Malnutrition is highly prevalent in hospitalized cirrhotic patients and associates with a poor outcome

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Abstract

Background and study aims: **The role of malnutrition on the prognosis of hospitalized cirrhotic patients is incompletely studied. Our aim was to determine the prevalence of malnutrition, functional scores and their impact on prognosis of hospitalized cirrhotic patients.**

Patients and methods: **This retrospective study included all patients with cirrhosis hospitalized in the gastroenterology unit at Saint-Luc university hospital, Brussels between April 2014 and September 2014. Nutritional status was evaluated according to minimum clinical summary diagnostic criteria. Cirrhosis-related complications or death occurrence were analysed in a one-year follow-up.**

Results: **95 cirrhotic patients were assessed for nutritional status and outcomes. Malnutrition affected 45.3% of patients and was more frequent with the severity of cirrhosis: 29% in Child-Pugh A, 48.8% in Child-Pugh B and 72.2% in Child-Pugh C patients. 58.9% of patients developed cirrhosis-related complications (60.7% in the malnutrition group vs. 39.3%, p<0.001, OR 5.06, IC95 1.90-14.58) and 33.7% of patients died (68.75% vs. 31.25%, p=0.002, OR 4.33, IC95 1.62-12.28). Adjusting for age, sodium, MELD, Charlson index, hepatocellular carcinoma, platelets, diabetes, prognostic nutritional index and Braden scale, malnutrition was significantly associated with higher mortality and morbidity rates with an OR of 3.56 (CI95 1.55-8.16) and 2.09 (CI95 1.16-3.77) respectively. Braden scale was significantly associated with higher mortality (p=0.027, OR 1.25, CI95 1.03-1.52) whereas prognostic nutritional index was associated with higher morbidity (p=0.001, OR 0.94, CI95 0.90-0.98).**

Conclusion: **Malnutrition is highly prevalent in hospitalized cirrhotic patients. Malnutrition, low prognostic nutritional index and low Braden scale are associated with poor outcomes in cirrhosis.** (Acta gastroenterol. belg., **2022,** 85, **311-319**).

Keywords: alcoholic liver disease, cirrhosis, nutrition, prognosis, malnutrition.

Introduction

Cirrhosis causes the death of one million people worldwide each year (1). Hepatitis B and C virus, alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD), also named metabolic dysfunction-associated fatty liver disease (MAFLD) (2) are the most frequent causes of cirrhosis (3). With the introduction of the new antiviral medications (4), the growing industrialisation in emerging countries and the worldwide global diet changes, NAFLD/MAFLD is a slowly increasing cause of cirrhosis (5,2,3). However, malnutrition remains frequent in cirrhotic patients, including in NAFLD-related cirrhotic patients (6). The prevalence of malnutrition in cirrhotic patients ranges from 23 to 60 % in the medical literature (7). Carvalho and Parise described 75% of cirrhotic outpatients suffering from malnutrition in their Brazilian prospective study (8). Malnutrition in cirrhosis is the consequence of multiple pathological modifications. These include loss of appetite (due to delayed gastric emptying, early satiety because of ascites, the alteration in the regulation in appetite-hormones (9) and the inflammatory cytokine activation (10)), poor intakes (salt-restriction, hepatic encephalopathy, iatrogenic fasting periods), malabsorption (fat-soluble vitamin deficiencies in cholestatic liver diseases (11), shunting of nutrients away from the liver because of portal hypertension (12) and protein-losing enteropathy secondary to portal hypertension (13)) and increase of the catabolic state (14). Gut microbiome dysbiosis in cirrhosis also seems to be associated with malnutrition and protein catabolism, bacterial translocation, inflammatory status and cirrhosis' complications (15,16).

A correlation is also observed between the evolution of the liver disease and the poor nutritional status (17). In 1984, Mendenhal already showed a greater prevalence of malnutrition in decompensated cirrhotic patients compared to patients with compensated liver diseases (18). In several studies, malnutrition seems to be associated with more medical cirrhotic related-complications, longer hospitalizations and death (19). These observations are confirmed with the follow-up of patients who benefited from liver transplantation. Malnourished transplanted patients have longer intensive care stays, more post-surgical complications and higher mortality rates (20).

