Predicting an unfavorable outcome in patients with liver failure associated with obstructive jaundice syndrome: a prospective observational study

Прогнозирование неблагоприятного исхода у больных с печеночной недостаточностью на фоне синдрома механической желтухи: проспективное наблюдательное исследование

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Abstract

INTRODUCTION: Specialized scales developed to assess survival and mortality of patients after liver transplantation have not been validated when applied to liver failure in the setting of obstructive jaundice. **OBJECTIVE:** To determine the prognostic value of multiparametric scoring scales and to identify predictors of unfavorable outcome in liver failure due to obstructive jaundice. **MATERIALS AND METHODS:** 53 patients with confirmed liver failure due to obstructive jaundice of benign etiology who underwent biliary decompression were included in this prospective, observational, single-center study. Depending on the outcome two groups were distinguished: with favorable ($n = 27$, 51 %) and with unfavorable outcome ($n = 26$, 49 %). The following time points were defined for the dynamic evaluation of the course of the disease: day 1, day 3, day 7, and day 11 after decompression. Statistical processing of the data was performed using IBM SPSS Statistics 22 software for social science data analysis. **RESULTS:** The sensitivity and specificity of the studied scales in predicting liver failure due to obstructive jaundice were calculated on the basis of receiver operating characteristic (ROC) analysis. The AUROC for the SOFA was 0.862, for the MELD — 0.882, for the APACHE II — 0.864, for the Child-Turcotte-Pugh — 0.813. The sensitivity and specificity values for the SOFA were 78.9 and 77.8 %, for the MELD — 80.8 and 79.7 %, for the APACHE II — 57.7 and 81.9 %, and for the Child-Turcotte-Pugh — 75.1 and 70.9 %, respectively. Albumin was an independent predictor of unfavorable outcome (AUC ROC 0.909, $p = 0.01$), sensitivity 88.6 %, specificity 85.2 %. **CONCLUSIONS:** The scales presented in the study and the biomarker candidate "albumin" showed significant prognostic ability, but low values of sensitivity and specificity (less than 80 %) in some points of the study require the

Реферат

АКТУАЛЬНОСТЬ: Специализированные оценочные шкалы, разработанные для оценки выживаемости и летальности пациентов после трансплантации печени, не валидизированы применительно к печеночной недостаточности (ПН) на фоне механической желтухи (МЖ). **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Определить прогностическую ценность многопараметрических оценочных шкал и выявить предикторы неблагоприятного исхода при ПН на фоне МЖ. **МАТЕРИАЛЫ И МЕТОДЫ:** В проспективное наблюдательное одноцентровое исследование включены 53 пациента с верифицированным диагнозом ПН на фоне МЖ доброкачественного генеза, подвергшиеся декомпрессии желчевыводящих путей. В зависимости от исхода заболевания выделено две группы: с благоприятным ($n = 27$, 51 %) и неблагоприятным ($n = 26$, 49 %) исходами. Для динамической оценки течения заболевания определены временные точки исследования: 1, 3, 7, 11-е сутки после декомпрессионного вмешательства. Статистическую обработку данных проводили с использованием пакета статистических программ анализа данных общественных наук IBM SPSS Statistics 22. **РЕЗУЛЬТАТЫ:** На основании логистического регрессионного анализа рассчитаны чувствительность и специфичность шкал в прогнозировании ПН на фоне МЖ. Площадь под кривой ошибок (area under the curve receiver operating characteristic, AUC ROC) для шкалы Sequential Organ Failure Assessment (SOFA) составила 0,862, для шкалы Model for End-stage Liver Disease (MELD) — 0,882, для шкалы Acute Physiology and Chronic Health Evaluation (APACHE II) — 0,864, для шкалы Child—Turcotte—Pugh — 0,813. Значения чувствительности и специфичности для шкалы SOFA составили 78,9 и 77,8 %, для шкалы MELD — 80,8 и 79,7 %,

search for additional predictors of unfavorable outcome of liver failure due to obstructive jaundice.

