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A Case-Control Study of Single-Pass Albumin Dialysis for Sub-Compensated Acute Liver Failure

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Abstract **Objective.** The aim of the study was to evaluate the effectiveness of the improved method of hemodiafiltration (HDF), based on the Single pass albumin dialysis (SPAD), for extracorporeal liver support in patients with acute liver failure (ALF). **Material and methods.** The retrospective case-control study. We identified 69 ALF and acute-on-chronic liver failure (ACLF) patients (38 SPAD-treated, 31 controls) between January 2011 and March 2020. The average age was 34 years, 57% were male. To evaluate the therapy efficacy, laboratory tests (bilirubin, urea, creatinine, ammonia, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP), prothrombin index (PTI) and INR) and the Model for End-Stage Liver Disease (MELD) score were used. **Results.** In patients with acute renal failure without concomitant hepatorenal syndrome, SPAD allowed stable stabilization and regression of the pathological process by the 5th day of treatment in 81.6% of cases, while in the control group this indicator was 45.2% (p=0.003). Total bilirubin (p <0.05), ammonia (p <0.05) ALT and CRP (p <0.05) significantly decreased after treatment with SPAD. **Conclusion.** An improved HDF technique using 2% albumin in ALF and ACLF patients allows for a stable regression of the disease. At the same time, good results of applying the proposed method were noted in the absence of initial manifestations of hepatorenal syndrome with a creatinine < 100 μmol/l.

Keywords Liver failure, Extracorporeal liver support, Hemodiafiltration, Single pass albumin dialysis

1. Introduction

The liver is a complex organ that performs vital functions of synthesis, heat production, detoxification and regulation; its failure carries a highly critical risk [1,2]. Every year, 250.000 cases of ALF are recorded in the world, which is the cause of 50% of deaths even in specialized hepatological centers, and takes the 6th place among all causes of death [3].

Today, there is a clear need for temporary prosthetics devices of liver function. Over the past two decades, some artificial liver devices began to develop with the aim of being used as supportive therapy until liver transplantation (bridge-to-transplant) or liver regeneration (bridge-to-recovery). The well-recognized devices are the Molecular Adsorbent Recirculating System (MARS), the Single-Pass Albumin Dialysis (SPAD) system and the Fractionated Plasma Separation and Adsorption system (Prometheus) [1,4].

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In the following years, experimental works and early clinical applications were reported, and to date, many thousands of patients have already been treated with these devices. The ability of artificial liver support systems to replace the liver detoxification function, at least partially, has been proven, and the correction of various biochemical parameters has been demonstrated [5,6,7]. However, the complex tasks of regulation and synthesis must be addressed through the use of bioartificial systems, which still face several developmental problems and very high production costs. Moreover, clinical data on improved survival are conflicting [8,9].

The aim of this study was to evaluate the effectiveness of the improved method of hemodiafiltration (HDF) based on the SPAD for patients with acute liver failure (ALF) and acute-on-chronic liver failure (ACLF).

2. Material and Methods

The retrospective case-control study. We identified 69 patients with various etiology of ALF and ACLF (38 SPAD-treated, 31 controls) between January 2011 and March 2020 (table 1).

Table 1. Liver failure etiology

Liver failure etiology	SPAD	Control
	n (%)	n (%)
Hepatitis B	6 (15,8%)	6 (19,4%)
Cardiac surgery	9 (23,7%)	7 (22,6%)
Tocsin hepatitis	5 (13,2%)	5 (16%)
Liver cirrhosis	18 (47,4%)	13 (42%)
Total	38 (100%)	31 (100%)

Patients were treated in the RSSPMCS named after V.Vakhidov (Tashkent, Uzbekistan) and in City Clinical Hospital No.4 (Almaty, Kazakhstan). The average age was 34 years, 57% were male. To evaluate the therapy efficacy, laboratory tests (bilirubin, urea, creatinine, ammonia, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP), prothrombin index (PTI) and INR) and the Model for End-Stage Liver Disease (MELD) score were used.

