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Predictive models of mortality and hospital readmission of patients with decompensated liver cirrhosis

Rui Gaspar*,[1], Susana Rodrigues[1], Marco Silva, Pedro Costa-Moreira, Rui Morais, Patricia Andrade, Helder Cardoso, Andreia Albuquerque, Rodrigo Liberal, Guilherme Macedo

Gastroenterology Department, Centro Hospitalar São João, Faculty of Medicine of the University of Porto, Porto, Portugal

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ABSTRACT

Introduction: Complications of cirrhosis are one the major causes of hospital admission associated with high morbimortality rates and social and economic charges.

The aims of this study were to evaluate hospital readmission and mortality rates and predictive factors for hospital readmission and mortality.

Methods: Patients with decompensated cirrhosis admitted to our institution between 2008–2014 were retrospectively analyzed.

Results: Included 427 admissions from 177 patients with cirrhosis with mean age of 59.0 ± 12.3 years. The major cause was alcoholic-related liver disease and the median duration of admission was 9.0 days (IQR 6.0–14.0).

During the follow-up period,there were 250 readmissions from 95 patients, with a median of 58 (IQR27-134) days for readmission, representing 58.5% of the total number of admissions.The 180-day mortality rate was 35.0%.

In the multivariate analysis, ascites, smoking and MELD Na were associated with 180-day mortality. Creatinine, albumin, esophageal variceal bleeding, previous variceal banding, lactulose, rifaximin and proton pump inhibitors use were independently associated with need of readmission. Based on regression analysis, two models were calculated to predict 180-day mortality (AUROC 0.74 (0.682−0.794)) and need for readmission(AUROC 0.821 (0.781−0.861)), $p < 0.001$.

Conclusion: The readmission rate and mortality of cirrhotic patients are still very high and it is a priority to determine preventable risk factors to improve patient outcome.

Two models were created to predict 180-day mortality(AUROC 0.74) and need for readmission(AUROC 0.821), that could guide the management of the patients at the time of admission.

1. Introduction

Cirrhosis is one of the major causes of morbidity and mortality in the entire world and the second leading cause of digestive disease mortality. [1] It accounts for 40,000 deaths in the United States (US) per year, similar to diabetes and higher than kidney diseases, presenting a mortality rate of 25.7 per 100,000 [2]. In Europe, it is estimated that 20 million people suffer from chronic liver diseases, with 0.1% of the European population being affected by cirrhosis and an estimated 170,000 deaths per year [3,4]. Recent data showed a 46% increase in mortality from 1990 to 2013 [5]. Cirrhosis is not only associated with higher mortality, but also with significant morbidity and health care costs, leading to more than 150,000 hospitalizations, with an estimated cost of nearly 4 billion dollars each year in USA [6]. The burden of liver disease and related costs are expected to continue to rise in the next years due to the increasing number of patients with hepatocellular carcinoma, long-standing HCV infection-related cirrhosis and non-alcoholic fatty liver disease [7].

The estimated rate of transition from compensated advanced chronic liver disease to decompensation is 11% per year [8]. Studies reported that, after a first episode of decompensation, the survival rates are 81.8% at 1 year and only 50.8% at 5 years [1,9]. Although

* Corresponding author at: Gastrenterology Department, Centro Hospitalar São João, Faculty of Medicine of the University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal.
E-mail address: ruilopesgaspar@gmail.com (R. Gaspar).
[1] These authors contributed equally to this manuscript.

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significant strides have been made in the management of decompensated patients with cirrhosis in the last years, there is still a high risk of hospital admission, leading to substantial financial costs to the health care system. The overall cost of cirrhosis not only includes the direct costs associated with the hospitalizations, laboratory tests and imaging studies and drugs, but also the indirect costs related to decreased on-the-job productivity and employee absence [10].

Another important fact is that once admitted for a cirrhosis-related complication, the reported readmission rate for the same or other cirrhosis-related decompensation is very high, with an overall probability of readmission at 30 days of 37% and of 45% at 1 year and an average cost of $20 000 in US and € 10,000 in Europe [1,5,11,12]. There are many possible reasons for this high readmission rate such as frailty, psychological aspects, substance abuse, poor health literacy and poor social support [3]. Several studies tried to identify risk factors for readmission in order to stratify the patients. Nevertheless, the majority of them are marred by the inclusion of patients through national databases or specific health care systems, resulting in inclusion of patients from various institutions with different care pathways.