In recent years, an abundant medical literature has emerged about these concerns in cirrhosis. The role of malnutrition is incompletely studied in hospitalized patients, especially in the setting of a tertiary referral centre with systematic personalized dietary counselling. Based on previous results, the identification of malnutrition is of high priority to improve a modifiable condition that could have important consequences. Lots of definitions and screening tools are found, based on

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Table 1. — **Definition of Malnutrition**

Malnutrition	Weight loss speed	Previous week food intake (%)	Body mass index
Adult < 70 y.	> 5% in 3 months	< 75	< 20,5
Adult > 70 y.	> 5% in 3 months	< 75	any

Table 2. — **Nutritional Risk Screening (NRS 2002)**

Table 1A – Initial screening			
		Yes	***No***
1	Is BMI < 20.5 ?		
2	Has the patient lost weight within the last 3 months ?		
3	Has the patient had a reduced dietary intake in the last week ?		
4	Is the patient severely ill ? (e.g. in intensive care)		

Yes : If the answer is "Yes" to any question, the screening in Table 1.B is performed. No : If the answer is "No" to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.

Table 1B. Final screening			
Impaired nutritional status		Severity of disease (~ increase in requirements)	
Absent = score 0	Normal nutritional status	Absent = score 0	Normal nutritional requirements
Mild score 1	Weight loss > 5% in 3 months or food intake below 50-75% of normal requirement in preceding week	Mild score 1	Hip fracture, chronic patients, in particular with acute complications (cirrhosis, COPD, chronic hemodialysis, diabetes, oncology)
Moderate score 2	Weight loss > 5% in 2 months or BMI 18.5-20.5 + impaired general condition or food intake 25-60% of normal requirement in preceding week	Moderate score 2	Major abdominal surgery, stroke, severe pneumonia, hematologic malignancy
Severe score 3	Weight loss > 5% in 1 mth (> 15% in 3 mths) or BMI < 18.5 + impaired general condition or food intake 0-25% of normal requirement in preceding week	Severe score 3	Head injury, bone marrow Transplantation, Intensive care patients (APACHE-score II > 10)
Score A =		Score B =	
Total score = score A + score B		Age > 70 years : + 1 to total score	
Score ≥ 3 : the patient is nutritionally at-risk and a nutritional care plan is initiated. Score < 3 : weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

body composition (muscle mass), anthropometric tools (midarm circumference and triceps skinfold thickness), functional assessment tools and global assessment tools. In 2019, GLIM criteria were published for the diagnosis of malnutrition, discussing a two steps approach. The first step is to identify at-risk patients, the second to evaluate the severity of malnutrition (21).

However, before this consensus guidelines, results varied across the studies in cirrhosis. Variations in the prognosis can also be highlighted (22). This puts emphasis on the importance of using standardized tools and scales in the definition and evaluation of malnutrition in future studies (23). A good malnutrition screening tool should be easy to use, not time-consuming, reproducible and with a high specificity and sensibility (24). Our aims were to determine the prevalence of malnutrition in a cohort of hospitalized cirrhotic patients, using easy and validated tools according to the European society for clinical nutrition and metabolism (ESPEN) guidelines, to confirm its association with morbidity and mortality, and to assess other functional tools including frailty (22, 25) that could be used to predict the morbidity and the mortality of hospitalized cirrhotic patients.

Methods

Study Design

This retrospective analysis was performed on a cohort including all consecutive patients with cirrhosis who were admitted in the department of gastroenterology and hepatology of *Cliniques universtaires Saint-Luc*, Brussels, from April 2014 to September 2014. Diagnosis of cirrhosis relied on clinical basis together

