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CLINICAL COURSE OF ASCITIC SYNDROME AND ACUTE KIDNEY INJURY IN THE SETTING OF NONSELECTIVE BETA-BLOCKERS OR ENDOSCOPIC VARICEAL LIGATION FOR PRIMARY PREVENTION OF BLEEDING IN CIRRHOTIC PATIENTS AWAITING LIVER TRANSPLANTATION

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Objective: to compare the effects of nonselective beta-blockers (NSBB) and endoscopic variceal ligation (EVL) on patient survival, ascites dynamics, and development of acute kidney injury (AKI) during primary prevention of bleeding from the esophageal varices and cardia in patients with decompensated cirrhosis on the liver transplant waiting list (LTWL). **Materials and methods.** A retrospective comparative study of the clinical data of patients with severe ascites and esophageal varices without a bleeding history at the time of their inclusion in the LTWL was performed. Group 1 patients (n = 84) were prescribed NSBB, alpha and beta-adrenoblockers in order to prevent bleeding and reduce progression of decompensated cirrhosis. Group 2 patients underwent EVL. **Results.** Demographic, laboratory and instrumental parameters of patients in the compared groups had no significant differences. In both groups, there were no significant differences between the indicators of severity of liver lesions (MELD-Na, Child–Turcotte–Pugh), frequency of severe ascites, frequency of varicose nodes grades 2–3. At follow-up, bleeding developed in 22 patients (13.25%) – 13 patients in the NSBB group and 9 patients in the EVL group (15.47% and 10.97%, respectively, $p > 0.05$). Patient survival was significantly higher in the EVL group than in the NSBB group. Incidence of refractory ascites, number of patients with grade 3 ascites, and AKI stages 2–3 in the NSBB group, were significantly higher ($p < 0.05$) than in the EVL group. MELD-Na was the independent predictor of mortality in the EVL group, while low mean arterial pressure (mAP) and presence of AKI were those for patients receiving NSBB. **Conclusion.** NSBB and EVL are effective methods of primary prevention of bleeding. Mortality rate, number of patients with refractory ascites and severe ascites, and number of patients with AKI stages 2–3 were higher in the NSBB group than in the EVL cohort. In EVL patients, the independent predictor of death was MELD-Na, while in NSBB patients, the independent predictors of mortality were low mAP and presence of AKI.

Keywords: liver transplant waiting list, ascites, variceal bleeding, endoscopic variceal ligation, nonselective beta blockers, acute kidney injury, MELD-Na, mean arterial pressure.

INTRODUCTION

NSBB and EVL are means of curbing the progression of decompensated cirrhosis after occurrence of the first decompensating event, most often ascites [1, 2]. The term "progression of decompensated cirrhosis" was introduced into clinical practice by the International Consensus on the Diagnosis, Treatment and Prevention of Cirrhosis Complications (Baveno VII) [3]. According to the authors of the Consensus, the term "progression of decompensated cirrhosis" implies the presence of a prognostic stage characterized by a higher patient mortality than in the first episode of decompensation [3]. Several factors are considered as drivers of progression of decompensated cirrhosis: variceal bleeding (VB) or gastric bleeding (GB), diuretic-resistant ascites or a significant increase in the clinical severity of ascites, manifestations of hepatic

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encephalopathy (HE) [3]. Measures to prevent progression of decompensated cirrhosis include prophylaxis of the first bleeding episode in patients with varices at low or high risk of VB or GB. Baveno VII experts prioritize traditional NSBB or carvedilol. In cases of intolerance or contraindications to the use of this class of drugs, an interventional procedure – EVL – is recommended. Despite the relative effectiveness of primary prevention of bleeding in patients with ascites, the first episode of decompensated cirrhosis is an indication for inclusion in the LTWL [3]. In all transplant systems in Europe, USA, Russia, etc. there is a gap between the number of LTWL patients and the number of LT performed. This is proportionally related to increased decompensated cirrhosis and, accordingly, indications for LT [1, 3] on one hand, and organ shortages [4–6] on the other hand. Increased LTWL time causes further decompensation due to the risk of recurrent events (bleeding, diuretic-resistant ascites, development of manifest HE, etc.). In this regard, therapeutic measures aimed at preventing further decompensation and, accordingly, at preserving the life of this group of patients, are extremely relevant [3, 7].