Readmissions represents a high cost burden for the healthcare system and are considered an important indicator of the quality of hospital care [13,14]. Therefore, it is of paramount importance to identify risk factors for hospital readmission and mortality in this susceptible population, in order to develop strategies to improve pre and post-discharge care and reduce morbimortality and costs of care [15].

The aims of this study were to evaluate hospital readmission and mortality rates as well as predictive factors for hospital readmission and mortality.

2. Methods

2.1. Study design, inclusion and exclusion criteria

A retrospective review was performed of all adult patients admitted to the ward of Gastroenterology Department between January 2008 and December 2014 at Centro Hospitalar Sao Joao. The Hospital is located in Porto and is the referral centre for the population of the North of the country. The Department of Gastroenterology and Hepatology is a tertiary, academic, non-transplant centre, and is the largest in the region both in terms of number of physicians and number of patients' referrals.

Study inclusion criteria included: 1) cirrhosis diagnosed by clinical data (based on imaging studies/endoscopy signs of portal hypertension and laboratory data) and/or histologically, 2) hospital admission with an episode of decompensation. For patients with multiple admissions, each was considered individually and were only included readmissions due to decompensated cirrhosis and not related to other causes.

Exclusion criteria were: 1) patients admitted to our centre, but not on the Gastroenterology ward; 2) when relevant clinical data was missing from the files (laboratory data, endoscopic or imaging studies); 3) patients whose laboratory work-up or imaging studies had been performed elsewhere; 4) elective hospital admission in our analysis (scheduled diagnostic or therapeutic procedure). (Fig. 1)

We also did not include patients that had no follow-up in our department

2.2. Data collection

Patient data were collected from electronic medical records. The etiological diagnosis of cirrhosis included a detailed drug history,

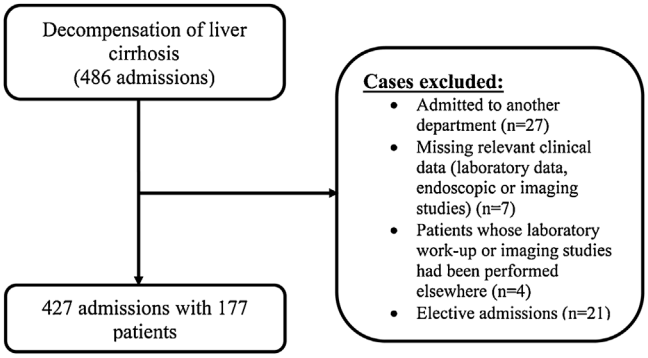

Fig. 1. Study flowchart.

body mass index, serology for hepatitis B virus (HBV) and hepatitis C virus (HCV), serum immunoglobulins and a panel of autoantibodies for the diagnosis of autoimmune hepatitis (AIH) or primary biliary cholangitis (PBC) according to established criteria [16,17] and the appropriate laboratory data to diagnose hemochromatosis, Wilson's disease and α-1 antitrypsin deficiency [18–20]. HBV DNA and HCV RNA were further tested to establish the diagnosis of chronic hepatitis B or C, respectively. Alcohol consumption was evaluated through the description of the medium quantity and type of drinks consumed.

Cirrhosis was labelled as cryptogenic whenever all the available investigations did not lead to or suggest a specific aetiology.

All laboratory work-up, as well as endoscopic and imaging studies, were performed at our Institution.

The causes of acute decompensation of cirrhosis that were included were hepatic encephalopathy, ascites, variceal bleeding, spontaneous bacterial peritonitis and hepatorenal syndrome.

Hepatic encephalopathy was classified according to West Haven criteria and diagnosed through clinical judgement and ammonia levels.

Ascites was defined the presence of fluid in the peritoneal cavity and considered the main reason for acute decompensation only when classified as grade 2 or 3.

Variceal bleeding was diagnosed according to the findings of gastrointestinal bleeding and the evidence of active or recent bled from gastroesophageal varices after performing upper endoscopy.

Spontaneous bacterial peritonitis was diagnosed according to EASL guidelines, as a cut-off of more than 250/mm^3 neutrophils count in the peritoneal fluid, in the absence of any intra-abdominal surgically treatable source of infection.

Hepatorenal syndrome was diagnosed as a progressive rise in serum creatinine in patients with chronic liver disease not responding of withdrawal of diuretics and volume expansion with albumin (1 g/kg) for 2 days.

Acute renal failure and the development of infections were also considered but not as main causes of acute decompensation and were included in one of the diagnosis previously referred. In the presence of more than one cause, we identified the main cause as the precipitant that lead to the admission of the patient.