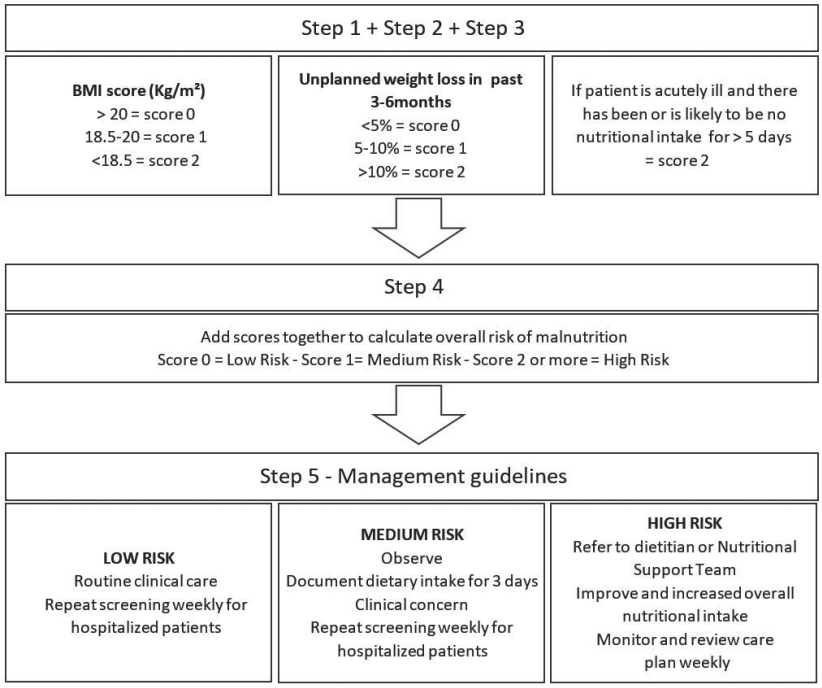

Figure 1.— Malnutrition universal screening tool
BMI= Body mass index.

with laboratory parameters, endoscopic evidence, imaging findings, and liver histology, if available. We recorded all disease specificities including aetiology of the liver disease, severity of the liver disease according to Child-Pugh classification and Model for End-Stage Liver Disease (MELD) score (26) and liver-disease-related medical background. We also registered the reason of hospitalization, the patients' particularities (body mass index –BMI–, the need for haemodialysis, active alcoholism) and other relevant comorbidities (cardiovascular diseases, diabetes mellitus, chronic obstructive pulmonary disease, renal impairment, and HIV infection). Active heavy alcoholism was defined by more than 14 drinks per week for women and more than 21 drinks per week for men within the previous 3 months (27). Re-hospitalizations, cirrhosis-related complications or death occurrence were analysed in a one-year follow-up. Cirrhosis-related complications included variceal bleeding, encephalopathy, infections, in particular spontaneous bacterial peritonitis (SBP), uncontrolled ascites and hepatorenal syndrome (HRS). We only took into account infections requiring hospitalization. Patients with unavailable nutritional data or with absence of follow-up were excluded, together with those suffering from alcoholic hepatitis and active malignancies, except hepatocellular carcinoma. The follow-up was ended prematurely in case of death or liver transplantation.

Nutrition assessment tools

All patients were assessed for malnutrition at admission during the referential hospitalization. Concerning patients hospitalized during the recruiting period and who were already hospitalized during the previous 6 months, data were collected from the first hospitalization. Nutritional diagnosis at baseline was performed according to the tool used in our hospital, the Minimum Clinical Summary diagnostic criteria, involving weight loss speed, intake reduction during previous week, and BMI. This tool adapts its cut-off for patient's age. Those diagnostic criteria are reported in Table 1. We also reported two nutritional scores validated by the ESPEN guidelines for each of our patients, the MUST (Malnutrition Universal Screening Tool (28) explained in Figure 1, and the NRS (Nutritional Risk Screening) 2002 detailed in Table 2 (29). Furthermore, we investigated the role of Onodera's Prognostic Nutritional Index (PNI) (30), another easy nutritional assessment tool, on the prognostic of cirrhotic patients. Onodera's Prognostic Nutritional Index (PNI) formula is: *10 × serum albumin value (g/dL) + 0.005 x total lymphocyte count in the peripheral blood (per mm³)*. It was designed to assess the nutritional status of gastrointestinal surgical patients with neoplasia. Onodera's PNI should not be confused with a prognostic nutritional index described by Buzby (31). All patients received nutritional counselling, and adaptation of their diet either by a dietician or by a physician. Diet was advised based on their condition, i.e. salt restriction in patients with ascites or low sugar diets for diabetic patients.

Comorbidities and frailty assessment tools

Finally, we also investigated the role of three others scales in the predicting of morbidity and mortality of our patients. First, The *Charlson comorbidity index*

(32) which predicts the ten-year mortality for a patient who may have a range of comorbid conditions. Ai-Freah *et al.* showed an increase of five times mortality in their cohort of 151 patients in a waiting list for liver transplantation with the presence of any comorbidity defined by Charlson comorbidity index (33). Secondly, *the Braden Scale for Predicting Pressure Ulcer Risk (34)*, which is a tool to help the nurses to assess a patient's risk of developing a pressure ulcer. It examines six criteria: sensory perception, skin moisture, activity, mobility, nutrition, friction & shear. And thirdly, the chronic liver failure-sequential organ failure assessment (*CLIF-SOFA)*, a modified SOFA score which considers specific features of cirrhosis (35). CLIF-SOFA is an important tool to evaluate the severity of the hospitalized patient and is linked to the 30-day mortality. The resting energy expenditure and the nutritional needs are linked to the systemic inflammation. We used this modified SOFA score for the diagnosis of organ failure and better characterization of the severity of our cohort (36). The CLIF-SOFA was calculated with parameters of the day of admission to hospital.