для шкалы APACHE II — 57,7 и 81,9 %, для шкалы Child—Turcotte—Pugh — 75,1 и 70,9 % соответственно. Независимым предиктором неблагоприятного исхода является альбумин (AUC ROC 0,909, *p* = 0,01), чувствительность — 88,6 %, специфичность — 85,2 %. **ВЫВОДЫ:** Представленные в исследовании шкалы (SOFA, MELD, APACHE II, Child—Turcotte—Pugh) и кандидатный биомаркер «альбумин» показали значимую прогностическую способность, но невысокие значения чувствительности и специфичности (менее 80 %), в некоторых точках исследования требуется поиск дополнительных предикторов неблагоприятного исхода ПН на фоне МЖ.

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Introduction

Obstructive jaundice (OJ) (synonyms: subhepatic, obstructive, obstructive) is a syndrome that occurs when the outflow of bile into the duodenum is impaired [1]. Mortality rates among patients with OJ, according to various authors, reach 20–60 % [2, 3].

The main reason for the unfavorable outcome is liver failure (LF) with rapidly developing liver dysfunction, increasing deterioration of biochemical parameters, decompensation of other organs and systems as the process progresses [2, 3]. The main principle of surgical tactics is the implementation of minimally invasive interventions aimed at decompressing the biliary tract in order to relieve OJ

and restore the outflow of bile into the duodenum [1, 4]. A quick and accurate assessment of the severity of LF against the background of OJ, along with predicting its further outcome, is a pressing issue in modern intensive care, determining tactical positions in the treatment of the patient [5, 6].

For an objective assessment of the severity of LF against the background OJ use various criteria, scales, the purpose of which is to determine the severity of patological process, assessing the prognosis of the disease and the formation of adequate treatment regimens [5, 6]. However the use of existing techniques does not always make it possible to ability to solve the above problems [7, 8]. Traditionally, to predict the course and outcome of LF against the background of OJ in the intensive care unit, scales are used to assess the

severity of the condition of patients with diseases of the hepatobiliary organs: a scoring scale for assessing end-stage liver diseases and prognosis of life in patients with end-stage LF (MELD) , Child-Turcotte-Pugh, Maddrey, Schindl their modifications and a number of others; as well as universal multiparameter scales for assessing the severity of the condition of critically ill patients: the Acute Physiology and Chronic Health Evaluation II (APACHE II) scale, the integral system for assessing organ dysfunction (Sequential Organ Failure Assessment, SOFA) [8, 9]. A number of authors, in their studies, demonstrate their lack of reproducibility and prognostic significance in relation to LF against the background of OJ [8]. Thus, the MELD score was developed in 2002 to predict mortality within three months after a transjugular intrahepatic portosystemic shunt procedure. Subsequently, it was found that it is important in determining the prognosis and prioritizing the tactical position in liver transplantation. In recent years, works have appeared devoted to the use of the MELD scale for predicting postoperative LF after liver resection [8, 10]. The Child-Turcotte-Pugh scale is an assessment technique designed to determine the severity of liver cirrhosis and patient survival, allowing to assess the likelihood of an unfavorable outcome of the disease. The method was first published in 1964 by medical scientists at the University of Michigan C. Child and D. Turcotte, in 1972 and improved by a group of British doctors led by Pugh. In the final version, the Child-Turcotte-Pugh scale includes an assessment of detoxification (bilirubin level, severity of encephalopathy) and synthetic (albumin level and international normalized ratio) liver functions, as well as an assessment of portal hypertension syndrome [11]. One of the most common integrated systems for determining the severity of a patient's condition is the APACHE II scale, developed and implemented by Knauss W.A. et al. (1981). The disadvantage of this scale is that it can only be used for severely ill patients in the intensive care unit due to fear of overestimating the degree of severity in other patients [12, 13]. The SOFA scale, which consists of a sequential assessment of organ failure and includes six main parameters (respiratory, cardiovascular, nervous system, renal, liver and blood coagulation) was created by a working group of the European Community of Intensive Care Medicine and adopted at the Paris Consensus Conference in 1994. But the above scale is more intended for quickly scoring and describing a number of complications in patients in critical condition than for predicting the outcome of the disease [14, 15].