Ascites is the most common decompensating event in cirrhosis, and it is associated with high morbidity and mortality rates [8, 9]. After the development of ascites, further decompensating events in cirrhosis may develop, which are subclassified as ascites-related (spontaneous bacterial peritonitis, dilutional hyponatremia and acute liver injury [10–12]), or ascites-unrelated (VB and HE [13]), which complicate the clinical course of the disease [9, 13].

MATERIALS AND METHODS

The comparative retrospective study included 166 cases with decompensated cirrhosis who were included in the LTWL between 2016 and 2022.

Inclusion criteria: ascites of varying severity, no variceal bleeding prior to inclusion in the LTWL, abstinence for at least 3 months (confirmed by addiction specialists) prior to inclusion in the list for patients with alcohol-related cirrhosis, virus-related cirrhosis (hepatitis B virus (HBV)- or hepatitis C virus (HCV)-associated etiology), cirrhosis of mixed etiology (virus-related and alcohol-related), cirrhosis classes B and C according to the Child–Turcotte–Pugh (CTP) classification.

Exclusion criteria: patients with any tumors, including hepatocellular cancer, accompanied by ascites, HE grade 2 and above, any infections, portal vein thrombosis, renal dysfunction at the time of inclusion in the study, refractory ascites, contraindications to NSBB (bradyarrhythmia, bronchial asthma, obstructive pulmonary disease), and diabetes mellitus.

Group 1 included 84 patients and group 2 had 82 patients. Both groups of patients with ascites, as the first episode of the beginning phase of decompensated cirrhosis, were included in the LTWL. Patients from the first group with signs of high risk of first VB received NSBB or carvedilol for primary prophylaxis. Group 2 patients underwent EVL for the same purposes due to intolerance and/or contraindications to NSBB or carvedilol.

Concurrently, we investigated the survival rates among patients who received NSBB or underwent EVL during primary prophylaxis of bleeding in those with decompensated cirrhosis included in the LTWL (primary endpoint of the study) and determined the effect of NSBB and EVL on the dynamics of ascites and AKI during primary prevention of bleeding in patients with decompensated cirrhosis included in the LTWL (secondary endpoint of the study).

All data, including demographic, clinical, and laboratory parameters, were obtained from a permanent, continuously updated electronic database of patients who were under follow-up after their inclusion in the LTWL, after approval of the study by the Local Ethics Committee, Center for Surgery and Donation Coordination, Rostov Regional Clinical Hospital.

Clinical and biochemical blood tests, hemostasis parameters, calculation of MELD-Na scores and liver injury class according to CTP were repeated at 3-month intervals where the patients' condition was stable.

Where patients' condition was stable, abdominal ultrasound was carried out every 6 months (of waiting for LT) after the patients' initial examination.

In all patients, esophagogastroduodenoscopy (EGD) was performed to screen for varices with high risk of VB. The Baveno VI [14] and World Gastroenterology Association (WGO) [15] guidelines were used to identify patients with varices requiring urgent therapy (medium and large varices).

The severity of ascites in patients included in the study was determined according to the International Ascites Club criteria [16]. To diagnose AKI, we used the criteria proposed by the experts of the International Kidney Disease Improving Global Outcomes (Kidney Disease Improving Global Outcomes), modified by experts from the International Ascites Club [17, 18].

Mean arterial pressure (mAP) was determined by the formula: $mAP = (DP) + {}^{1}/_{3}(SP - DP)$, where SP is systolic pressure, and DP is diastolic pressure [19].