For SPAD (multiFiltrate; Fresenius Medical Care, Germany), dialysis flow rates were set to 700 ml/h. One thousand millilitres of fluid was removed from a 5000-ml dialysis solution bag and replaced with 1000 ml of 20% albumin containing 19.2 g of human albumin; 125 mmol/L Na^+; maximum 100 mmol/L Cl^-, HCl or NaOH for pH adjustment; 16 mmol/L caprylate; and 16 mmol/L *N*-acetyl-d,l-tryptophan. This resulted in a final human albumin concentration of 2%.

The sample size calculations were based on the data of 69 patients of the retrospective study. The sample size calculations and the statistical analysis by means of linear mixed-effect models were performed with R statistical software. Changes in laboratory and clinical parameters before and after treatment were compared using the Wilcoxon signed-rank test.

3. Results

Both therapies (SPAD and standard medical intensive therapy – control group) led to a significant reduction of total plasma bilirubin levels without significant differences at first 5 days after. Nevertheless, on the 7th day in the SPAD-group total plasma bilirubin level was significantly better (95.5±6.4 μmol/L versus 119.6±7.3 μmol/L, respectively).

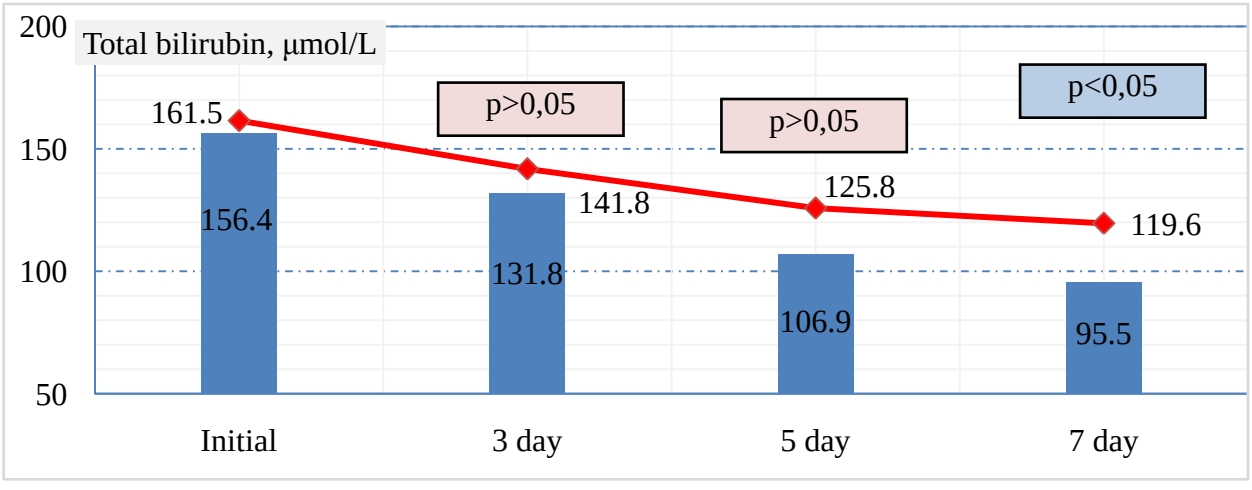
Similar dynamics in both groups was noted in plasma ammonia levels, which significantly decreased only on the 7th day after treatment (from 71.4±5.2 mmol/L to 44.2±3.74 mmol/L and from 69.8±4.8 mmol/L to 56.54±3.38 mmol/L, respectively). It is noteworthy that renal dysfunction parameters (urea and creatinine) in both groups did not tend to significantly decrease, and only 7 days after SPAD a significant decrease in plasma urea level was noted (from 9.7±0.6 mmol/L to 8.7±0.4 mmol/L) (Fig. 1).

As can be seen from Fig. 1, in both groups there was a normalization of intoxication syndrome parameters by 7 days after treatment, however, a significant difference is observed only in the reduction of bilirubin ($t=2.48$; $p<0.05$) and ammonia ($t=2.39$; $p<0.05$).

A significant decrease in ALT level (Fig. 2) to the initial one begins from 5 days after the application of SPAD (from 324.6±15.2 UI/L to 255.8±14.3 UI/L), and AST on 7 days (from 295.5±13.4 UI/L to 238.9±11.6 UI/L), unlike control. In control group, a significant decrease in ALT level from the initial value begins only on the 7th day (from 311.3±14.3 UI/L to 269.4±13.1 UI/L). Nevertheless, a significant difference in ALT levels was observed on day 7 in favor of SPAD ($t=14.49$; $p<0.05$).