Thus, in the current literature there is little information about the possibility of using the above scales to predict LF against the background of OJ, and the use of existing criteria does not always provide a complete assessment of the severity of the disease, which affects the amount of treatment provided [5, 8]. Of course, the leading place in treatment tactics for OJ is occupied by decompression of the biliary system using various methods (x-ray, endoscopic, surgical). Intensive therapy includes the use of hepatoprotectors, which play an important role in reducing the level of bilirubin fractions, infusion therapy (aimed at restoring microcirculation, removing toxic endogenous substances from the body) [4]. With the development of such complications of OJ as acute renal failure and LF, extracorporeal treatment methods become especially relevant, which is especially important for patients at risk of an unfavorable outcome [16].

Objective

To determine the prognostic value of multiparametric rating scales and identify predictors of unfavorable outcome in LF against the background of OJ.

Materials and methods

This prospective observational single-center study of a continuous sample included 53 patients with LF associated with benign OJ. Personal data of patients is anonymized. The diagnosis of the disease was established based on the results of clinical, laboratory and instrumental research methods using clinical recommendations developed by the working group on OJ of the Russian Society of Surgeons (2018) [1]. Etiologically, the patient population is represented by: choledocholithiasis in 66 cases (66 %); in 30 cases, cicatricial strictures of the bile ducts (30 %); intraoperative damage to the common bile duct in 4 cases (4 %). According to the classification of the severity of OJ by E.I. Halperin [5], 11 patients (21 %) were classified as class C, 28 (53 %) as class B and 14 (26 %) patients as class A.

In accordance with the clinical recommendations for OJ developed by the working group of the Russian Society of Surgeons (2018), all patients, for the purpose of decompression of the biliary tract, underwent various options of antegrade minimally invasive interventions under the control of ultrasound and X-ray television against the background of pathogenetically based complex conservative therapy in the conditions intensive care units.

Inclusion criteria for the study: patients over 18 years of age with benign liver lesions who underwent antegrade decompression of the biliary tract to resolve OJ during the 1st day of hospitalization; absence of chronic inflammatory liver diseases. Exclusion criteria from the study: age under 18 years, inability to assess factors included in the study, decompensated concomitant pathology; chronic inflammatory liver diseases.

Monitoring the development of impaired functional state of the liver based on clinical and laboratory data with assessment of the severity of the patients' condition using the APACHE II, SOFA, MELD, Child-Turcotte-Pugh scales [2], carried out on the day of hospitalization, on the 3rd, 7th and 11th day after decompression intervention. To characterize the severity of the condition, the following laboratory parameters were analyzed: the level of platelets, leukocytes,

and serum hematocrit (automatic hematology analyzer "UniCel DxH800" Beckman Coulter, USA); level of bilirubin, albumin, creatinine, blood electrolytes (biochemical analyzer "AU480" Beckman Coulter, USA); markers of the hemostasis system — international normalized ratio (automatic coagulometer "AMAX DESTINY-plus", Ireland); gas composition, acid-base state and lactate level in blood serum (automated analyzer "ABL-800 Flex" Radiometer, Denmark). Hemodynamic parameters were monitored using the Mindray BeneView T1 bedside monitor from Mindray, China. The severity of ascites was assessed using the SonoScape S11 ultrasound apparatus from SonoScape, China.

Statistical processing of data was carried out using the statistical software package for analyzing social science data IBM SPSS Statistics 22. Presentation of indicators included calculation of the median (Me), 25th and 75th percentiles (p25 % and p75 %, respectively). To predict the risk of death, methods of logistic regression and ROC analysis, MedCalc and SPSS 17 statistical packages were used. The area under the operating characteristic curve (AUROC, Area Under Receiver Operator Curve) shows how well the model differentiates patients with a favorable and unfavorable prognosis. For models predicting mortality, reliable resolution (as measured by AUROC) was greater than 0.9. In order to verify the accuracy of the results obtained, in this study, methods recommended for small samples were used, such as two-factor nonparametric (rank) Friedman analysis of variance, Kruskal-Wallace H-test for nonparametric (rank) one-way analysis of variance, Mann-Whitney U-test. Statistically significant results were considered at $p < 0.05$.