The diagnosis of depression was always performed by a psychiatrist as the patients were followed in a psychiatry outpatient clinic in our hospital.

Clinical data collected included age, sex, race, marital status, history of alcohol and tobacco consumption, medication, comorbidities (type 2 diabetes, depression) hepatocellular carcinoma, portal vein thrombosis, previous episodes of decompensation and number of emergency department visits before admission. Laboratory data included haemoglobin, white cell and platelet count, international normalized ratio (INR), albumin level, aspartate aminotransferase level (AST), alanine aminotransferase level

Table 1a
Characteristics of 177 individuals admitted for acute decompensation of liver cirrhosis.

	General Population (n = 177)	Readmissions			180-day Mortality		
		Y (n = 79)	N (n = 98)	p value	Y (n = 61)	N (n = 106)	p value
Mean age (years) ± SD	59.0 (±12.3)	60.716071 (±11.8)	58.6 (±12.4)	0.291	59.77 (±12.8)	58.7 (±11-7)	0.635
Male sex, n (%)	138 (78.4)	62 (78.5)	76 (77.6)	0.360	44 (77.0)	94 (88.7)	0.534
Civil State, n (%)				0.380			0.377
• Married	99 (59.9)	47 (59.5)	52(53.1)		34 (55.7)	65 (61.3)	
• Single	20 (11.3)	12 (15.2)	8 (8.1)		6 (9.8)	14 (13.2)	
• Widowed	17 (9.6)	7 (8.9)	10 (10.2)		5 (8.2)	12 (11.3)	
• Divorced	9 (5.1)	5 (6.3)	4 (4.1)		3 (4.9)	6 (5.7)	
• Unknown	32 (18.1)	8 (10.1)	24 (24.5)		13 (21.3)	19 (17.9)	
Residence status, n (%)	123			0.072			0.966
• Accompanied	(69.5)	54 (68.4)	69 (70.4)		43 (70.5)	80 (75.5)	
• Alone	22 (12.4)	14 (17.7)	8 (8.1)		7 (11.5)	15 (14.2)	
• Assisted living	7 (4.0)	4 (5.1)	3 (3.1)		2 (3.3)	4 (3.8)	
• Unknown	25 (14.1)	7 (8.9)	18 (18.4)		9 (14.8)	16 (15.1)	
Cirrhosis diagnosis, n (%)				0.083			0.166
• Clinical	137 (77.4)	54 (68.4)	83 (84.7)		47 (77.0)	90 (84.9)	
• Histological	30 (22.6)	25 (31.6)	15 (15.3)		14 (23.0)	16 (15.1)	
Cirrhosis etiology, n (%)				0.274			0.804
• Alcohol	114 (64.4)	45 (57.0)	69 (70.4)		39 (63.9)	75 (70.8)	
• Alcohol + virus (HBV or HCV)	24 (13.6)	15 (19.0)	9 (9.2)		10 (16.4)	14 (13.2)	
•HCV	11 (6.2)	6 (7.6)	5 (5.1)		4 (6.6)	7 (6.6)	
• Metabolic syndrome-associated	8 (4.5)	3 (3.8)	5 (5.1)		1 (1.6)	7 (6.6)	
• HBV	6 (3.4)	5 (6.3)	1 (1.1)		4 (6.6)	2 (1.9)	
• Auto-immune hepatitis	5 (2.8)	1 (1.3)	4 (4.1)		0	5 (4.7)	
• Hemochromatosis	3 (1.7)	0	3 (3.1)		3 (4.9)	0	
• Wilson's disease	1 (0.6)	0	1 (1.1)		0	1 (0.9)	
• Cryptogenic	5 (2.8)	4 (5.1)	1 (1.1)		0	5 (4.7)	

(ALT), total bilirubin level, creatinine level and sodium level. In each admission, an abdominal ultrasound was performed to exclude hepatocellular carcinoma, even if the readmission was before 30 days, and the Model for End-Stage Liver Disease (MELD) and Child-Pugh score was always calculated.

Patients were followed until their last follow-up hospital visit, death or transplantation.

2.3. Outcome variables

Our primary outcomes were 180-day mortality and readmission rates. We considered readmission as a new admission in our department and analysed mortality for all causes. We also analysed the readmission rate between the 7 years of follow-up (2008–2014), as well as the emergency department recurrence without admission.