With regard to CRP, a significant decrease after SPAD was also noted on the 5th day (from 22.3±1.2 mg/L to 16.4 ± 0.9 mg/L), in contrast to control, after which this parameter significantly began to decrease towards 7 days (from 21.8±1.3 mg/L to 18.4±0.9 mg/L). A significant difference between the groups in CRP levels was noted from 5 days in favor of SPAD ($t=2.18$; $p<0.05$) and persists for 7 days ($t=2.46$; $p<0.05$).

The dynamics of hypocoagulation in terms of INR and PTI levels are shown in Fig. 3.



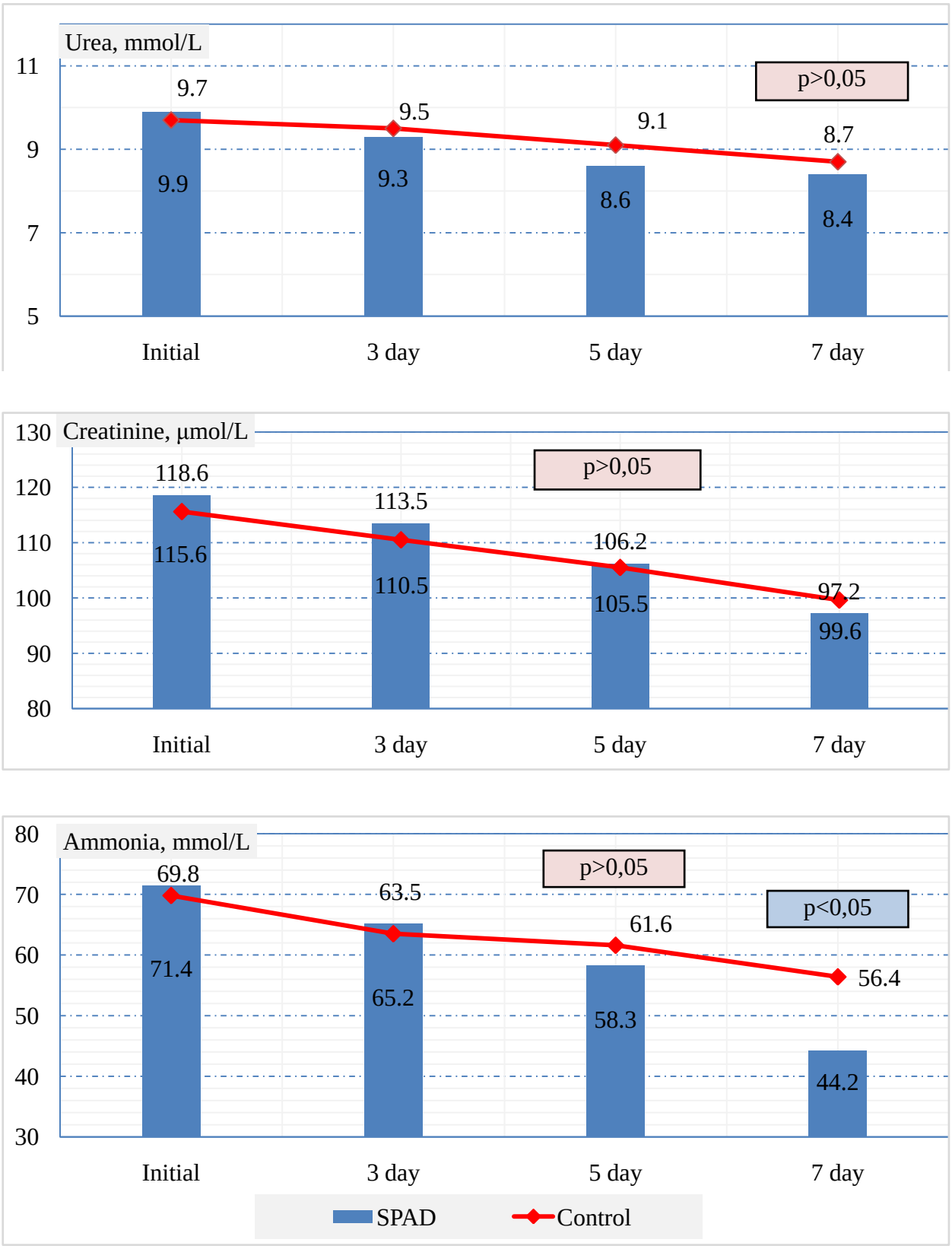


Figure 1. Bilirubin and kidney retention parameters during treatment