In order to prevent "further decompensation", we performed primary prophylaxis of VB using the traditional NSBB (propranolol, nadolol) and carvedilol. Propranolol was initiated at a starting dose of 40 mg/day, with a maximum dose of 240 mg/day; nadolol was 40 mg/day and 80 mg/day, respectively. The starting dose of carvedilol was 6.25 mg/day and the maximum dose was 25 mg/day. Heart rate, SP, DP and mAP were monitored in all patients using these drugs. Drug doses were adjusted whenever these parameters decreased.

A multi-band ligation kit was used to perform EVL. EGD was performed under sedation for this purpose.

EVL began at the gastroesophageal junction and proceeded proximally. Typically, 2 to 4 rubber ligatures were used depending on the size of varices. A repeat EVL was performed 4 weeks after the first, and subsequent EVLs were repeated until all varices, subject to emergency treatment criteria [14, 15], were obliterated. After achieving the result (obliteration of esophageal varices), control EGDs were performed at 3-month intervals. Where there are recurrences (appearance of new varices), repeat EVL was performed.

Patients in both groups received diuretics; paracentesis was performed in patients with diuretic-resistant ascites. Patients with AKI stage 2–3 were considered as a priority group for priority LT. During the waiting period for LT, patients with AKI stage 2–3 were discontinued from diuretics and received intravenous infusions of albumin and terlipressin.

According to the guidelines for the treatment of patients with HBV- and HCV-associated cirrhosis who are waitlisted for LT, antiviral therapy with nucleoside alternatives and a combination of direct-acting antivirals was performed, respectively [20].

The obtained data were analyzed using IBM SPSS Statistics (version 23). The type of distribution of the obtained variables of sample indicators (normal and non-normal distribution) was determined by calculating the Kolmogorov–Smirnov test. In the case of normal distribution, the variables were presented as arithmetic mean (M) with determination of standard deviation (SD); significance of differences between compared values was determined by Student's t-test. In the case of non-normal distribution, variables were expressed by means of median (Me) and interquartile range (IQR, interval between the 75th and 25th percentiles of the data). To determine the significance of differences between variables, the following nonparametric criteria were used: Wilcoxon test for pairwise comparisons of dependent variables, Mann–Whitney U test and Pearson's Chi-square for comparison of independent variables. Frequency and proportion (%) analysis was used to compare qualitative parameters. The p value <0.05 was accepted as the criterion of statistical significance between compared parameters. Patient survival in the compared groups was determined by the Kaplan–Meier method. The significance of differences between compared curves was determined by calculating the logarithmic test [Log-Rank (Mantel-Cox)].

To determine the probability of an event depending on the values of independent variables (risk factors or predictors), we used a binary logistic regression method with stepwise removal of insignificant predictors by the backward elimination (Wald) method. To assess the quality of the regression model (predictive ability), the ROC (Receiver Operating Characteristic) curve was plotted and the area under the ROC curve (AUC) was calculated. The null hypothesis was that the AUC ROC curve did not differ from 0.5. The Mantel–Haenszel odds ratio (OR) was used to assess the association between the tested outcome and the risk factor, and the 95% confidence interval (CI) for this indicator was determined. A comparative assessment of accumulated risks in the groups was performed using a mathematical model of proportional risks (Cox regression). The risk of occurrence of the test event (HR, hazard ratio) was calculated with determination of 95% confidence interval (CI) for this indicator.

RESULTS

Data on demographic, clinical, laboratory parameters, indices (MELD-Na, CTP) in the groups of patients who received NSBB (n = 84) or underwent EVL (n = 82) during LTWL stay are presented in Table 1 and Table 2.

As can be seen from the tables presented, the demographic, laboratory and instrumental parameters of patients with decompensated cirrhosis in the compared groups had no significant differences. In both groups of patients included in the LTWL, there were no significant differences between the severity of liver injury represented by MELD-Na score and CTP class.