2.4. Statistical analysis

Continuous variables are expressed as means (standard deviation) or median (range), according to the distribution of normality. Categorical variables are reported as absolute (n) or relative frequencies (%). Analysis of variance was used to compare the differences in variable between groups. Group comparisons of categorical variables were analysed with X^2-test or Fisher's exact test. Group comparisons of continuous variables were analysed with Mann-Whitney test. The statistical significance of survival data using the

Kaplan–Meier curves was tested using the log-rank test. A multivariate logistic regression

was performed using the variables that provided a statistically significant association with 180-day mortality and readmission on the univariate analysis. The area under the receiver-operating characteristics curve (AUROC) was used to evaluate the performance of the models created for 180-day mortality and readmission. *P* values <0.05 were considered significant. Data were analysed using SPSS 21.0 (IBM Corp, Armonk, NY, USA).

Table 1b
Characteristics of 177 individuals admitted for acute decompensation of liver cirrhosis at the time of admission.

Features, n (%)	n = 177	Readmissions n = 79	180-Mortality n = 61
Type 2 Diabetes Mellitus	51 (28.8)	23 (29.1)	16 (26.2)
Ascites	114 (64.4)	58 (73.4)	45 (73.8)
Hepatocellular carcinoma	23 (13.0)	13 (16.5)	13 (21.3)
Portal vein thrombosis	15 (8.5)	9 (11.4)	11 (18.0)
Depression	29 (16.4)	12 (15.2)	6 (9.9)
Active drinkers	90 (50.8)	34 (43.0)	28 (45.9)
Active smokers	49 (27.7)	23 (29.1)	13 (21.3)

2.5. Ethical considerations

This study was conducted according to the Declaration of Helsinki. The ethical approval for this retrospective study was obtained from the Ethics Committee of Centro Hospitalar São João.

3. Results

3.1. Study population

Over the 7-year study period (January 2008 to December 2014), 486 admissions from 184 patients with cirrhosis were considered. Although, 59 admissions were not considered - 7 due to missing relevant clinical data (laboratory data, endoscopic or imaging studies), 27 as were admitted to another department, 21 as were elective admissions and 4 as performed laboratory work-up or imaging studies in other hospital. In total, 427 admissions from 177 patients were included.

The mean age was 59.0 years (±12.3) and 78.4% were male. The most common etiologies were alcoholic liver disease (64.4%), alcoholic liver disease and viral simultaneously (HBV or HCV) (13.6%), and HCV infection (6.2%).

The median Child-Pugh score was 10 (IQR 8–11), the median MELD score was 13 (IQR 9–18).

Clinical characteristics are displayed in Tables 1a and 1b.

3.2. Admissions

During the period of analysis, there were 427 admissions of 177 individuals (Fig. 1).

The main cause of admission was hepatic encephalopathy (35.1%), followed by variceal bleeding (27.1%) and ascites (25.5%). Regarding hepatic encephalopathy, the most common triggers were infection (31.3%) and constipation (20.0%). Supplementary Table S1 depicts the causes of admission.

Regarding infectious complications, 28.6% of the admissions presented an infection, being spontaneous bacterial peritonitis (SBP) the most common (39.3%), followed by urinary tract infection (33.4%), pneumonia (12.8%), cellulitis (7.7%) and undetermined (6.8%).

Concerning the clinic appointment, 80.3% had a clinic appointment after discharge with the specialist in hepatology responsible for his follow-up, with a median time of 30 days after discharge (IQR 16–62).

The mean number of consultations to emergency department before admission was 1.34 ± 0.97.

The majority of the patients were classified at admission as Child-Pugh C (52.0%), the remaining were Child-Pugh B and A in 40.0% and 8.0% of the cases, respectively. Laboratory data are shown in Supplementary Table S2.

The median duration of hospital stay was 9.0 days (IQR 6,0–14,0).

3.3. Readmissions

The median follow-up was 10 months (IQR 2–30) and the patients till loss of follow-up or death.

During the follow-up period, there were 250 readmissions, representing 58.5% of the total number of admissions of decompensated cirrhosis. The median time for readmission was 58 [26.8–133.8] days, with a 30-day readmission rate of 31.2%.

Among the 250 readmissions, the main causes were hepatic encephalopathy (45.4%), ascites (24.7%) and esophageal variceal bleeding (16.3%). The most important precipitating factors for hepatic encephalopathy were infection (31.6%) and constipation (20.2%).

Akin to infectious complications, 32.7% of the readmissions presented an infection, being SBP (38.8%) the most common, followed by urinary tract infection (32.7%), pneumonia (11.1%), cellulitis (8.7%) and undetermined (8.7%).