Results

The study included 53 patients: 26 (49 %) men and 27 (51 %) women, average age 60 ± 3.8 years. Depending on the outcome of the disease, patients were divided into two categories: group 1 with a favorable outcome (27/51 %) and group 2 with an unfavorable outcome (26/49 %) of the disease. The assessment was based on the results of 30-day mortality. The causes of unfavorable outcome were LF (8/31 %), multiple organ failure (6/26 %), cholangitis (4/15 %), renal failure (4/15 %), sepsis (3/12 %), gastrointestinal bleeding (1/4 %). In the presented study, the groups of patients were comparable not only in gender and age, but also did not have statistically significant differences in the main rating scales (Table 1).

At the first stage of the study, multiparameter rating scales were analyzed in relation to the population of patients with LF against the background of OJ, traditionally used in the intensive care unit. All severity rating scales analyzed (SOFA, MELD, APACHE II and Child-Turcotte-Pugh) showed very good predictive accuracy regarding the development of an unfavorable outcome of LF due to OJ. The SOFA score, when analyzed at four study time points, demonstrated a sensitivity of 78.9 % (73.1–84.6 %), specificity of 77.8 % (74.1–81.5 %), area under the ROC curve (AUC) 0.862 (0.820–0.904) [95 % CI 0.707–0.823 ... 0.933–0.985], $p = 0.04$, cut-off point more than 8 points. The MELD scale sensitivity in this study was 80.8 % (73.1–88.5 %), specificity — 79.7 % (74.1–85.2 %), area under the ROC curve (AUC) 0.882 (0.872–0.892) [95 % CI 0.779–0.806 ... 0.965–0.984], $p = 0.01$, cut-off point 15 points. For the APACHE II scale, sensitivity was 57.7 %, specificity — 88.9 %, area under the ROC curve (AUC) 0.864 [95 % CI 0.550–0.777], $p = 0.04$, cut-off point more than 30 points. The area under the operational characteristic curve (AUROC) for the Child-Turcotte-Pugh score was 0.810 (0.758–0.863) [95 % CI 0.629–0.966], $p = 0.03$, cut-off point greater than 12 points with sensitivity and specificity values of 75.1 % (69.2–80.8 %) and 70.9 % (63.0–88.9 %), respectively.

The above results of statistical analysis of predicting outcome in PN against the background of breast syndrome for the APACHE II and Child-Turcotte-Pugh, SOFA and MELD scales are presented in Table 2.

ROC curves of logistic models with the considered predictors (SOFA and MELD scale) for predicting an unfavorable outcome of LF in OJ syndrome are presented in Figure 1 and 2.

Table 1. The distribution of the groups of patients included in the study based on sex, age, and clinical assessment scoring systems

| Characteristic	1st group (*n* = 27)	2st group (*n* = 27)	*p*
Patient age avg. (minimum–maximum), years (AA)	63.5 (37–85)	61.9 (35–88)	< 0.09
Men/women, % (AA)	14/13 (51.9/48.1)	12/14 (48.3/51.7)	< 0.05
SOFA, Me points (IR)	7.4 (4.0–9.0)	8.8 (6.0–10.0)	< 0.05
APACHE II, Me points (IR)	21.1 (9.0–28.0)	23.8 (12.0–32.0)	< 0.05
MELD, Me points (IR)	16.8 (10.0–23.0)	18.2 (13.0–28.0)	< 0.04
Child-Turcotte-Pugh, Me points (IR)	12.1 (11.0–14.0)	14.2 (12.0–15.0)	< 0.04
Significant intergroup difference *p* < 0.05. AA — arithmetic average; IR — interquartile range; Me — median.			
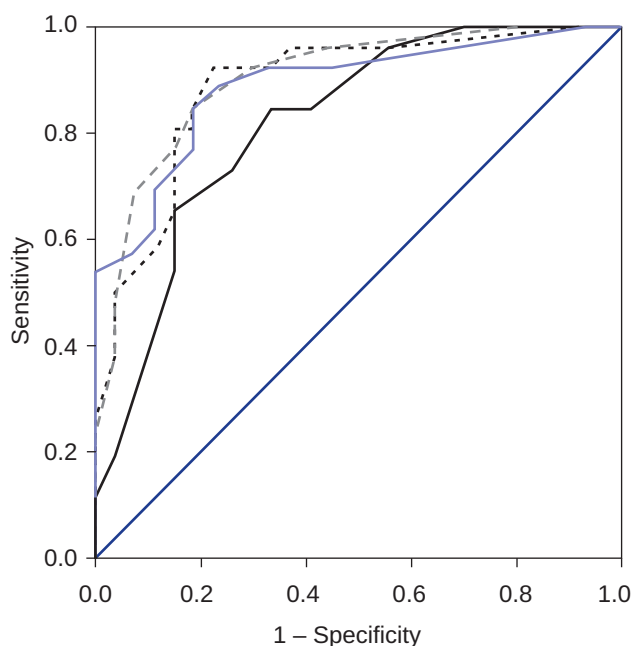
Curve source: predictor "SOFA scale"