There were no significant differences in the pattern of etiology (virus-related, alcohol-related, mixed) in the compared groups of patients with decompensated cirrhosis. In patients enrolled in LTWL, grade 2 ascites prevailed without significant differences between the groups; the incidence of grade 3 ascites was also comparable in the compared groups ($p > 0.05$). Grade 2 varices prevailed in both groups without significant differences between groups ($p > 0.05$). There were also no significant differences ($p > 0.05$) in the incidence of grade 3 varices among the compared groups of patients.

During the follow-up period up to 18 months of LTWL stay, VB developed in 22 patients (13.25%) – 13 patients in NSBB group and 9 in EVL group (15.47% and 10.97%, respectively, $p > 0.05$).

During the LT wait period, 53 patients (31.92%) died in both groups: 36 patients in the NSBB-treated group and 17 patients in EVL group (42.85% and 20.73%, respectively, $p < 0.05$). Thus, patient survival was significantly higher in EVL than in NSBB group, as determined by the Kaplan–Meier method (Log Rank = 0.004) (Fig. 1).

While waiting for LT during 18 months of follow-up, both patient groups developed refractory ascites (20 patients, 10.75%). The frequency of refractory ascites in NSBB group was significantly higher ($p < 0.05$) than in EVL group (Table 3). The number of patients with grade 3 ascites and AKI stages 2–3 increased in NSBB group compared to EVL group during the mentioned LTWL stay period (Table 3).

To search for possible risk factors for death and predictors influencing mortality, a comparative analysis was performed in the groups of deceased and survivors at the time of follow-up, who received NSBB in LTWL

or underwent EVL. Using the binary logistic regression method with stepwise removal of insignificant predictors by the backward Wald exclusion method, we were able to identify significant predictors of mortality (Table 4).

As shown in Table 4, MELD-Na, CTP class, platelet and leukocyte counts were significant predictors of mortality in EVL group. To test the suitability of the regression model for predicting the risk of waitlist mortality, ROC analysis of the identified predictors was performed to obtain ROC curves and calculate the area under them (AUC) (Table 5 and Fig. 2).

From Table 5 and Fig. 2, it can be concluded that the predictors included in the regression model (MELD-Na, platelet and leukocyte counts) significantly affect waitlist

Table 1

Comparative characteristics of the indicators in the NSBB and ELV groups (normal and non-normal distribution)

Indicator	NSBB (n = 84) M ± SD	EVL (n = 82) M ± SD	Statistical significance
Normal distribution (M ± SD)			
Age	51.36 ± 11.43	49.57 ± 11.98	p > 0.05
Hemoglobin (g/L)	110.57 ± 24.18	114.57 ± 25.83	p > 0.05
Leukocytes ($\times 10^9$/L)	3.25 ± 0.67	3.19 ± 0.79	p > 0.05
Platelets ($\times 10^9$/L)	79.87 ± 32.75	75.67 ± 35.39	p > 0.05
Plasma albumin (g/L)	38.78 ± 4.67	36.23 ± 4.25	p > 0.05
MELD-Na	22.12 ± 4.57	21.49 ± 5.21	p > 0.05
mAP (mmHg)	76.35 ± 21.54	77.54 ± 24.35	p > 0.05
SP (mmHg)	111.15 ± 29.34	109.56 ± 31.05	p > 0.05
DP (mmHg)	62.21 ± 19.31	67.54 ± 18.57	p > 0.05
Non-normal distribution (Me; IQR)			
INR	2.02 (1.59–2.43)	1.90 (1.81–2.18)	p > 0.05
Bilirubin (μmol/L)	69.0 (57.5–108.5)	65.0 (53.00–105.00)	p > 0.05
Creatinine (μmol/L)	92.0 (68.55–120.5)	88.0 (63.5–119.5)	p > 0.05
Na (mmol/L)	137.5 (118.5–149.5)	134.5 (104.5–170.5)	p > 0.05