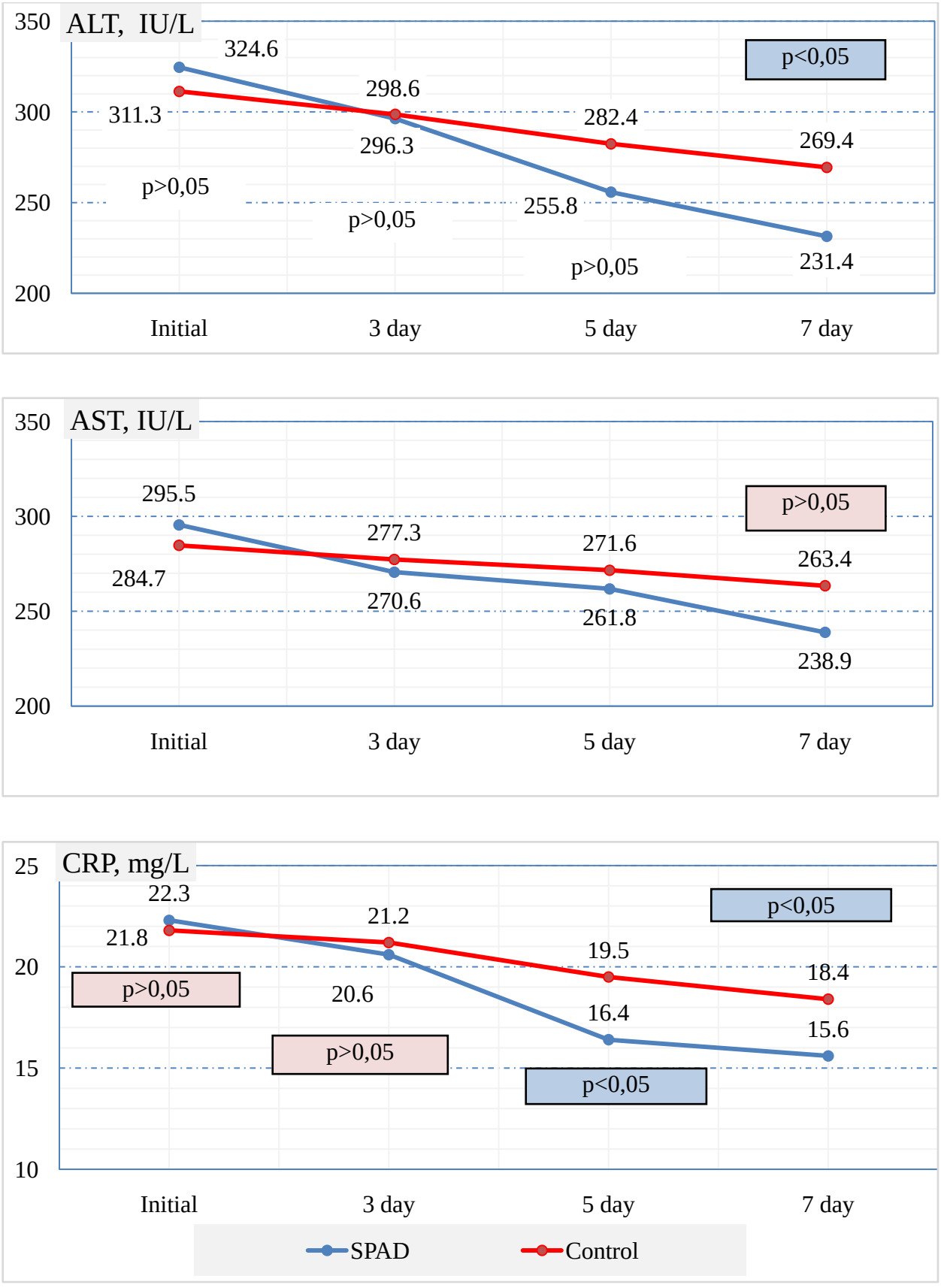


Figure 2. Comparative dynamics of inflammation and cytolysis markers

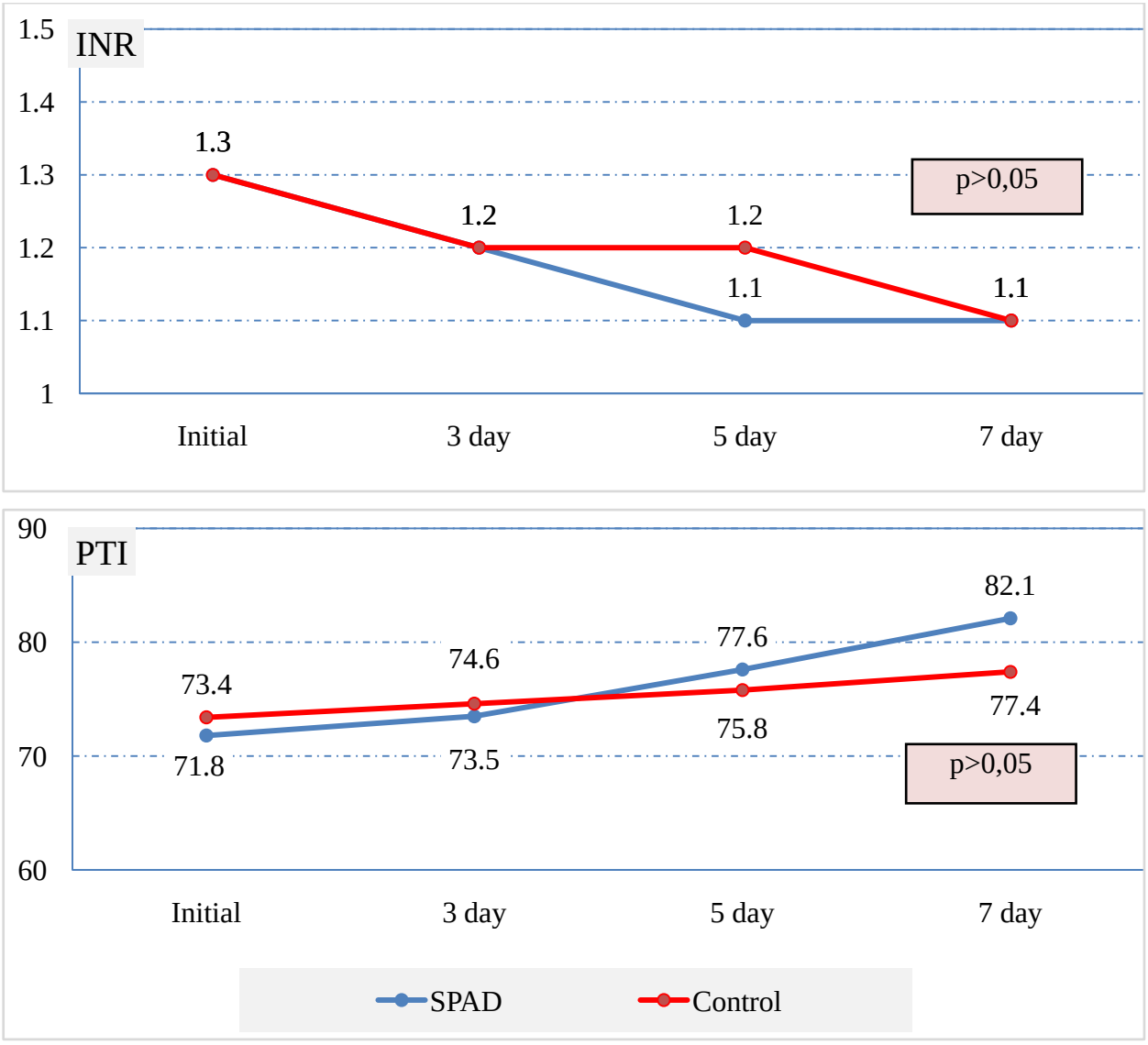


Figure 3. Comparative dynamics of hemostatic system parameters

Table 2. The timing of the onset of liver failure regression in SPAD and control groups