At readmission, 54.5% were under diuretics (furosemide in 47.8% and spironolactone in 46.6%), 58.2 under lactulose, 24.7% were being treated with beta-blocker, 60.6% on proton pump inhibitor (PPI), 25.9% under rifaximin and 19.5% were under SBP prophylaxis with norfloxacin or trimethoprim-sulfamethoxazole. With respect to alcohol and tobacco consumption, 43.8% were active drinkers and 27.5% active smokers.

Seventy-eight patients were readmitted in the 30-days after discharge, with hepatic encephalopathy (41.0%), ascites (32.1%) and esophageal variceal bleeding (14.1%) as the major causes of readmission. When analyzing the readmissions after 30-days of discharge, the causes were similar: hepatic encephalopathy (37.5%), ascites (26.1%) and esophageal variceal bleeding (25.0%).

In the univariate analysis, the following were associated with readmission: creatinine ($p = 0.001$), albumin ($p < 0.001$), sodium ($p = 0.013$), hepatic encephalopathy ($p < 0.001$), esophageal variceal bleeding ($p < 0.001$), ascites at admission ($p = 0.018$), lactulose use ($p < 0.001$), rifaximin use ($p < 0.001$), PPI use ($p < 0.001$), SBP prophylactic antibiotic ($p < 0.001$), previous variceal banding ($p < 0.001$) and previous paracentesis ($p < 0.001$).

In the multivariable analysis, creatinine, albumin, esophageal variceal bleeding, previous variceal banding, lactulose use, rifaximin use and PPI were associated with readmission (Table 2a) and we built the multivariable logistic regression model using these statistically significant variables.

Table 2a
Predictors of readmission – multivariate analysis.

Variable	Odds Ratio [95% CI]	p-value
Creatinine	1.363 [1.094–1.698]	0.006
Albumin	0.944 [0.898–0.992])	0.023
Esophageal variceal bleeding	0.282 [0.160–0.496]	< 0.001
Previous esophageal variceal banding	5.312 [2.888–9.769]	< 0.001
Lactulose use	2.911 [1.712–4.981]	< 0.001
Rifaximin use	5.795 [2.143–15.667]	0.001
PPI use	1.810 [1.073–3.052]	0.026

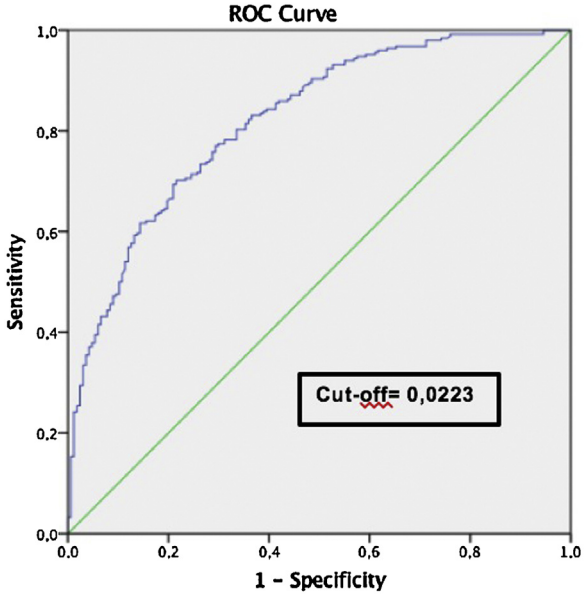

Fig. 2. Predictive model for readmission.

Fig. 2 depicted the ROC curves produced by our logistic regression model. Our model achieved the area under the curve (AUC) values: 0.821 (95% confidence interval[CI]: 0.781–0.861). The optimum cut-off was determined by the point on the ROC curve which was nearest to the upper left corner. At the cutoff of 0.0223, our logistic regression model obtained sensitivity of 80% and specificity of 67%. The model created has the following formula:

Predictive model readmission = 10.749 + (0.310×Creatinine) + (−0.058×Albumin) + (−1.268×esophageal variceal bleeding) + (−1.072×Lactulose use) + (−1.670×previous variceal banding) + (−1.757×Rifaximin use) + (−0.593×PPI use).

In our predictive model for readmission, with the cutoff of 0.0223, we created two groups: a high-risk group, with a readmission rate of 80.2%, and a low-risk group, with a readmission rate 19.8% (Fig. 4a).