| —— Day 1 | – – Day 3 | · · · Day 7 |
| —— Day 11 | —— Reference line | |

Fig. 1. ROC-curves predicting adverse outcome of liver failure due to obstructive jaundice at four time points with "SOFA score"
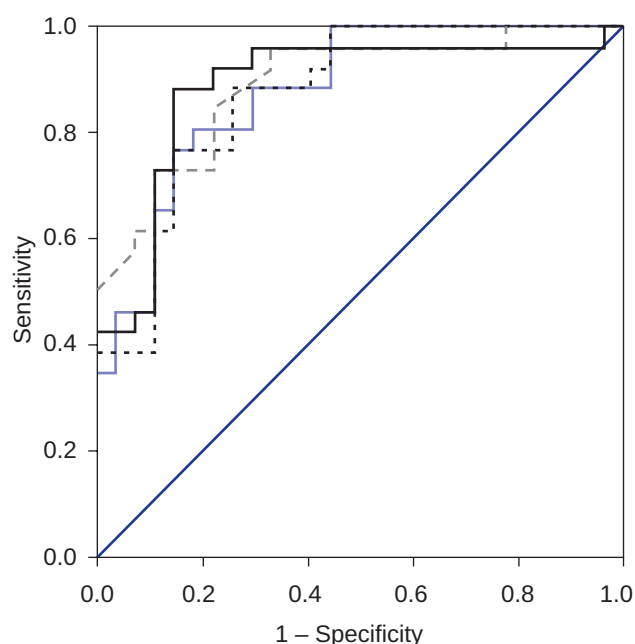
Curve source: predictor "MELD scale"

| —— Day 1 | – – Day 3 | · · · Day 7 |
| —— Day 11 | —— Reference line | |

Fig. 2. ROC-curves predicting adverse outcome of liver failure due to obstructive jaundice at four time points with "MELD score" predictor

Table 2. Results of ROC analysis of a logistic model predicting the severity of liver failure syndrome caused by obstructive jaundice with the predictors "APACHE II", "Child-Turcotte-Pugh score", "SOFA score" and "MELD score" in dynamics

Day	Area under the ROC curve	Standard error	Value (p)*	Asymptotic 95 % confidence interval		Se, %	Sp, %
				Bottom line	Upper limit		
APACHE II scale							
1	0.864	0.058	0.04	0.750	0.977	57.7	88.9
Child-Turcotte-Pugh scale							
1	0.867	0.050	0.05	0.769	0.964	69.2	88.2
3	0.758	0.066	0.01	0.629	0.887	80.8	63.0
7	0.863	0.052	0.05	0.761	0.966	73,1	78.9
11	0.769	0.067	0.01	0.638	0.900	69.2	77.8
MELD scale							
1	0.887	0.049	0.00	0.791	0.984	88.5	85.2
3	0.892	0.044	0.00	0.806	0.978	73.1	77.8
7	0.872	0.048	0.01	0.779	0.965	76.9	74.1
11	0.876	0.046	0.01	0.785	0.967	80.8	85.2

Day	Area under the ROC curve	Standard error	Value (p)*	Asymptotic 95 % confidence interval		Se, %	Sp, %
				Bottom line	Upper limit		
SOFA scale							
1	0.820	0.058	0.05	0.707	0.933	73.1	74.1
3	0.904	0.041	0.04	0.823	0.985	76.9	76.9
7	0.890	0.046	0.04	0.801	0.980	80.8	81.5
11	0.890	0.046	0.04	0.800	0.979	84.6	81.5