Table 2

Comparative characteristics of indicators (sex, etiology of cirrhosis, severity of ascites, severity of esophageal varices, class of cirrhosis) in the NSBB and ELV groups

Indicator	NSBB (n = 84) (%)	EVL (n = 82) (%)	Statistical significance
Male	62 (73.81%)	63 (76.83%)	p > 0.05
Virus-related cirrhosis	49 (58.33%)	47 (57.32%)	p > 0.05
Alcohol-related cirrhosis	25 (29.77%)	27 (32.92%)	p > 0.05
Cirrhosis of mixed etiology	10 (11.90%)	8 (9.76%)	p > 0.05
Ascites, grade 2	62 (73.81%)	63 (76.83%)	p > 0.05
Ascites, grade 3	22 (26.19%)	19 (23.17%)	p > 0.05
Esophageal varices, grade 2	59 (70.24%)	57 (69.51%)	p > 0.05
Esophageal varices, grade 3	25 (29.76%)	25 (30.49%)	p > 0.05
CTP class B	5 (5.95%)	7 (8.54%)	p > 0.05
CTP class C	79 (94.05%)	75 (91.46%)	p > 0.05

Table 3

Comparative characteristics of indicators in the NSBB and ELV groups 18 months since start of the study

Indicator	NSBB (n = 84) (%)	EVL (n = 82) (%)	Statistical significance
Refractory ascites	16 (19.05%)	4 (4.88%)	p < 0.05
Ascites, grade 2	24 (28.57%)	56 (68.29%)	p < 0.05
Ascites, grade 3	44 (52.38%)	22 (26.83%)	p < 0.05
AKI, stage 1	6 (7.14%)	4 (4.88%)	p > 0.05
AKI, stage 2	13 (15.48%)	2 (2.44%)	p < 0.05
AKI, stage 3	11 (13.10%)	3 (3.66%)	p < 0.05

mortality at 18 months. At the same time, MELD-Na is an independent predictor of mortality.

Since the AUC ROC values for leukocyte and platelet counts and CTP class were below 0.5, these indicators were excluded from the analysis due to their unsuitability for use as independent predictors in the mathematical model.

The Mantel–Haenszel OR for mortality in EVL group if the MELD-Na score at LTWL inclusion was >25 was 2.077 (95% CI 1.562–2.92); if MELD-Na ≤25, the OR was 0.238 (95% CI 0.155–0.365); $p < 0.0001$.

To clarify the association between NSBB, AKI and waitlist mortality, we used Cox proportional hazards mathematical regression model with calculation of risk of death (HR) and determination of 95% confidence interval (CI).

As shown in Table 6, two independent risk factors, mAP score and AKI (HR = 2.220; p = 0.001; 95% CI [0.890–5.534] and HR = 4.601; p = 0.005; 95% CI [1.747–11.163], respectively), significantly influenced mortality rates in NSBB group.