Statistical analysis

Data processing was performed by using the software packages SPSS version 23 (SPSS Inc., Chicago, IL). Data were expressed as mean ± SD. For comparison of categorical variables, chi-square and Fisher's exact χ^2 tests were used, and for continuous variables, Mann–Whitney test for unpaired data and Wilcoxon sign rank test for paired data were used, as appropriate. Pearson's correlation coefficient was used to assess correlation of nutritional parameters with liver disease severity and of PNI with nutritional status. ANOVA test was used for comparison in multiple groups. Kaplan–Meier method was used to assess the correlation of nutritional status with survival and differences between the curves being tested using the log rank test. The probability level of $p < 0.05$ was set for statistical significance.

Results

On 662 single patients hospitalized during the study period, 113 patients were cirrhotic patients. Among those cirrhotic patients, 18 were excluded (1 due to unavailable nutritional data and 17 due to loss of follow-up). The remaining 95 patients were assessed for nutritional status and outcomes. The recruitment process is illustrated in Figure 2.

Patient characteristics

Patient characteristics are showed in Table 3. There were 71 men (74.8%). Mean age was 60 years (range 20-84 years). Two-thirds of the patients were hospitalized electively (68.4%). Aetiology of cirrhosis was ALD in 56 patients (58.9%), viral hepatitis in 28 patients (29.5%), with 4 hepatitis C virus-related cirrhosis and 1 hepatitis B virus-related one, NAFLD/MAFLD in 5 patients (5.3%) and other rare causes in 6 patients (6.3%) (hemochromatosis, alpha1-antitrypsin deficiency, autoimmune hepatitis and primary biliary cholangitis). Mean MELD score was 13.4 ± 6.6 points. 40% of patients had a Child-Pugh A score, 41% a Child-Pugh B score and 19% a Child-Pugh C score. Mean BMI was 27.1 kg/m².

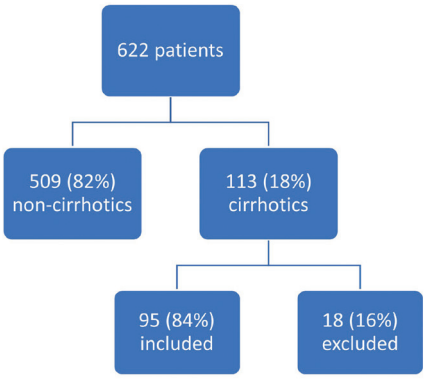

Figure 2. — Recruitment flowchart.

Table 3.— **Patient characteristics**

Variables	Values
Males, n (%)	71 (74,7%)
Mean age, years (range)	60 (20-84)
Aetiology of cirrhosis, n (%)	alcohol = 56 (58,9%)
	hepatitis B or C viruses = 28 (29.5%)
	NAFLD = 5 (5.3%)
	other = 6 (6.3%)
Mean BMI, kg/m² (± SD)	27.1 (± 6.7)
HCC[ii], n (%)	44 (46.3%)
Diabetes mellitus, n (%)	35 (36.8%)
Mean MELD[i], points (± SD)	13.4 (± 6.6)
Mean Charlson comorbidity index, points (± SD)	6 (± 2.3)
Mean serum sodium level, mmol/L	135 (± 5.55)
Mean albumin level, g/L (± SD)	33 (±6,7)
Mean prealbumin level, g/l (± SD)	0.09 (±0.05)
Mean bilirubin level, g/dl (± SD)	2.9 (±3.6)
Total lymphocyte count was (per/µL) (± SD)	1.31 (±0.70)
Mean platelet count (per/µL) (± SD)	125.00 (±60.00)
Mean INR (± SD)	1.40 (±0.45)
Mean vitamin D level (ng/mL) (± SD)	21.20 (±17.0)

[i] BMI : Body Mass Index. [ii] HCC : Hepatocellular carcinoma. [iii] MELD : Model for End Stage Liver Disease.