* Significant intergroup difference $p < 0.05$ according to the Mann-Whitney U-test.
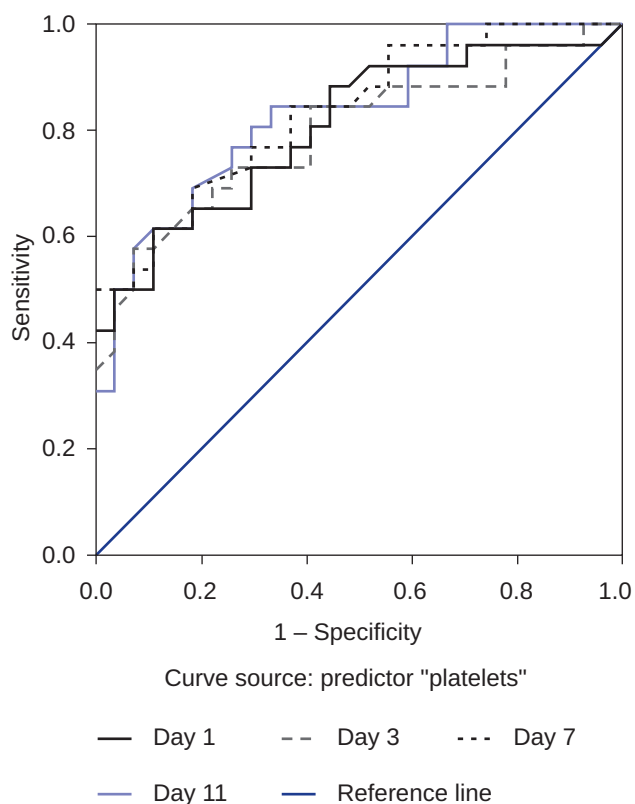Se — sensitivity; Sp — specificity.

Fig. 3. ROC curves predicting adverse outcome of liver failure due to obstructive jaundice at four time points with predictor "platelets"
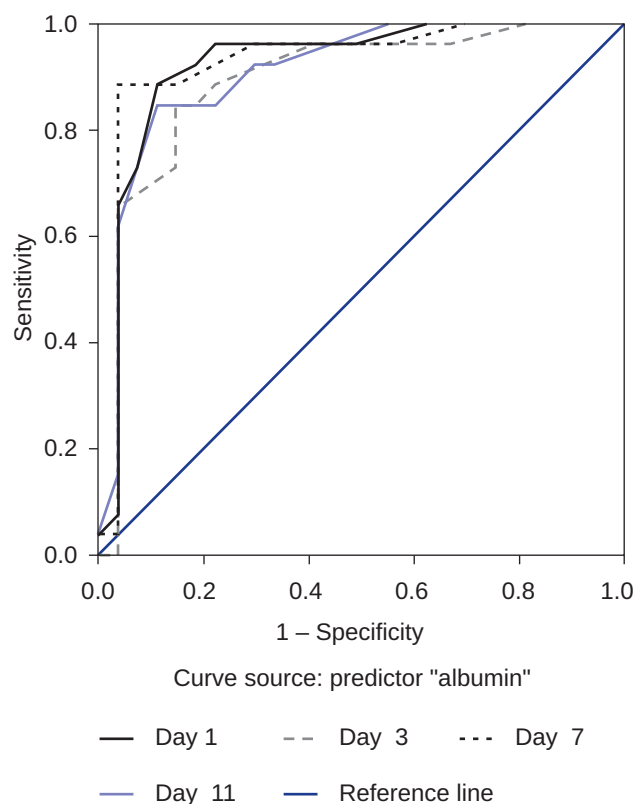

Fig. 4. ROC curves predicting adverse outcome of liver failure due to obstructive jaundice at four time points with predictor "albumin"

The results obtained indicate the high predictive ability of multiparameter severity rating scales, but insufficient sensitivity and specificity values do not allow their use as an independent predictor of an unfavorable outcome of LF in OJ syndrome, which determines the need to search for additional predictors.

At the next stage of the study, the statistical significance of laboratory data routinely used in practice was tested as independent predictors of an unfavorable outcome of the disease. From this perspective, regression analysis revealed only two laboratory biomarkers: platelets and albumin.