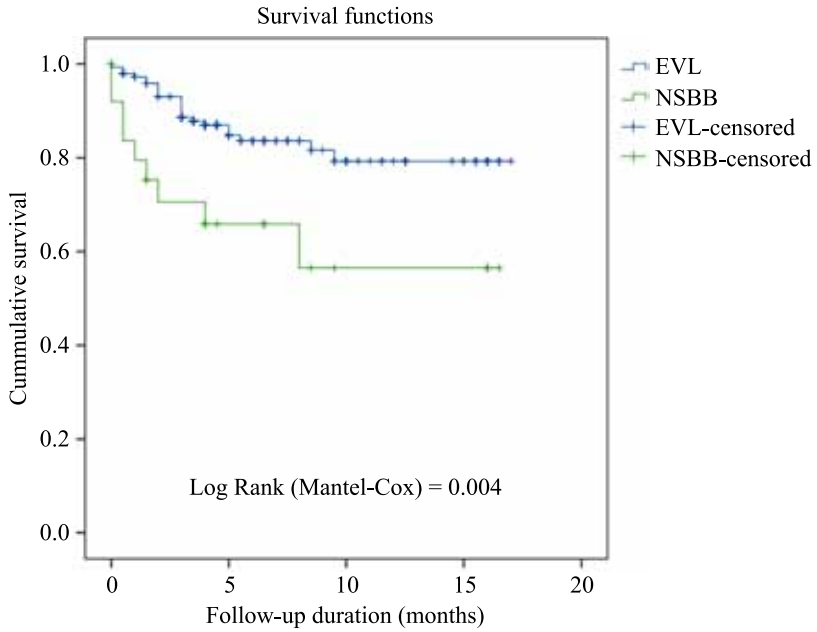

Fig. 1. Patient survival in the EVL and NSBB groups (Kaplan–Meier estimate with Log-Rank test)

Table 4

Variables in the binary logistic regression equation

Variable	B	Root mean square error	Wald	p-value	Exp (B)	95% CI for Exp (B)	
						Lower bound	Upper bound
MELD-Na	0.080	0.041	3.874	0.049	1.083	1.000	1.173
Platelets	–0.012	0.006	3.952	0.047	0.988	0.976	1.000
Leukocytes	–1.130	0.280	16.261	0.001	0.323	0.187	0.560
CTP class	1.723	0.767	5.051	0.025	5.601	1.247	25.163
Constant	1.374	1.563	0.773	0.379	3.950		

Note. Independent variables (creatinine and albumin levels) whose values were not significant (p > 0.05) are not shown in the table.

Table 5

Characteristics of the predictive value of the resulting model

Variables	Area under the curve	Standard error	Asymptotic significance	Asymptotic 95% CI	
				Lower bound	Upper bound
MELD-Na	0.737	0.042	<0.001	0.655	0.818
CTP class	0.476	0.040	0.569	0.398	0.555
Platelets	0.288	0.037	<0.001	0.214	0.361
Leukocytes	0.225	0.033	<0.001	0.160	0.289

DISCUSSION

Introduction of the main provisions of the Baveno VII Consensus into clinical practice led to a change in the way portal hypertension (PH) is treated. The main task was not to control the course (treatment) of ascites, but to prevent "progression of decompensated cirrhosis" (i.e. influence on the mechanisms of cirrhosis progression) and reduce patient mortality [3].

We found that when primary prophylaxis of bleeding in patients with decompensated cirrhosis included in the LTWL, survival was significantly higher in the group of patients who underwent EVL than in the NSBB group. This difference was due to a higher mortality rate in NSBB group compared to EVL group (42.85% and 20.73%, respectively, $p < 0.05$).

Similar results to our work were obtained in a randomized clinical trial (RCT) that included patients with severe ascites and varices requiring primary prevention of bleeding. It was shown that the survival rate of patients treated with NSBB (propranolol) was lower than in the EVL group (76.0% and 89.7%, respectively, $p = 0.02$) [21].

In another study involving two groups of patients with compensated cirrhosis (with and with no NSBB), NSBB was found to improve patient survival at up to 3 years of follow-up [22]. In particular, the use of NSBB resulted in increased survival in the group of patients awaiting LT compared to patients not receiving these drugs (HR: 0.319, 95% CI: 0.120–0.848; $p = 0.022$). However, compared with our study and the RCT cited above [21], most patients had compensated cirrhosis in this study and a relatively low MELD score (51.1%, CTP class A, MELD: 12.1 ± 3.8). In our study, CTP grade C was dominant among patients in both groups (94.05% and 91.46%, respectively), MELD scores also had a higher gradation (22.12 ± 4.57 and 21.49 ± 5.21, respectively).

In our study, both methods of primary prevention of bleeding were quite effective, as evidenced by the low incidence of VB during an 18-month follow-up period.