3.4. Mortality

During the period of follow-up, in a total of 177 patients, 98 patients died (55.4%), 69 patients survived (39.0%), 4 patients (2.3%) were transplanted and 6 lost follow-up (3.4%). The 30-day mortality rate was 13.6% and 180-day mortality rate was 35.0%. The major causes of death were liver failure (53%) and sepsis (15.3%).

In the univariate analysis, we used 5 variables that were associated with 180-day mortality: white cell count ($p = 0.001$), readmission ($p = 0.03$), ascites ($p < 0.001$), smoking ($p = 0.026$) and MELD Na ($p < 0.001$).

Table 2b
Predictors of 180-day mortality – multivariate analysis.

Variable	Odds Ratio [95% CI]	p-value
MELD Na	1.128 [1.081–1.177]	< 0.001
Ascites	1.959 [1.135–3.380]	0.016
Smoking	1.913 [1.090–3.359]	0.024

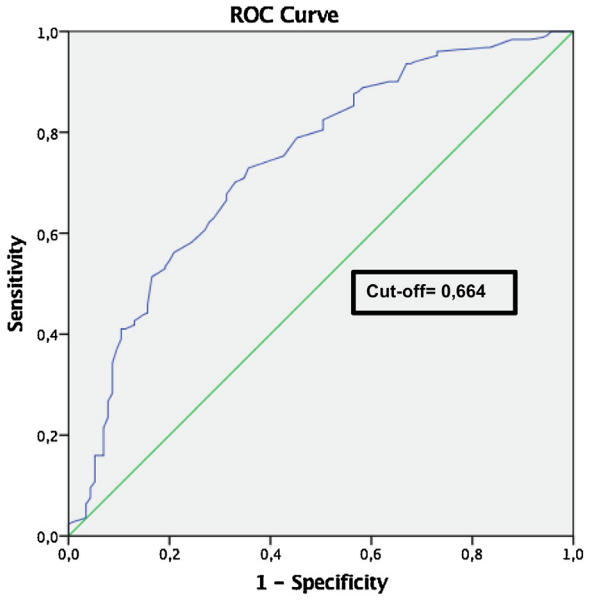

Fig. 3. Predictive model for 180-day mortality.

In the multivariable analysis, MELD Na ($p < 0.001$), smoking ($p = 0.024$) and ascites ($p = 0.016$) were associated with 180-day mortality (Table 2b) and we built the multivariable logistic regression model using these statistically significant variables.

Fig. 3 depicted the ROC curves produced by our logistic regression model. Our model achieved the area under the curve (AUC) values: 0.74 (95% confidence interval [CI]: 0.682–0.794). The optimum cut-off was determined by the point on the ROC curve which was nearest to the upper left corner. At the cutoff of 0.664, our logistic regression model obtained sensitivity of 70% and specificity of 67%.

The model created has the following formula:

Predictive model_180-day mortality = −4.721 + (0.672 × ascites) + (0.649 × smoking) + (0.12 × MELD Na)

In our predictive model for 180-day mortality, with the cutoff of 0.664, we created two groups: a high-risk group, with a 180-day mortality rate of 50%, and a low risk group, with a 180-day mortality rate of 18%.

4. Discussion

In this large retrospective study spanning 7 years of hospitalized patients with decompensated cirrhosis, we found 427 admissions from 177 patients. During the period of follow-up, there were 250 readmissions, representing 58.5% of the total number of admissions. This result is in concordance with other studies, with a readmission rate ranging from 50% to 78% [2,5,12]. In agreement with other reports, this study also shows a 30-day readmission rate of 31.2% [7,11,12,21,22].

The main causes of admission were hepatic encephalopathy, esophageal variceal bleeding and ascites and the median duration of hospital stay was 9.0 days. In line with other studies, the main causes for readmission were hepatic encephalopathy, ascites and esophageal variceal bleeding [2,5,12].

Readmissions represent a valuable opportunity to improve care. Therefore, understanding the reasons and possible strategies to implement to reduce the readmission rate, namely through preventive measures, are of paramount importance [13].

In our study, in the multivariable analysis, we identified creatinine, albumin, esophageal variceal bleeding, previous variceal banding, lactulose use, rifaximin use and PPI use as independent predictors of hospital readmission and created a predictive model for readmission with a c-statistic value of 0.821, indicating a strong predictive ability, which permitted us to create risk groups. The model permitted a stratification of the population in two groups: a high-risk group, with a readmission rate of 80%, and a low risk group, with a readmission rate of around 20% (Fig. 4a). Although previously associated with mortality, in our study readmission as a variable presented only borderline significance ($p = 0.005$) [11]. As expected, patients with higher values of creatinine and lower levels of albumin presented a higher risk of readmission. Contrarily, esophageal variceal bleeding, previous variceal banding, lactulose use, rifaximin use and PPI use were considered as protective factors for readmission. The presence of esophageal variceal bleeding as a protective factor could be explained by the fact that these patients are immediately enrolled in a structured secondary prophylaxis program to prevent re-bleeding, probably diminishing the risk of readmission due to more frequent ambulatory visits.