The "platelet" indicator demonstrated statistically significant results for the integral indicator of the quality of predicting an unfavorable outcome of the disease (area under the ROC curve (AUC) 0.816 (0.796–0.835) [95 % CI 0.967–0.991 ... 0.978–0.994], $p = 0.01$), but low values of sensitivity and specificity (71.15 % (65.4–76.9 %) and 72.3 % (70.4–74.1 %), respectively) with a cut-off point of 115×10^9/l.

Table 3. Parameters of logistic models of laboratory predictors-indicators for prognosis of severity of liver failure caused by obstructive jaundice syndrome in dynamics

Biochemistry indicator	Odds ratio*	Asymptotic 95 % confidence interval	p**	Se, %	Sp, %	Area under the ROC curve	Cut off threshold
When patients are admitted to the hospital							
Platelets	0.984	0.975–0.993	0.01	65.4	70.4	0.806	114×10^9/l
Albumen	0.635	0.498–0.810	0.01	92.3	81.5	0.925	25.5 g/l
On the 3rd day of treatment in hospital							
Platelets	0.986	0.978–0.994	0.01	73.1	74.1	0.796	115×10^9/l
Albumen	0.698	0.579–0.841	0.01	84.6	81.5	0.891	28.0 g/l
On the 7rd day of treatment in hospital							
Platelets	0.979	0.967–0.991	0.01	76.9	70.4	0.835	110×10^9/l
Albumen	0.574	0.434–0.759	0.01	88.5	92.6	0.927	26.0 g/l
On the 11rd day of treatment in hospital							
Platelets	0.981	0.971–0.992	0.01	76.9	70.4	0.830	105×10^9/l
Albumen	0.592	0.452–0.775	0.00	84.6	77.8	0.910	26.5 g/l

* Reducing the risk of death by 1 unit. ** Significant intergroup difference $p < 0.05$ according to the Mann-Whitney U-test.
Se — sensitivity; Sp — specificity.

The "albumin" indicator, as an independent predictor of an unfavorable outcome of the disease, using the logistic regression method demonstrated sensitivity of 88.6 % (84.6–92.3 %), specificity of 85.2 % (77.8–92.6 %), area under the ROC curve (AUC) 0.909 (0.891–0.927) [95 % CI 0.434–0.759 ... 0.579–0.841], $p = 0.01$ with a cut-off point of 28.3 g/l.

The results of statistical analysis of the "platelet" and "albumin" indicators from the standpoint of predicting an unfavorable outcome of PN in breast syndrome are presented in Table 3.

ROC curves of logistic models with the considered predictors of predicting an unfavorable outcome of LF in OJ syndrome are presented in Figure 3 and 4.

The results obtained indicate the high predictive ability of albumin, but the low values of sensitivity and specificity at some points of the study (days 3 and 11) do not allow us to consider them as reliable predictors of an unfavorable outcome of LF against the background of OJ syndrome.

Discussion

The number of patients with diseases of the hepatopancreatoduodenal organs, complicated by OJ syndrome, continues to increase, maintaining high postoperative mortality, reaching 12.5 % [2, 13, 17]. The main reason leading to an unfavorable outcome and deterioration of the results of surgical treatment for OJ syndrome is progressive LF, the problem of treatment of which remains serious and relevant today [4].

Assessing the severity of the condition of patients with LF due to OJ syndrome who are in the intensive care unit is an integral part of the diagnostic and treatment process. All kinds of criteria and scales are used, the purpose of which is to timely determine the severity of the pathological process with the subsequent formation of adequate treatment regimens [6, 9, 18, 19]. However, to date, there is very little data in the literature on their prognostic ability regarding the outcome of LF against the background of OJ syndrome [9, 20].

In this study, patients were analyzed, divided into two groups depending on the outcome of the disease, with a diagnosis of LF against the background of benign OJ syndrome. In the presented study, the groups of patients were comparable not only in gender and age, but also did not have statistically significant differences in the main rating scales.