Previously, we obtained similar results comparing NSBB and EVL for primary prevention of VB at follow-up periods ranging from 1 month to 36 months in the LTWL [23]. Similar results to our data were obtained by Singh et al. [21]. The RCT authors found that the

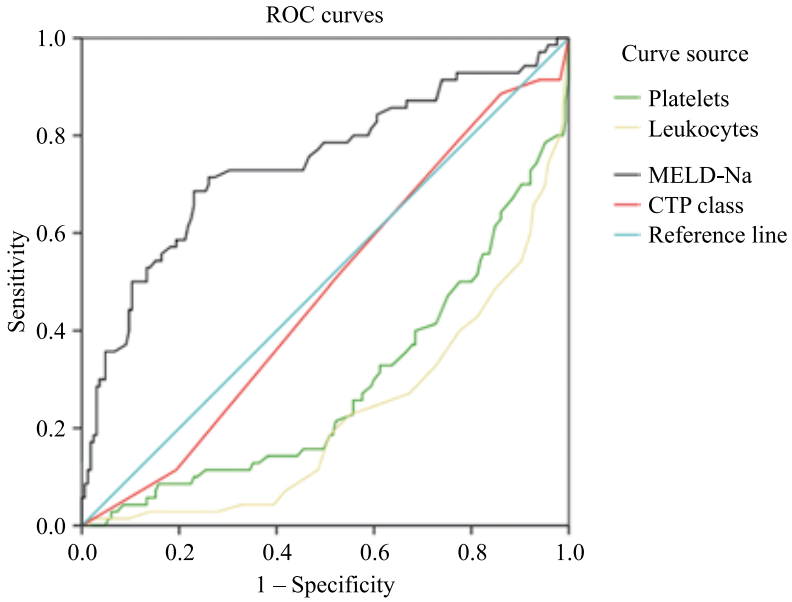

Fig. 2. ROC curves of predictors of mortality during LTWL stays of up to 18 months in EVL subjects

Table 6

Variables in the Cox regression equation (proportional hazards model)

Variable	B	Root mean square error	Wald	p-value	Exp (B)	95% CI for Exp (B)	
						Lower	Upper
Leukocytes	–0.629	0.201	9.843	0.053	0.533	0.360	0.790
Creatinine	0.005	0.004	1.630	0.202	1.005	0.997	1.012
mAP	0.797	0.032	2.926	0.001	2.220	0.890	5.534
MELD-Na	0.036	0.046	0.602	0.438	1.037	0.360	0.790
AKI	1.723	0.767	5.051	0.005	4.601	1.747	11.163

incidence of VB when comparing NSBB group and EVL group was 7.5% and 2.5%, respectively, p = 0.13.

Pérez-Ayuso et al. [24] showed no significant differences in the incidence of bleeding when comparing NSBB (propranolol) and EVL used in primary prophylaxis of VB.

Wei et al. [25] found NSBB (carvedilol) and ELV to have equal efficacy in primary prophylaxis of bleeding at 6, 12, 18 and 24 months of follow-up.

Pfisterer et al. [26] found no significant differences between the efficacy of NSBB (propranolol, carvedilol) and EVL in primary prophylaxis of VB at up to 3 years follow-up period. The study authors showed that bleeding rates at 1 year for NSBB and EVL were 7.5% and 9.9%, respectively, (p > 0.05); at 2 years, 15.5% and 16.7%, respectively (p > 0.05); and after three years, 18% and 19.7%, respectively (p > 0.05).

We found that both compared groups developed refractoriness to the current therapy for ascites, the incidence of which was significantly higher in NSBB patients than in EVL group. In addition, the proportion of patients with grade 3 ascites increased in NSBB cohort.

Singh et al. [21] also noted a significant increase in the proportion of patients with worsening ascites in NSBB (propranolol) group compared to EVL group (15% and 5%, respectively, p = 0.03), as well as an increase in the proportion of patients who developed diuretic-resistant ascites (13.7% and 3.7%; respectively, p = 0.02).