Table 4. — **Nutritional scores according to CHILD-PUGH score**

Child-Pugh Score	Number of patients	MUST Score				
		0	1	2	3	4
A	51	78%	6%	14%	2%	0%
B	44	64%	23%	9%	2%	2%
C	18	39%	22%	11%	17%	11%
TOTAL	**113**	**66%**	**15%**	**12%**	**4%**	**3%**

Child-Pugh Score	Number of patients	NRS 2002			
		0	1	2	3
A	51	71%	22%	6%	2%
B	44	50%	27%	23%	0%
C	18	28%	22%	33%	17%
TOTAL	**113**	**56%**	**24%**	**17%**	**4%**

Child-Pugh Score	Number of patients	MALNUTRITION	
		No	Yes
A	51	76%	24%
B	44	52%	48%
C	18	28%	72%
TOTAL	**113**	**59%**	**41%**

Diabetes mellitus was present in 36.8% of patients. 19 patients (20%) had addiction: 45 patients (47.4%) with a history of tobacco consumption, 67 patients (70.5%) with a history of alcoholism. 15 patients (15.8%) were patients with active alcohol use dependence and 5 patients (5.3%) were drug abusers. Patients took a mean of 5 drugs (medication). Other biological data are summarized in Table 3.

Malnutrition, based on our nutritional tool, affected 45.3% of patients: 29% with Child-Pugh A, 48.8% with Child-Pugh B and 72.2% with Child-Pugh C. MUST scoring system was null in 59 patients (62.1%), 1 point in 16 patients (16.8%), 2 points in 12 patients (12.6%), 3 points in 5 patients (5.3%) and 4 points in 3 patients (3.2%). NRS 2002 scoring system was null in 51 patients (53.7%), 1 point in 21 patients (22.1%), 2 points in 19 patients (20%) and 3 points in 4 patients (4.2%). We summarized the three scores regarding to Child-Pugh in Table 4. Mean Braden scale was 21.54 ± 2.25; 46.3% of patients had a Braden scale <23. Charlson comorbidity index was < 4 in 7 patients (7.4%). Mean CLIF-SOFA score was 4.20 in our cohort, with 11 patients (11.6%) with a CLIF-SOFA ≥ 7.

Survival rates of cirrhotic patients

During the follow-up, 59 patients (62.1%) developed a complication. Complications were ascites in 42.4% (25 patients), variceal bleeding in 10.2% (6 patients), overt hepatic encephalopathy in 52.5% (31 patients), infection requiring hospitalization in 39% (23 patients), including SBP in 56.5% of them (13 patients in total), HRS in 18.6% (11 patients), deep vein thrombosis in 6.8% (4 patients), hepatocellular carcinoma in 3.4% (2 patients) and transjugular intrahepatic portosystemic shunt (TIPS) placement in 6.8% (4 patients). Among patients who developed complications (n = 59), 17 (28.8%) were in Child's class C, 31 (52.5%) B and 11 (18.7%) A. Among patients who died (n = 32), 13 (40.6%) were in Child's class C, 17 (53.1%) in Child's class B and 2 (6.3%) in Child's class A. The 30-day readmission rate was 9.5% (9 patients). During follow-up, 43 patients (45.3%) were hospitalized (unplanned hospitalizations). 24 patients were admitted to the intensive care unit and 14 patients were transplanted.

60.7% patients developed complication in the malnutrition group *vs*. 39.3% in the well-nourished group (p<0.001, OR 5.06, CI 95 1.90-14.58) and 32 patients (33.7%) died (68.75% in the malnutrition group *vs.* 31.25%, p=0.002, OR 4.33, CI 95 1.62-12.28). The 30-day mortality rate was 6.3% (6 patients) and the 90-day mortality rate was 13.7% (13 patients). These results are reported on a Kaplan-Meier curve in Figure 3.

Morbidity & Mortality Prognostic factors

Factors significantly associated with morbidity in univariate analysis were serum sodium (Na) <135 mmol/L (p<0.001), a MELD score >15 (p<0.001), PNI <40 (p<0.001) (Figure 4), Braden scale <23 (p=0.005), malnutrition (p<0.001) and the presence of hepatocellular