Day of therapy	SPAD		Control	
	n	%	n	%
1-2 days	6	15,8%	2	6,5%
3 day	21	55,3%	5	16,1%
5 day	4	10,5%	7	22,6%
7 day	2	5,3%	4	12,9%
Progression of disease	5	13,2%	13	41,9%
Total	38	100,0%	31	100,0%
	χ^2=16,345; df=4; p=0.003			

A significant improvement in PTI level was noted only after the application of SPAD-therapy on the 7th day (from 71.8±3.1 to 82.1±2.5), while the INR parameter began to significantly improve on the 5th day (from 1.3±0.05 to 1.1±0.04), and in control – on the 7th day (from 1.3±0.07 to 1.1±0.05). Significance of differences between groups was not noted.

According to the timing of the onset of regression of liver failure, it was noted that against the background of the use of SPAD, on 1-2 days, regression of ALF was observed in 6 (15.8%) patients, on the 3rd day - in 21 (55.3%), on day 5 - in 4 (10.5%), on day 7 - in 2 (5.3%). Progression of multiple organ dysfunction was noted in 5 (13.2%) patients (table 2).

Against the background of the use of IT, the onset of liver failure regression on day 1-2 was observed only in 2 (6.5%) patients, on day 3 - in 5 (16.1%), on day 5 - in 7 (12.9%), on the 7th day - in 2 (5.3%). In control, progression of multiple organ dysfunction was noted in 13 (41.9%) patients.

A significant reduction of the MELD score was observed in the SPAD-group (from 21.4±0.4 to 18.2±0.4; t=5.66; p<0.05) and control (from 21.2±0.4 to 19.6±0.4; t=2.83; p<0.05).

A comparison of the dynamics of MELD scores is presented in Fig. 4. So, the significance of differences in the MELD score between the groups was observed on days 5 and 7 (t=2.47; p<0.05).