We also found that over the 18-month LTWL stay, the proportion of patients with stage 2–3 AKI significantly increased in those receiving NSBB compared to the EVL-treated group.

An increase in the proportion of patients with AKI while receiving NSBB compared to patients receiving EVL was noted in the work of Singh et al. [21]. AKI was diagnosed in 26.2% of cases for NSBB and in 12.5% of cases for EVL, p = 0.02.

Lai et al. [27] showed that the use of NSBB in patients undergoing LTWL was associated with stage 2 AKI (HR = 1.8; 95% CI 1.26–2.57) in patients with decompensated cirrhosis (CTP grade C). The authors concluded that in patients with decompensated cirrhosis awaiting LT, the use of NSBB is undesirable because it is associated with a high risk of AKI.

We found that MELD-Na score is an independent predictor of mortality in patients undergoing EVL. It was shown that the risk of mortality in this category of patients (Mantel–Haenszel OR) depends on MELD-Na score. If MELD-Na score >25, the Mantel–Haenszel OR is 2.077 (95% CI 1.562–2.92), and if MELD-Na score <25, mortality risk is significantly lower (OR = 0.238 (95% CI 0.155–0.365); p < 0.0001.

Our findings about MELD-Na as an independent predictor of LTWL mortality are confirmed by Sinh et al. [21], who obtained similar results. Lai et al. [27] found that the risk of mortality in patients with cirrhosis, CTP class, awaiting LT was associated with NSBB (HR = 1.45; 95% CI 1.03–2.03).

We showed, using a mathematical Cox proportional hazards regression model, that two independent risk factors determine the development of mortality while taking NSBB: mAP score and AKI (HR = 2.220; p = 0.001; 95% CI [0.890–5.534] and HR = 4.601; p = 0.005; 95% CI [1.747–11.163], respectively).

In addition to the MELD-Na score, mAP <82 mmHg was also considered an independent risk factor for mortality, which is supported by our study [21].

In another study, multivariate analysis showed that the presence of ascites (HR: 3.901, 95% CI: 1.352–11.251; p = 0.012) and pre-existing renal impairment (HR: 4.315, 95% CI: 1.054–17.672; p = 0.012) were independent risk factors for AKI with NSBB in a cohort of patients with cirrhosis and varices requiring therapy [22].

In a prospective study, Sersté et al. [28] showed that NSBB was associated with lower mAP compared with the group of patients who did not receive these drugs (78 ± 3 mmHg and 87 ± 5 mmHg, respectively, p < 0.0001). Among patients taking NSBB during 168 days of follow-up, 89.6% (95%CI, 74.9–95.9%) developed AKI, compared with 50.4 (95%CI: 39.0–60.7) in patients not taking NSBB; p = 0.0001). In a multivariate analysis, the authors found independent predictors of AKI: high MELD score and NSBB. Ngwa et al. concluded that patients who took NSBB were more likely to develop AKI within a 90-day period than patients who did not take these drugs (22% and 11%, respectively, p = 0.048) [29].

CONCLUSION

Receiving NSBB and performing EVL in patients with cirrhosis, varices and ascites are effective methods of primary prevention of VB.

At the same time, mortality rates in patients receiving NSBB while waiting for LT was higher than in the group of patients undergoing EVL.

In NSBB group, there was an increased number of cases of diuretic-resistant ascites compared to EVL group, and there was an increased number of patients with more severe ascites.

In addition, the proportion of patients with AKI stages 2–3 in the group of patients who received NSBB during 18 months of LTWL stay increased significantly compared to EVL group.

MELD-Na score is an independent predictor of mortality in EVL patients. The risk of mortality (Mantel–Hentzel OS) in this category of patients depends on MELD-Na score.

Two independent risk factors determine mortality rates in patients who took NSBB: low mAP and presence of AKI.

The authors declare no conflict of interest.

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