirrhosis. It is recognized as the leading cause of death in the compensated phase, especially in patients with HCV. (Capocaccia R, 2007; Perz, J.F, 2006)

1.2 Indication of liver transplantation and survival models

Liver transplantation is the treatment of choice in acute and chronic irreversible liver failure of different etiologies, in primary liver tumors and when an impaired quality of life appears by manifestations of liver disease, as intractable pruritus and hepatic osteodystrophy.

The most commonly used survival models to assess the degree of liver failure and to prioritize patients on the waiting list for liver transplantation are: the Child-Pugh score (Oellerich M, 1991) and Model for End Stage Liver Disease (MELD) score (Malinchoc M, 2000). Although currently used primarily MELD, both have been included among the criteria for liver allocation in the United States and Europe (Freeman RB Jr, 2004; Adler M, 2005).

The Child-Pugh score has been widely used both in research and in clinical practice. For these reason, candidates for liver transplantation were prioritized mainly by these score, which included subjective measures of encephalopathy and ascites, and time waiting on the list. However, the need for a more accurate system in which the urgency of assignment was a relevant criterion, determined the introduction of the MELD score that is also very valuable as a predictor of mortality and allocation of organs for patients on the waiting list. The MELD score had been previously validated as a predictor of 3-month mortality for patients with chronic liver disease. (D'Amico G, 2006; Botta F, 2003)

The MELD system appears superior for comparing populations and has had a positive impact on allocation and survival in liver transplantation; however, it is still far from perfect. One of the disadvantage of the MELD formula is the loss of prognostic accuracy in periods longer than 3 months. The Child-Pugh classification provides superior results for periods exceeding one year. For these reasons, some authors recommend implementing both systems. (Forman LM, 2001; D'Amico G, 2006; Prieto M, 2007; Durand F, 2005.)

The Child-Pugh score evaluates five parameters: ascites, encephalopathy, bilirubin, prothrombin time and albumin. Although never formally validated, has been the most

widely used for decades. It is easy to apply and has proved useful in estimating the prognostic index of survival. But some limitations are pointed out such as, not all variables have an independent effect, it includes subjective variables like ascites and encephalopathy, the cutoff points for quantitative variables are not optimal, and it does not take into account certain important prognostic factors such as renal function. (Oellerich M, 1991; Prieto M, 2007)

The MELD model uses a mathematical formula with simple and objective variables such as, serum concentrations of bilirubin, creatinine and international normalized ratio (INR) of prothrombin time. From these variables, you get a score that is predictive of survival. Initially it also included the etiology of the disease, but this variable was excluded because a minimal influence was observed. (Vargas V 2003) Nevertheless, its application is less practical because of the need of computer systems. One of its major limitations is its variability due to changes in creatinine and bilirubin. These parameters can be altered by treatment, sepsis or hemolysis. The value of creatinine is often affected by diuretics and other factors such as age, sex and body mass, which may introduce a bias independent of the severity of liver disease. Moreover, the severity of some medical complications, are not well reflected in the MELD score. (Prieto M, 2007; Vargas V, 2003; de la Mata, 2004)

Research is still going in an effort to improve this mathematical model. Many studies have proposed the addition of variables that may be of prognostic significance. Recently it has been suggested that the addition of sodium to the MELD formula could improve its accuracy. Some studies showed that serum sodium lower than 126 mEq/L is an independent predictor of mortality among patients listed for transplantation, and the addition of sodium to the MELD score increases its prognostic value. In patients with portal hypertension and cirrhosis, hyponatremia may be the earliest harbinger of refractory ascites and hepatorenal syndrome, and possibly a more sensitive marker than rising creatinine. (Taddei TH, 2007) However, this new formula is also subject to interassay variations, as well as the potential manipulation can be generated inadvertently by the use of diuretics. It is also unknown if its use can lead to increased mortality by neurological causes. For all this, it seems premature to use as long as no data are available for validation in larger groups and different cohorts. (Cárdenas A, 2008; Jiang M, 2008) Among the new proposals are to include the introduction of the measurement of the Hepatic Venous Pressure Gradient (Taddei TH, 2007), to include ascites, encephalopathy (Ripoll C, 2005; Stewart CA, 2007), sex (S Huo; 2007) or exclude the INR (Heuman DM, 2007). But is too premature to make conclusions.

Recently, a new estimator has been projected: the Cuban model Bioclim. This is a score calculated by a mathematical model that evaluates the creatinine and bilirubin biochemical parameters. It also takes into account: clinical encephalopathy, ascites and variceal upper gastrointestinal bleeding, considering the positive or negative response to treatment. Compared with Child-Pugh and MELD, the authors of this model (Vilar E, 2009) concluded that Bioclim score seems to have a greater discriminatory power in the short-term survival (4 to 12 weeks), intermediate term (24 to 52 weeks) and long-term (104 weeks).