In relation to the population of patients with LF on the background of OJ syndrome, scales that allow assessing the severity of the condition of patients with diseases of the hepatobiliary organs (MELD, Child-Turcotte-Pugh) and universal multiparameter scales for assessing the severity of the condition of critically ill patients (APACHE II and SOFA) were analyzed. All analyzed rating scales demonstrated very good predictive accuracy regarding the unfavorable outcome of LF due to OJ syndrome, but insufficient sensitivity and specificity values. Thus, the area under the operational characteristic curve (AUROC) for the SOFA scale is 0.862 (0.820–0.904), $p = 0.04$, the cut-off point is more than 8 points, which indicates the highest risk of death when registering above the specified; sensitivity 78.9 % (73.1–84.6 %), specificity 77.8 % (74.1–81.5 %). Unfortunately, there values is no data in the literature on the

prognostic ability of this scale for predicting the outcome of LF in the setting of OJ cancer.

For the APACHE II scale, the area under the ROC curve (AUROC) was 0.864 [95 % CI 0.550–0.777], p = 0.04, cut-off point more than 30 points, with little significant sensitivity (57.7 %) and specificity (81.9 %). A similar result was obtained in the work of Kądziołka I. et al., which showed a significant underestimation of the severity of patients with OJ syndrome using the APACHE II scale compared to other scoring systems, which does not allow it to be recommended for predicting the course and outcome of the disease [12].

The sensitivity of the MELD scale, throughout the study, was in the range of 73.1–88.5 % (80.8 %), specificity 74.1–85.2 % (79.7 %), area under the ROC curve (AUC) 0.882 (0.872–0.892) [95 % CI 0.779–0.806 ... 0.965–0.984], p < 0.01, cut-off point more than 15 points. The American College of Surgeons National Surgical Quality Improvement Program study found the MELD score to be good at predicting 30-day mortality for patients with scores between 10 and 22, but underestimated the risk for patients with higher scores [21]. This, obviously, can explain the insufficient predictive ability of the scale under consideration in relation to the population of patients with LF against the background of OJ syndrome.

The Child-Turcotte-Pugh scale in our study has an area under the ROC curve (AUC) of 0.813 (0.758–0.867) [95 % CI 0.0629–0.966], p = 0.03, cut-off point more than 12 points, sensitivity 75.1 % (69.2–80.8 %) and specificity 70.9 % (63.0–78.9 %). In their work, Mohamed Elmeliegy et al. pointed out the limitations of using the Child-Turcotte-Pugh scale for the category of patients with oncological pathology, since hypoalbuminemia, encephalopathy and ascites may be associated with the course of the oncological process or metastases, and not with impaired liver function. This does not allow us to recommend the use of the Child-Turcotte-Pugh scale other than its main purpose [22], which obviously explains the result obtained in our study.

Thus, the analyzed multivariate rating scales have a high, but still insufficient predictive ability regarding the outcome of LF against the background of OJ syndrome (at some points in the study, sensitivity and specificity values are less than 80 %), which determines the need to search for additional predictors.

A number of authors indicate that the main predictors of an unfavorable outcome of LF in OJ syndrome are age over 50 years, bilirubin levels over 340 µmol/l and creatinine over 132 µmol/l, prothrombin time over 35 seconds [23, 24]. Our study found that two laboratory biomarkers had statistically significant changes reflecting the likelihood of an unfavorable outcome of the disease: platelets (area under the ROC curve (AUC) 0.816 (0.796–0.835) [95 % CI 0.967–0.991 ... 0.978–0.994], p = 0.01, with sensitivity 71.15 % (65.4 %–76.9 %) and specificity 72.3 % (70.4–74.1 %)) and albumin (area under the ROC curve (AUC) 0.909 (0.891–0.927) [95 % CI 0.434–0.759 ... 0.579–0.841], p = 0.01, with sensitivity 84.6–92.3 % and specificity 77.8–92.6 %).

The results obtained indicate a good predictive accuracy of platelets and excellent for albumin, however, the values of sensitivity and specificity at some study points also do not allow us to consider them as reliable independent predictors of an unfavorable outcome of LF against the background of OJ syndrome.

Conclusion

Thus, the multiparametric assessment scales of the severity of the condition SOFA, APACHE II, Child-Turcotte-Pugh, MELD demonstrated good, and the candidate biomarker "albumin" excellent predictive ability regarding the development of an unfavorable outcome in patients with LF against the background of OJ syndrome. However, insufficient sensitivity and specificity values (less than 80 %) at some study points do not allow us to consider them as independent predictors of an unfavorable outcome. This requires further search for factors that predict the development of LF in OJ syndrome.

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