As reported previously, one of the major causes of admission and readmission in cirrhotic patients is hepatic encephalopathy. Another important finding was that lactulose and rifaximin use were protective of readmission. This could be explained because these patients were referred to specialist Hepatologist clinic and treatment was optimized. As hepatic encephalopathy is a potentially preventable cause of readmission, prompt referral to Hepatology clinic is key to ensure proper management.

Some studies have reported a higher risk of Clostridium difficile infections, SBP and encephalopathy in cirrhotic patients taking PPI, mainly due to alteration in gut microbiota composition [23,24]. Its use must be managed cautiously and in very precise indications such as post-peptic ulcer bleeding or following band-ligation. Indeed, our findings of a protective effect of readmission may be clarified by evidence that use of PPIs was shown to decrease the risk of variceal hemorrhage or severe medical complications after esophageal variceal banding [25,26]. Therefore, mainly when used in the appropriate setting PPI should also play a role in cirrhotic patients, preventing readmissions in this frail population.

The 30-day mortality was 13.6%, only mildly higher than previously reported [15,27], and 180-day mortality was 35%.

In our study, we identified total ascites, active smoking and MELD Na as risk factors for 180-day mortality and created a predictive model with a c-statistic value of 0.74, indicating a moderate predictive ability.

The model allowed a stratification of the population in two groups: a high-risk group, with a 180-day mortality rate of 50%, and a low-risk group, with a 180-day mortality rate of 18% (Fig. 4).

Ascites represents an important landmark in the progression of cirrhosis, worsening the prognosis, presenting a mortality of 15–20% within 1 year and 44% within 5 years.

MELD-Na is an important prognostic tool in patients with liver disease, being higher values associated with higher mortality [28]. A potential modifiable factor associated to higher mortality that we found was smoking. There were some studies reporting an indirect and direct effect of smoking on cirrhosis mortality, not only because is highly associated with alcohol consumption, with the probability of alcohol dependence increasing with the number of cigarettes smoked per day, but also for some cohort data revealing a direct influence of tobacco in liver cirrhosis [29]. This is, in fact, a frequently overlooked aspect in patients with cirrhosis. Smoking