1.3 Studies of survival and prognostic factors

In order to improve prognostic models many factors have been studied in relation to the survival of patients with liver cirrhosis.

In a review of 118 studies conducted by D'Amico (D'Amico G, 2006) the Child-Pugh was reported as the best predictor of mortality in cirrhosis, followed by the five components measured individually.

Said (Said A, 2004) noted that in one year follow up of cirrhotic patients, male gender, MELD score, Child-Pugh and encephalopathy, were associated with increased mortality. Independent predictors were the Child-Pugh and encephalopathy.

Botta (Botta F, 2003) compared the survival of cirrhotic patients at 6 and 12 months using a multivariate analysis including variables of Child-Pugh, MELD and a quantitative test of liver function test monoethylglycyl-L-glutamate (MEGX). At six months, MEGX, creatinine and prothrombin time were disposed as predictive factors of lower survival. The ascites was added at 12 months.

Attia (Attia KA, 2008) reported as independent predictors of mortality in 172 African patients with cirrhosis, the Child-Pugh score, MELD index, and creatinine.

London (London MC, 2007), in a study of 308 cirrhotic patients on the waiting list for liver transplantation, described the serum sodium and MELD score as independent predictors of survival at 3 and 12 months.

Samada (Samada M, 2008) conducted a study in 144 patients with liver cirrhosis and transplant candidates. The variables associated with lower survival at 12 months were: prothrombin time, bilirubin, albumin, cholesterol, serum sodium, sex, history of ascites and encephalopathy. Also MELD index and Child-Pugh stages were evaluated. But only the Child-Pugh score and spontaneous bacterial peritonitis were independent predictors of survival.

In conclusion we can state that detailed clinical evaluation of patients with liver cirrhosis and knowledge of prognostic factors associated with survival, could lead to proper management of these patients, the appropriate indication for liver transplantation and increased survival. This has been the principal motivation of the present study, in order to recognize the prognostic factors for survival in patients with cirrhosis within a three year period.

2. Methods

We performed a descriptive, prospective, and longitudinal study in 194 patients with liver cirrhosis. All were referred to the consultation of hepatology and liver transplantation at CIMEQ hospital between January 2004 and April 2011. The sample was composed of 144 patients who met the following inclusion criteria: diagnosis of liver cirrhosis (confirmed by laparoscopy, liver biopsy or ultrasound) and rolling up at least 36 months (three years). Patients who underwent liver transplantation during the study period, those who were lost to follow-up, died of causes unrelated to liver disease, and those who at the time of assessment presented hepatocellular carcinoma, cholangiocarcinoma or other malignancies were excluded. Were also excluded four patients with spontaneous bacterial peritonitis and hepatorenal syndrome. The frequency of evaluations was determined by clinical assessment of patients at least twice a year.

The confirmation of alcoholic and viral etiology was performed. The surface antigen for hepatitis B virus (HBsAg) by UMELISA HBsAg and antibody for HCV by HCV-UMELISA,

both produced by the National Center for Immunoassay in Havana, Cuba were investigated. HCV infection was confirmed by qualitative PCR (UMELOSA) produced by the National Center for Immunoassay in Havana, Cuba. The criterion for toxic alcohol intake was: 60 g daily intake for men and 40 g for women over 10 years. (Cavalry J, 2002) Patients with HBV or HCV and alcohol were included in the viral etiology, because liver damage is increased more by the virus than by alcohol. (Safdar K, 2004)

2.1 Variables studied

The variables studied were:

- Sex and age.
- Laboratory variables: INR, total bilirubin (normal up to $17\mu\text{mol/L}$), albumin (normal value 35-48 g/L) and creatinine (normal value up to $123\mu\text{mol/L}$).
- Presence of esophageal varices: established in present or absence depending on the report of the upper digestive tract endoscopy, once these were classified according Paguet. (González M, 2007)
- Variables related to complications of cirrhosis: diagnostic criteria considered for the purposes of the study were selected taking into account the complications of the cirrhotic disease established AEEH guides. (Berenguer J et al, 2001).
- Ascites: fluid in the abdominal cavity detected by physical examination and/or abdominal ultrasound. We determined the presence of this complication if the patient had ascites at the time of assessment or had a history of it.
- Hepatic encephalopathy: presence of neuropsychiatric disorders that occur in patients with severe liver dysfunction. We used this complication if it was present at the time of the evaluation or the patient's history, family and clinical summary of the center of origin.
- Upper gastrointestinal bleeding (UGB): presence of hematemesis or melena associated with esophageal varices and/or portal gastropathy. We evaluated the history of this complication by questioning the patient, the clinical summary sent by the center of origin or having been submitted for evaluation.
- Hepatocellular carcinoma, we sought the presence of hepatocellular carcinoma during follow-up by surveillance strategy for this disease in cirrhotic patients. The strategy was based monitoring by abdominal ultrasound and determination of serum alpha-fetoprotein every 6 months (twice a year).
- Classification of Child-Pugh: used to evaluate the degree of liver failure in patients with cirrhosis. It has three stages according to score: A, B, C (see Table 1). (Pugh RNH, 1973)
- MELD: score used to assess the degree of liver failure and prioritize patients on transplant waiting list. The MELD score was calculated according to the original formula proposed by the Mayo Clinical group as follows: $[9.57 \times \log_e \text{creatinine mg/dL} + 3.78 \times \log_e \text{bilirubin mg/dL} + 11.20 \times \log_e \text{INR} + 6.43 \text{ (constant for liver disease etiology)}]$. (Kamath PS, 2001)
- Compensated liver cirrhosis: patients with or without varices but who have not showed any of the complications of cirrhosis.
- Decompensated liver cirrhosis: defined by the presence of ascites, variceal bleeding, encephalopathy and/or jaundice. (Gines P, 1987)
- Survival time: defined from the first assessment in consultation until the date the study was closed.

Parameter	Child-Pugh classification		
	A	B	C
Ascites	none	slight-moderate	tense
Hepatic encephalopathy (grade)	none	I-II	III-IV
Serum bilirubin ($\mu\text{mol/L}$)	<51	51-102	>102
Serum albumin (g/L)	>34	25-34	<25
Prothrombin time (%)	>60	46-60	<46
Score	5 to 6	7 to 9	10 to 15

The total score classifies patients into grade A, B, or C (ordinal scale) according to the points on continuous 5-15-point scale, which depends on ascites, encephalopathy, jaundice, serum albumin, and prothrombin time prolongation (Pugh RNH, 1973)

Table 1. Child-Pugh classification for the survival prognosis in liver cirrhosis

2.2 Statistical analysis

The data were processed using SPSS 13.0 for Windows. The results are presented as means \pm standard deviations and confidence intervals of 95% for quantitative variables and as percentages for categorical variables. For comparison of continuous variables the t test comparison of independent means and chi-square test to compare categorical variables was used. Survival analysis was performed using the Kaplan-Meier curves; we used the cutoff points at 36 months (three years). We performed a Cox regression analysis to estimate the independent effects of potential predictors of survival that had been significant in univariate analysis. For all tests a significant level of 0.05 was set.

3. Results

Of the 144 patients, 94 (65.2%) were male and 50 (34.7%) females. Everyone had a minimal follow up of 36 months with a mean of 43.27 ± 12.97 , minimum of three months for those who died and up to 73 months for the rest.

The average age was 47.8 years with a standard deviation of 12.9. Younger age was 18 years old and the oldest 87. The group with the highest number was between 40 and 60 years old with 84 patients (58.35%) as shown in Table 2.

All patients	144
Follow-up time (months)	43.27 ± 12.97 (3-73)
Sex (Male/Female)	94/50
Age (years)	47.8 ± 12.97 (18-87)
<40 years	33 (22.9%)
40-60 years	84 (58.3%)
>60 years	27 (18.8%)

Table 2. Baseline characteristics of all patients

The most common cause of cirrhosis in the study was HCV (42 patients, 29.1%), followed by alcohol (33 patients, 22.9%). The group "others" (46 patients, 31.9%) involved autoimmune hepatitis, primary biliary cirrhosis, sclerosing cholangitis, Wilson's disease, congenital hepatic fibrosis and cryptogenic (Table 3).

Etiology of cirrhosis	Patients
Alcohol	33 (22.92%)
Hepatitis C virus	42 (29.17%)
Hepatitis B virus	23 (15.97%)
Others	46 (31.94%)
Total	144 (100%)

Table 3. Etiology of cirrhosis

Table 4 and 5 show the clinical and laboratory characteristics of all patients. At the beginning of the evaluation 40 (27.7%) had not developed complications of cirrhosis and 104 (72.2%) had one or more of them.