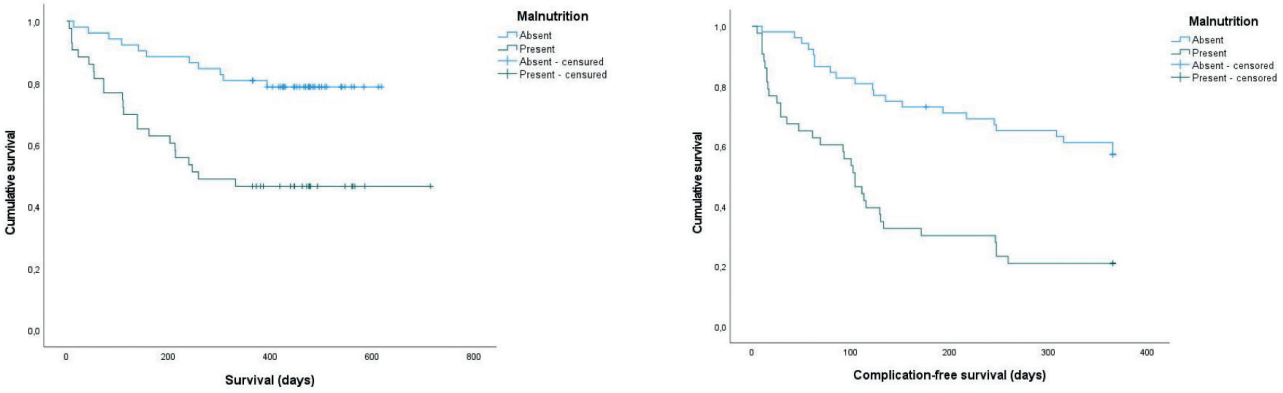

Figure 3. — Kaplan-Meier curves showing cumulative survival and complication-free survival during follow-up. Survival in well-nourished patient vs malnourished patients (68.75% in the malnutrition group *vs.* 31.25%, p=0.002, OR 4.33, CI 95 1.62-12.28). Complications in well-nourished patients vs malnourished patients (p<0.001, OR 5.06, CI 95 1.90-14.58).

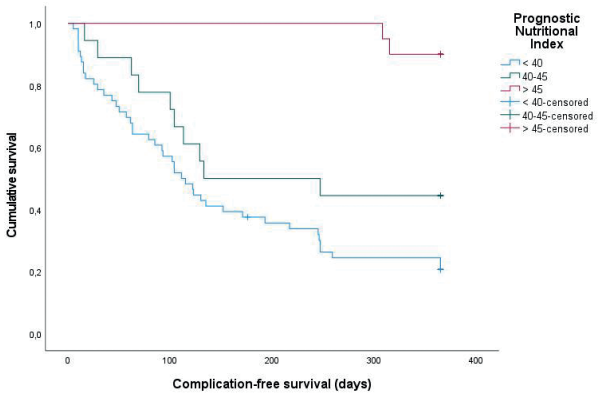

Figure 4. — Association of Prognostic Nutritional Index (PNI) levels with morbidity. In a univariate analysis, PNI <40 is significantly associated with poor survival compared to PNI between 40 and 45 and PNI >45 (p<0.001).

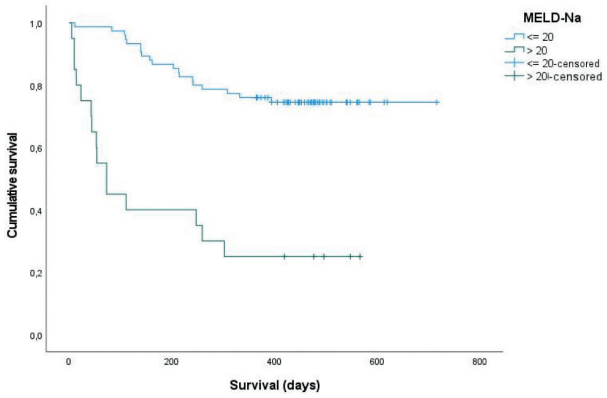

Figure 5. —Association of MELD-Na score level with survival. A MELD-Na score >20 is significantly associated with mortality compared to MELD-Na < 20 (p<0.001)

carcinoma (p=0.013). In multivariate analysis, factors significantly associated with morbidity were serum Na <135 mmol/L (p=0.033), PNI <40 (p=0.001) and malnutrition (0.014). Age ≥65 (p=0.912), diabetes mellitus (p=0.780), Charlson comorbidity index ≥4 (p=0.120) and thrombocytopenia <150000/µL (p=0.144) were not significantly associated with morbidity.

Factors significantly associated with mortality in univariate analysis were serum Na <135 mmol/L (p<0.001), a MELD score >15 (p<0.001), a MELD-Na score >20 (p<0.001) (Figure 5), PNI <40 (p=0.003) (Figure 4), Braden scale <23 (p=0.047) and malnutrition (p<0.001). In multivariate analysis, factors significantly associated with mortality were serum Na <135 mmol/L (p=0.091), a MELD score >15 (p<0.001), Braden scale <23 (p=0.027), malnutrition (p=0.003) and the Charlson comorbidity index ≥4 (p=0.016). Age ≥65 (p=0.446), HCC (p=0.661), diabetes mellitus (p=0.486), Charlson comorbidity index ≥4 (p=0.642) and thrombocytopenia <150000/µL (p=0.940) were not significantly associated with mortality.