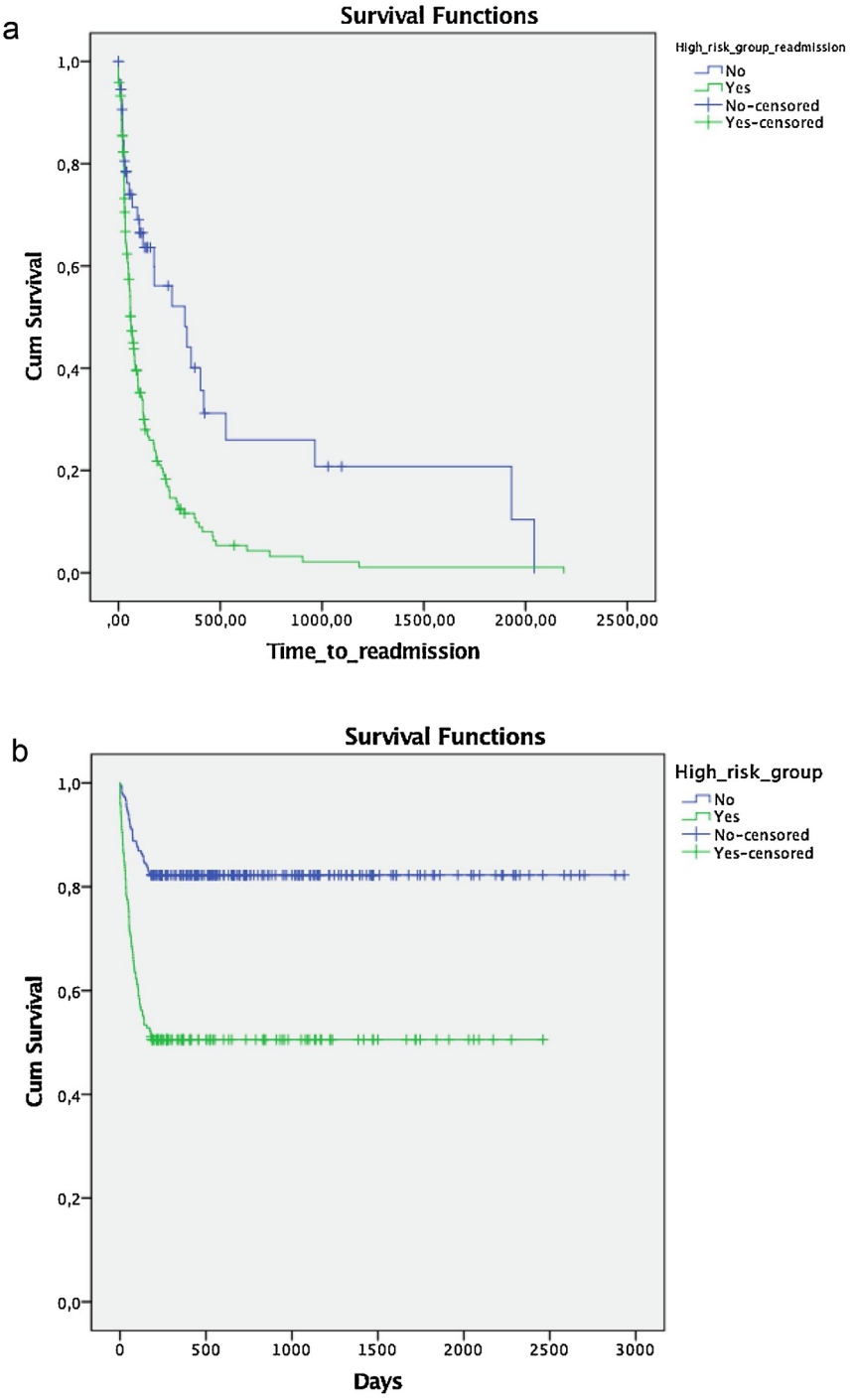

Fig. 4. (a) Kaplan-Meier curve for readmission according to the stratified groups (Log rank <0.001). (b) Kaplan-Meier curve for 180-day mortality according to the stratified groups (Log rank <0.001).

cessation is advocated particularly in patients on the transplant waiting list, but neglected in the remaining patients.

Our aim was to stratify patients into high and low risk groups in order to implement measures to reduce readmissions and mortality. Thereby, the high-risk group of patients would benefit of an intensive plan after discharge, with closer follow up. Some interventions that should be implemented in this subset of patients are a careful discharge plan, not only in the presence of the patient, but also the family, outlining clearly all the medications and how to deal with possible side effects to improve the adherence to treatment. It should also be provided social support facilities, encouraging adherence to programs of substances misuse, promote effective techniques to facilitate activity and early outpatient follow-up with skilled nurses and specialists for early detection and treatment of complications. A Danish study reported an improved survival in patients that attended a rehabilitation clinic for cirrhotic patients [30].

This study has some important limitations beyond its retrospective nature with inherent biases. Our study is a single institution study that could limit the external validity and we only included cirrhosis-related admissions, which could underestimate the admissions in this group of patients. Another limitation is that

as we considered each admission individually in patients with multiple admissions, the relative impact of the predictive variables could vary in time depending on whether it was the first or second admission.

Regarding the model of 180-day mortality, we included all the variables used in the univariate analysis, that could lead to overfitting and considered as a limitation of the study.

The lack of validation of the final model predictors of hospital readmission and 180-day mortality is another drawback to this analysis.

Our study has several strengths. First, it is based on real-life data, where all the patients were studied in the same way, by the same team of Gastroenterologists with and intensive follow-up, and not based in National databases that are dependent of correct coding, as in the majority of the previous studies. Second, we developed two models to predict readmission and 180-day mortality that could help so stratify our patients, defining priorities and strategies to improve health care. Finally, our study identified modifiable factors associated with higher risk of readmission and mortality that we can target, improving outcomes of a susceptible population.

In conclusion, hospital readmissions and mortality in cirrhotic patients are common and it is of paramount importance to identify risk factors and stratify the patients into low and high-risk groups, so measures to improve the outcome can be implemented. Our study provided several factors to target in order to curb readmissions and mortality. Establishing on-admission predictive models that could be applied to advanced chronic liver disease are key to enhance the care of patients with decompensated cirrhosis and reduce the high rates of readmission and mortality in this population.

Conflict of interest

None Declared.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.dld.2019.03.016.

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