Compensated cirrhosis (yes/no)	40 (27.8%) / 104 (72.2%)
Presence of varices (yes/no)	96 (66.7%) / 48(33.3%)
Compensated cirrhosis(yes/ no)	15 (37.5%) / 25 (62.5%)
Decompensated cirrhosis(yes/no)	81(77.8%)/23 (22.1%)
Child Pugh classification	
A	56 (38.8%)
B	46(31.94%)
C	42(29.16%)
Child - Pugh score	8.02 ± 2.6
MELD score	13.36 ± 5.74
Previous encephalopathy (yes/no)	21 (14.65)/123(85.4%)
Previous ascites (yes/no)	92 (63.9%) / 52 (36.15%)
Previous variceal bleeding (yes/no)	35 (24.3%) / 109 (75.7%)
Hepatocellular carcinoma (yes/no)	7 (4.9%) / 137 (95.1%)

Table 4. Clinical characteristics

According to Child-Pugh stages predominated A (56 patients, 38.8%), followed by B (46 patients, 31.9%) and C (42 patients, 29.1%). The average score was 8.02 ± 2.6. The mean MELD score was: 13.36 ± 5.74.

Laboratory test	
Bilirubin (µmol/L)	48.06 ± 59.4
Albumin (g/L)	34.10 ± 8.30
INR	1.45 ± 0.51
Creatinine (µmol/L)	83.53 ± 25.35

Table 5. Laboratory characteristics

96 patients showed esophageal varices (66.7%). Of these, 15 (37.5%) were in compensated stage and 81 (77.8%) in the decompensated one. Of these, 35 (24.3%) had at least one episode of gastrointestinal bleeding.

The most frequent complication was ascites (92 patients, 63.9%), followed by bleeding from esophageal varices (35 patients, 24.3%) and hepatic encephalopathy (21 patients, 14.6%).

Seven patients were diagnosed with hepatocellular carcinoma during follow-up and in two patients who were in Child A stage, it was considered as the cause of decompensation.

3.1 Survival of patients at three years

Of the 144 patients studied, 65 (45.1%) died from complications of liver cirrhosis between January 2004 and April 2011. Overall survival was 62.5% at three years follow-up, with a mean of 48.05 months and 95% between 43.2-52.8 months (see Figure 1).

As shown in Figure 2 and Table 6, survival of patients with compensated liver cirrhosis was 85% at three years with a mean of 60.27 months (CI 53.96-66.58). Patients who had complications had a survival rate of 53.8% with a mean of 42.4 months (CI 36.59-48.20) ($p < 0.001$). Of the patients with compensated liver cirrhosis at a baseline, the seven who died during the follow-up period were due to complications of the disease. Two of them presented HCC.

Cirrhosis	Median (months)	CI 95%	P
Compensated	60.27	53.96 - 66.58	$p < 0.001$
Decompensated	42.40	36.59 - 48.20	

Table 6. Survival of patients with compensated and decompensated liver cirrhosis

As presented in Table 7, univariate analysis showed continuous variables that were associated with significantly poorer survival such as, age of the patients ($p = 0.017$), bilirubin ($p = 0.04$), albumin ($p < 0.001$), the INR ($p < 0.001$), Child-Pugh score ($p < 0.001$) and MELD score ($p < 0.001$). Creatinine did not behave the same way ($p = 0.779$).

Categorical variables that were associated with a significantly lower survival were, male sex ($p = 0.033$), history of ascites ($p = 0.001$), of hepatic encephalopathy ($p = 0.032$), and the development of hepatocellular carcinoma ($p = 0.003$). The bleeding, did not behave the same way. (Table 7).

Value	Surviving	Deceased	p
Patients	79	65	
Sex (male/female)	46/33	48/17	0.033
Age (years, SD)	45.4 ± 13.2	50.66 ± 12.09	0.017
Previous ascites (yes/no)	41/38	51/14	0.001
Previous encephalopathy (yes/no)	7/72	14/51	0.032
Hepatocellular carcinoma (yes/no)	0/79	7/58	<0.001
Previous variceal bleeding (yes/no)	18/61	17/48	0.639
Compensated cirrhosis (yes/no)	32/47	8/57	<0.001
Bilirubin (µmol/L)	35.18 ± 50.18	63.72 ± 66	0.04
Albumin (g/L)	37.56 ± 7.74	29.97 ± 7.03	<0.001
INR	1.31 ± 0.49	1.62 ± 0.49	<0.001
Creatinine (µmol/L)	84.03 ± 24.6	82.94 ± 26.32	0.779
Child- Pugh score	7.0 ± 2.1	9.27 ± 2.63	<0.001
MELD score	11.45 ± 4.99	15.67 ± 5.77	<0.001

Table 7. Clinical and biochemical characteristics of the 144 cirrhotic patients at 3 years follow-up