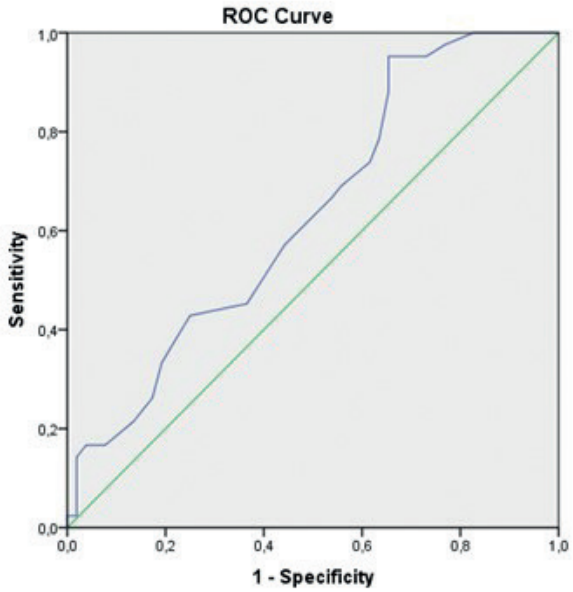

Figure 6. — ROC Curve of Prognostic Nutritional Index (PNI) for the diagnosis of malnutrition in cirrhosis. The correlation between PNI and malnutrition is low AUC=0.633.

Adjusting for age, serum Na, MELD score, Charlson index, HCC, platelets, diabetes mellitus, PNI and Braden scale, malnutrition was significantly associated with higher mortality and higher morbidity rates with odd ratios of 3.56 (CI 95 1.55-8.16) and 2.09 (CI 95 1.16-3.77) respectively. Braden scale was significantly associated with higher mortality (p=0.027, OR 1.25, CI 95 1.03-1.52) whereas PNI was associated with higher morbidity (p=0.001, OR 0.94, CI 95 0.90-0.98).

Subgroup analyses

We also performed subgroup analyses for patients with diabetes mellitus or HCC to assess the impact of nutritional status. Concerning diabetes mellitus, malnutrition was present in 15 patients out of 36 diabetic patients (41.7%) compared to 31 patients out of 59 non-diabetic patients (52.5%). Death rate was similar in both groups (35.6% in diabetic patients *vs*. 30.6% in non-diabetic patients) (p=0.486). Concerning HCC, malnutrition was present in 17 patients out of 44 (38.6%) compared to 29 patients out of 51 without HCC (56.9%). 1-year mortality was 37.3% in non-HCC patients *vs*. 29.6% in patients with HCC (p=0.661). Interestingly, patients with HCC were mainly Child-Pugh A (56.8%) in comparison to patients without HCC (only 25.5% being Child-Pugh A). Concerning alcohol use dependence, malnutrition was present in 29 patients out of 56 alcohol-related cirrhotic patients (51.8%) compared to 17 patients out of 39 non-alcohol-related patients with cirrhosis (43.6%). 1-year mortality was 37.5% in alcohol-related cirrhosis vs. 28.2% in patients with cirrhosis of another aetiology. Regarding to the 14 patients transplanted, 7 were malnourished (50%), 5 had a Meld score > 15 (35,7%) and 8 had and HCC (57,1%).

PNI as a marker of malnutrition in cirrhosis?

We found a poor correlation between malnutrition and PNI in cirrhosis, with an area under the curve of 0.633 as shown in Figure 6.

Discussion

Assessment of nutrition is important in the care of cirrhotic patients. It is essential to screen it early during the hospitalization, and in the follow-up of outpatients. In our study, we found a prevalence of 45.3% of malnutrition, which is like what has been reported in previous studies (22,37). Our cohort of patients was similar to other studies: a majority of men, alcohol as a major aetiology of cirrhosis, presence of diabetes mellitus, and mean MELD score. We have a high proportion of HCC since our centre is a referral centre for loco-regional treatment of HCC. Mean BMI was quite high (more than 25 kg/m²) despite a high proportion of malnutrition. The combination of malnutrition with loss of skeletal muscle and obesity with gain of adipose tissue is now observed in lot of cirrhotic patients (38). Otherwise, high BMI is also explained by Na and water retention. Indeed, 43 patients (45.3%) presented ascites at the beginning of the follow-up. We used the composite score of our hospital to define malnutrition. Even though BMI was used as a component and is increased with ascites in cirrhosis, the score gives good results in distinguishing two groups of inpatients with different prognosis. We demonstrated that malnutrition is associated with significantly higher morbidities and mortality. These complications result in an increased length of hospitalization and higher medical costs. With the same MELD score, malnutrition has an important influence on the clinical evolution. Unfortunately, MELD score ignores the nutritional state of the patient. Stickel *et al.* (39), highlighted an inaccurate prediction of survival after liver transplantation in 15-20% of cases because of not including a nutritional assessment. It is important to note that our results of important mortality in malnourished patient are found despite personalized nutritional counselling by a dietician, including all ESPEN recommendations (e. g. late evening snack) at the beginning of the follow-up. We only used a classification of malnutrition at the baseline and studied its impact on the morbidity and mortality. We didn't include evolution of the nutritional status of our patients with their nutritional counselling and we didn't study its impact on morbidity and mortality. Further studies are needed to improve nutritional management in cirrhosis and to assess the positive impact of dietary measures on eventual survival. Currently, dietary management has only shown a relative benefit in Child A patients (6).