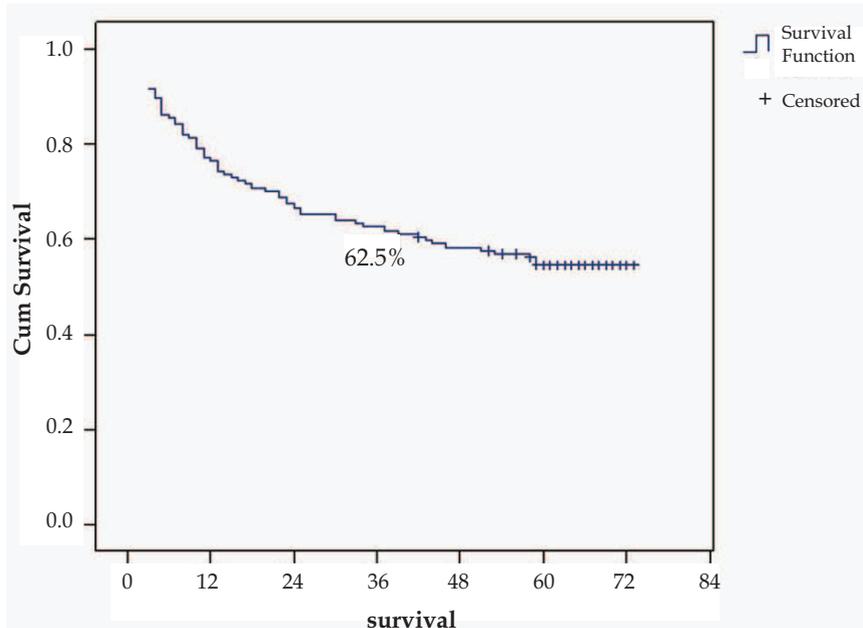


Fig. 1. Overall survival

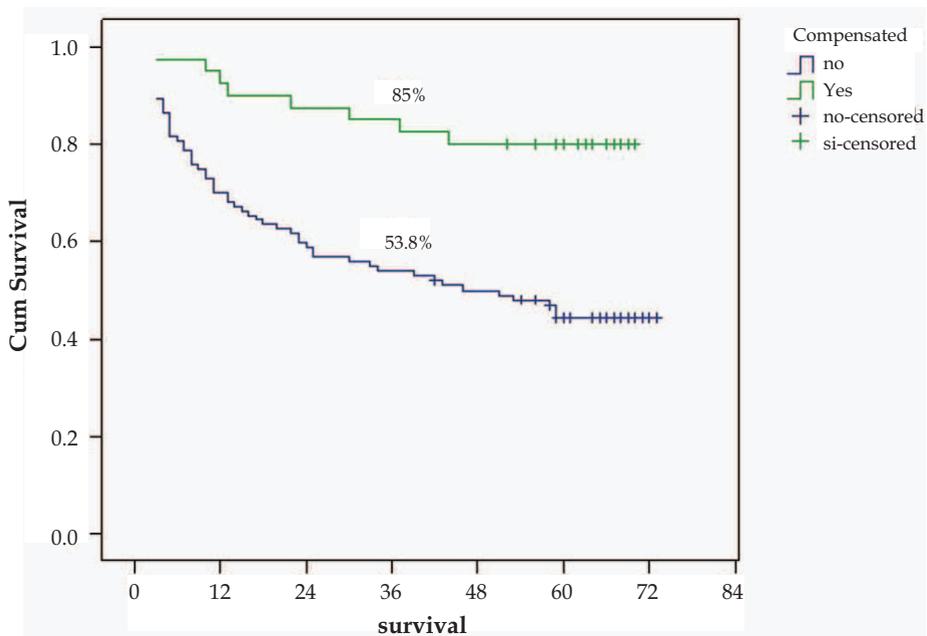


Fig. 2. Survival of patients with compensated and decompensated liver cirrhosis

In the analysis of the survival curves of Kaplan-Meier, categorical variables that had significantly lower survival were male gender (56.4%, average 43.69, 47.56-61.0), the history of ascites (51.1%, average 41.3 months; 35.06-47.53) hepatic encephalopathy (38.1%, mean 30.85 months, 17.67, 44.04), the development of hepatocellular carcinoma (0%, average 11.42, 4.09-18.76) and Child-Pugh stages with 80.8% survival for stage A, 69.9% for B and 31% for C (Table 8). Upper gastrointestinal bleeding for varicose veins was not associated with survival.