Furthermore, we showed that low Na is linked to poor prognosis. Na is the only parameter, with malnutrition, to be linked to both higher morbidity and mortality in multivariate analysis in our study. Indeed, serum Na is now used in the MELD score, which is then called MELD-Na (40). It has also a strong predictive value in surviving in our population. Since PNI is linked to albumin level, it reflects more the severity of the underlying cirrhosis than the poor nutritional status in these patients. We analysed the link between PNI and malnutrition in our cohort and we found a poor ROC curve with an AUC of 0.633, meaning that PNI is not correlated with malnutrition in cirrhosis.

We also investigated other tools in the prediction of mortality. The frailty is known to be an important predictor of mortality in geriatric patients (41). More recently, this concept began to gain importance in the evolution of cirrhotic patients. For example, *Fried Frailty Index* and *the 6-minute walk test* have been validated in the assessment of mortality in the waiting-list for transplantation (42, 43). The Braden Scale was developed to predict pressure ulcer risk in patients. We included it in our analysis because it is composed by a subjective assessment of the ability of the patient to feed himself. In our cohort, a low Braden scale was significantly associated with higher mortality. Tapper *et al*. already showed a correlation between 90-day mortality and a low Braden Scale (25). However, this low Braden Scale is probably more a reflection of the poor status of the patients than a cause of the 1-year mortality.

Limitations of our study are its retrospective nature, the small size of the cohort, the fact that it is a single-centre study and the lack of consensus in the definition of malnutrition in cirrhotic patients. Otherwise, we were not able to use classic functional scores (triceps skinfold, 6 minutes' walk test, handgrip strength) bioelectrical impedance analysis) or the Liver Frailty Index (44) because of the retrospective nature of the study and the fact that those tests were not used routinely in our centre. Hence, real assessment of functional outcome has not been performed. Therefore, we are not able to compare real functional scores of our population to previous studies and make a significative conclusion about its impact on the morbidity-mortality. However, Braden Scale is a setting that could be studied retrospectively. This scale, reported by the nurses, is systematically included in the medical field of our patients. With its description of mobility, activity, ability to feed himself and need for assistance of the patient, Braden Scale is a reflect of the others functional scores and could be included in future studies on functional scores despite its part of subjectivity. Frailty concept could have been highlighted in our study with the clinical frailty score, well-know to be predictive of mortality (45), but we weren't able to add it because of the retrospective nature of our study. Finally, sarcopenia, closely linked to malnutrition and frailty, is an emerging concept (46). It has been shown to increase the risk of morbidity dans mortality on the waiting list of transplantation (47). Changes in muscles mass and composition could be evaluated on CT-scan and seems to be linked in the progression of all decompensated cirrhosis (48). Compare nutrition status, frailty status, and objective measures of muscle quantity/quality could

be an additional issue for further investigations. Which of the available methods (functional or morphological) to evaluate sarcopenia is the most efficient to predict morbidity and mortality? Unfortunately, we had a relatively high amount of lost-to -follow-up (17 patients, 15% of the total of cirrhotic patients identified during the inclusion period). It is mainly explained by the fact that our hospital is a referral centre.

In conclusion, malnutrition is highly prevalent in hospitalized cirrhotic patients, affecting more than 45% of them, despite high median BMI in this population. Malnutrition, low PNI and low Braden scale are associated with poor outcomes in cirrhosis: malnutrition with morbi-mortality, low PNI with one-year morbidity and low Braden scale with one-year mortality rates. Screening for malnutrition, education on nutrition for health workers and therapeutic efforts should be implemented in medical institutions to improve outcomes in cirrhosis.

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