Variable	Survival at 36 months (%)	Median (months)	CI 95%	p
Sex: Female	74%	54.28	47.56- 61.0	0.033
Male	56,4	43.69	37.52- 49.87	
Ascites: No	82.7	57.722	51.75- 63.69	0.001
Yes	51.1	41.300	35.06- 47.53	
Encephalopathy: No	66.7	50.95	45.96- 55.92	0.032
Yes	38.1	30.85	17,67- 44.04	
Variceal bleeding: No	61.5	47.85	42.23- 53.46	0.639
Yes	65.7	47.68	38.62- 56.73	
HCC: No	65.7	49.92	45.07-54.77	<0.001
Yes	0	11.42	4.09-18.76	
Child- Pugh: A	80.8	58,04	52.28-63.81	<0.001
B	69.6	51.71	44.30-59.13	
C	31.0	26.42	17.88-34.97	

Table 8. Univariate analysis of categorical variables to three years of survival

	Exp(β)	p
Age	1.024	0.029
HCC	2.377	<0,001
Child-Pugh	1.378	<0,001

Table 9. Predictors of survival of liver cirrhosis at 3 years follow- up Cox regression

4. Discussion

According to different authors, cirrhosis caused by alcohol and HCV are more frequent in the fifth and sixth decades of life, and in males. (Safdar K, 2004; Sagnelli E, 2005; Benvegnù L, 2004) Recent series described that the most common causes of liver cirrhosis are due to HCV, HBV, and alcoholism. These causes can vary between them by geographic area. (Dehesa-Violante M, 2007; Fattovich G, 2008)

These conclusions coincide in this series, since the average age was 47.8 ± 12.95 years. The group more frequent were in patients between 40 to 60 years, male sex and the most frequent causes of cirrhosis were HCV and alcohol.

Cirrhosis is often manifested as a silent disease. In the compensated phase the diagnosis can be made by nonspecific manifestations or laboratory findings, whereas in later stages the disease may debut by its complications. (Heidelbaugh JJ, 2006) At the beginning of the study 27.8% of patients were in compensated phase and 72.2% had developed complications.

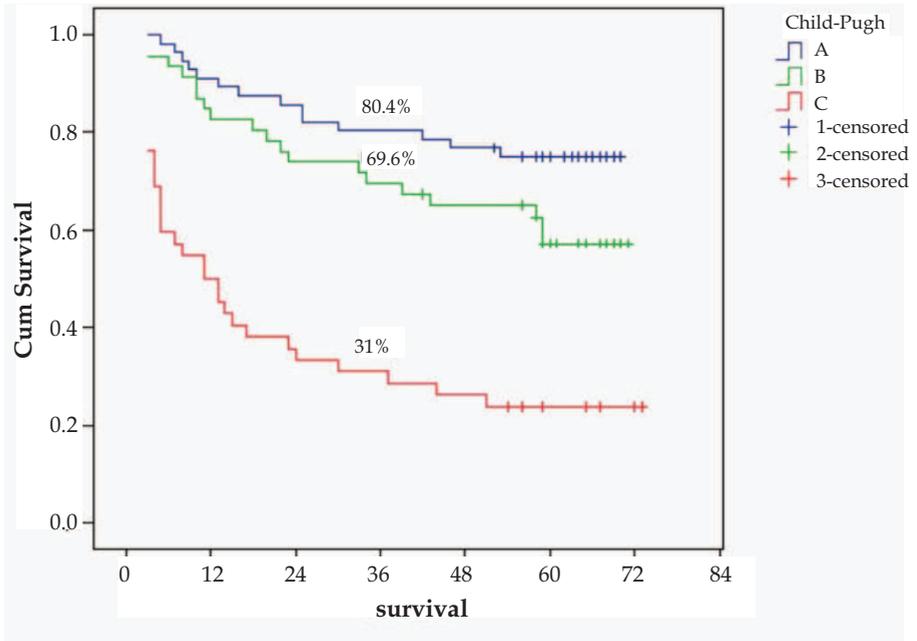


Fig. 3. Survival of patients according the Child-Pugh score

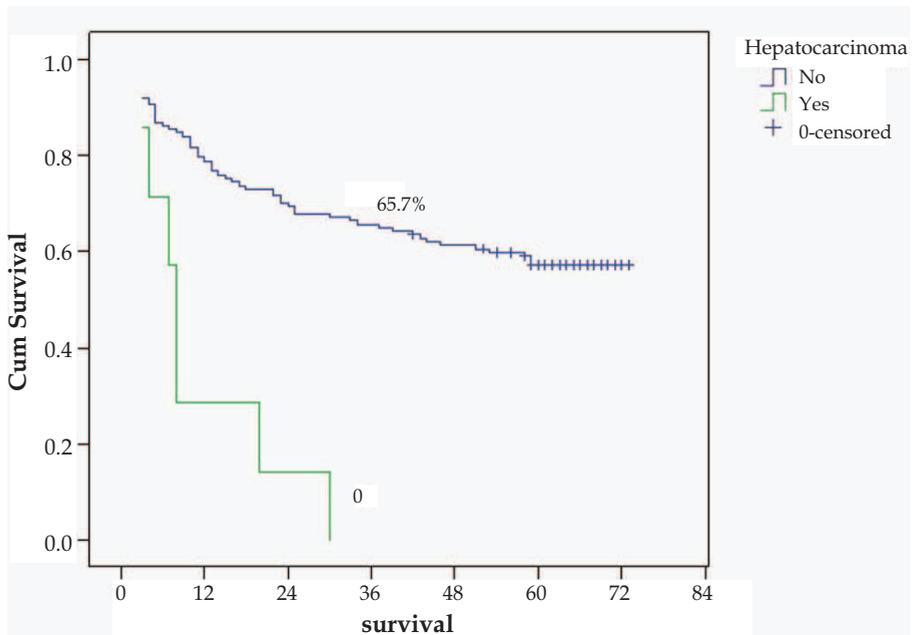


Fig. 4. Survival of patients according the diagnosis of hepatocellular carcinoma

The presence of esophageal varices was more frequent in decompensated liver cirrhosis. Ascites was the most common complication followed by gastrointestinal bleeding, which coincides with reports of other authors (Gines P, 1987). As is known, the higher frequency of esophageal varices is also associated with ascites and with the advanced stage of Child-Pugh. (Samada M, 2008; Sarwar S, 2005; Dib N, 2005)

In this series, overall survival at three years follow-up was 62.5%, which approximates to the average values to the review of natural history and survival in cirrhosis of 118 studies conducted by D'Amico. (D'Amico G, 2006) They reported on 32 studies of survival, with median follow-up of 33 months, cumulative survival of 61%.

Overall survival is less specific because patients are very heterogeneous regarding the presence or absence of complications. In conducting the study it was observed that patients that were at the beginning of the evaluation in compensated and decompensated stage, presented survival rates with significant differences, with 85% and 53.8% respectively. It is reported that the development of hepatocellular carcinoma is a major cause of mortality in patients in compensated phase and the transition to the decompensated stage may be 5 to 7% per year (D'Amico G, 2001). In the present study, HCC was the cause of death in 28.5% of patients who were compensated and the rest died of other cirrhosis complications.

As identified by D'Amico (D'Amico, 2006), compensated cirrhosis by the absence of complications includes two states, patients without varices or ascites (state 1) and patients with varicose veins but without ascites (state 2). Although they have different prognoses, mortality is low (1% per year for state 1 and 3.4% for state 2). On the other hand, decompensated cirrhosis (stages 3 and 4) has a significantly higher mortality (20% per year for the state 3 and up to 57% in 4). This classification was accepted at the Consensus Conference of Portal Hypertension, Baveno IV (De Franchis R, 2000) and modified states Baveno decompensated phase V (D'Amico G, 2011)

Many factors have been studied in relation to the survival of patients with liver cirrhosis and to improve forecasting models. In the study by D'Amico (D'Amico, 2006), it was reported that the Child-Pugh was the best predictor of mortality in cirrhosis, followed by the five components measured individually. Age was the only variable that was predictive of survival in more than 10 studies, and that was not part of the Child-Pugh score. These data are consistent with those presented by the authors of this paper. The univariate analysis showed that in addition to Child-Pugh, MELD, age, sex and liver cancer were associated with lower survival of the five variables of Child-Pugh, bilirubin, albumin, INR from prothrombin time, ascites and encephalopathy.

In our series, creatinine was not a factor associated with survival, which corresponds with other authors. (Degre D, 2004; Ruf AE, 2005) In relation to sex as a prognostic factor, we must consider that the United States 56 409 deaths related to hepatitis C in the period 1995-2004, there was an increase in mortality from 1.09 to 2.44 per 100 000 inhabitants. This represented an increase of 123% in the period studied, a male predominance with 144% and 81% in females. Alcohol was a cofactor related and could be underestimated. These data confirm the higher male mortality by the two leading causes of cirrhosis, hepatitis C and alcohol (Wise M, 2008)

Ascites is one of the earliest and most frequent complications of liver cirrhosis. Approximately 50% of patients with compensated cirrhosis, can develop ascites within 10 to

15 years after diagnosis, with a mortality of 15% per year and 44% within five years follow-up (Planas R, 2006). In this study, the survival at three years follow-up was 51.1%, indicating that all patients with ascites should be evaluated for liver transplantation, preferably before they develop renal dysfunction, and worsening prognosis.

Encephalopathy is a complication involving low survival. Bustamante et al. (Bustamante J, 1999), followed for 12 ± 17 months 111 patients with cirrhosis who had a first episode of acute encephalopathy, and found that 74% died during follow-up, with a survival rate of 42% per year. In this series the survival at three years was 38.1%.

Hepatocellular carcinoma was the complication that had lower survival; within 11.4 months mean follow-up there was no survivor. This complication can occur at any stage of cirrhosis and is associated with increased frequency in viral causes, so it is very important to increase surveillance programs for early diagnosis and thereby obtain prolonged survival rates. (Capocaccia R, 2007; Perz JF, 2006) In studies of cirrhosis caused by HBV and HCV has been the leading cause of mortality, especially in patients with HCV. (Perz JF, 2006)

In the survival analysis of MELD and Child-Pugh, it was observed that as they grow, the rate decreases in relation to time tracking. Although the MELD system is the outcome of choice to give priority to patients on the waiting list for liver transplantation in the Consensus Document of the Spanish Society for Liver Transplantation published in 2008, it is argued that currently there are not available data for the Child-Pugh classification no longer used in favor of the MELD system and recommend to apply both models with their advantages and limitations in the future to decide which method is most convenient. Spanish Society for Liver Transplantation. (Spanish Society for Liver Transplantation, 2008)

In the work developed in short and long term, the Child-Pugh score has proven to be a good predictor of mortality. In a review by Cholongitas (Cholongitas E, 2006) on studies that compare the MELD and Child-Pugh, performed with patients on the waiting list for liver transplantation that included 12 532 cirrhotic patients, only 4 of 11 studies showed that the MELD is superior to Child-Pugh in predicting short-term mortality and Gotthardt et al (Gotthardt D, 2009) from the results of their work, consider that for the prediction of long-term mortality (estimated at one year) and removal from the waiting list of patients awaiting transplantation, monitoring should be better by Child-Pugh score than by MELD. This might have implications for the development of new improved scoring systems

In this series, we found on univariate analysis similar significance of Child-Pugh and MELD index as predictors of survival at three years follow-up. But the Child-Pugh acted as an independent predictor of survival.

The prediction of MELD can rise to associate other factors such as clinical or biochemical. Some studies have shown the prognostic contribution of the addition of sodium to MELD (Ruf AE 2005, Biggins SW 2005), as well as ascites and encephalopathy. (Somsouk M, 2009, Stewart CA, 2007) It has been shown that patients with severe ascites and low sodium, low MELD even have very poor prognosis and suggest incorporating these two elements to the MELD (Heuman DM, 2007).

In another review of prognostic models for priority to liver transplantation, with numerous suggestions for additions to the MELD concluded that the MELD-sodium score is better able to predict survival on the waiting list than the Standard MELD score. (Cholongitas E, 2010)

Biselli M et al (Biselli M 2010) evaluated the survival of patients with advanced liver cirrhosis, liver transplant candidates at 3, 6 and 12 months. Six scoring systems used, included the modified Child Pugh (MCTP) and the standard MELD, and four of its modifications. The modified CTP (Huo TI, 2006) was obtained by assigning an additional point in patients whose serum bilirubin was > 8 mg/dL, prothrombin time prolongation >11 seconds, or albumin <2.3 g/dL, accordingly a mCTP score of 16-18 was defined as class D, which identifies severely decompensated cirrhosis. In this study population, the prognostic power of mCTP did not differ from that of MELD, MELD-sodium and integrated MELD were the best prognostic models.

Although these models are used to assess the short-term survival and give priority for liver transplantation, it would be interesting to determine their behavior in pursuit of longer than one year.

5. Conclusions

Age, Child-Pugh score and the development of hepatocellular carcinoma behaved as independent predictors of survival within three years of monitoring.

Undoubtedly, the Child-Pugh has a good long-term predictive capacity and the development of hepatocellular carcinoma can vary the prognosis of these patients in the short term, so you should keep a surveillance system for early detection.

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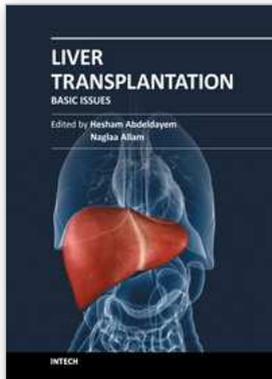
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This book covers a wide spectrum of topics including history of liver transplantation, ischemia-reperfusion injury, immunology of liver transplantation, viral hepatitis and liver transplantation, other indications for liver transplantation, prognostic factors and perioperative period. The authors of the chapters are experts in their respective fields. They are proponents covering different aspects of liver transplantation and come from many centers across the world. The interdisciplinary approach and the authority of the contributors resulted in a valuable reference to anyone interested in developing a global view in liver transplantation including medical students, residents, fellows, nurses, and practicing physicians and surgeons as well as researchers in the field of liver transplantation.

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