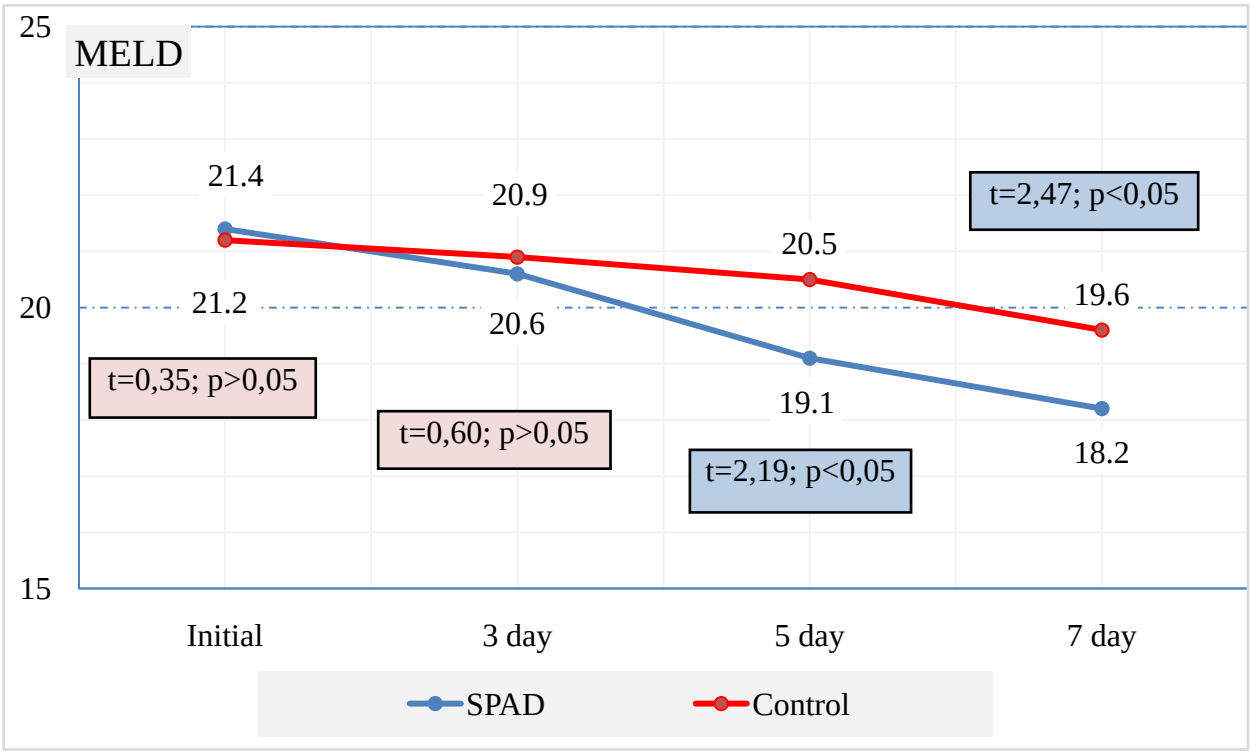


Figure 4. The significance of differences in the MELD score in the SPAD and control groups

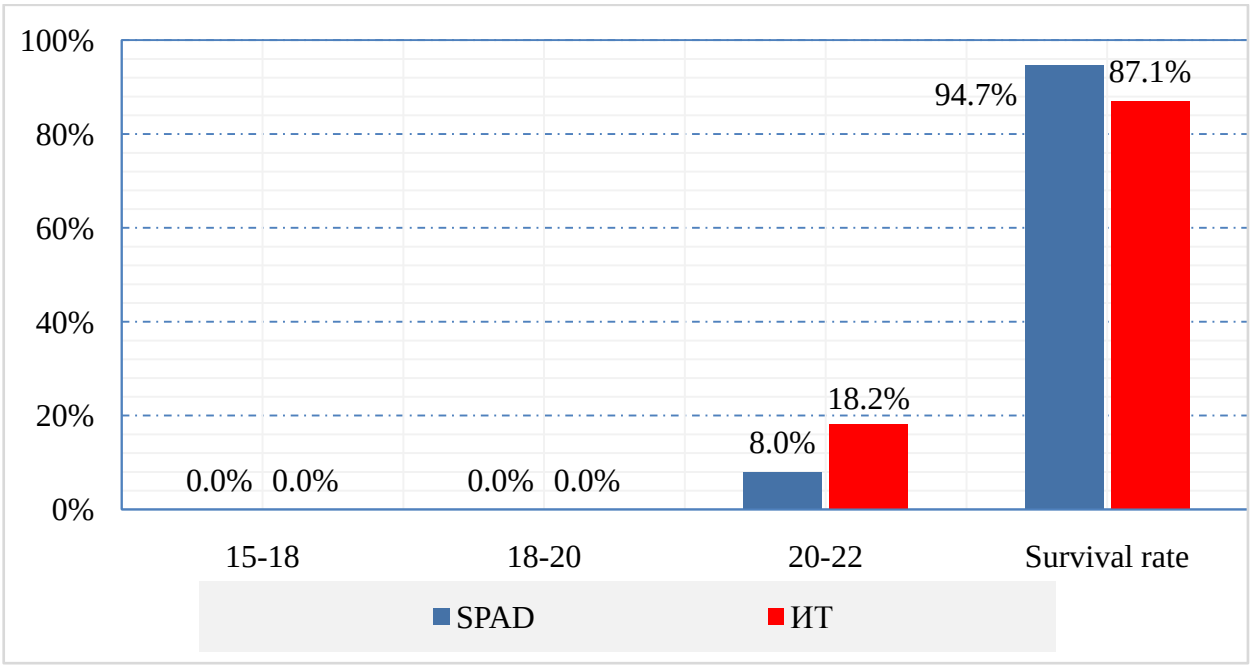


Figure 5. Treatment outcome depending on the MELD score

Detailing the treatment outcomes depending on MELD scores is shown in Fig. 5.

Fatal outcome was observed only in patients with MELD 20-22. A satisfactory result was observed in 94.7% of patients after SPAD and in 87.1% cases in control (Fig. 5). The mortality rate was 5.3% and 12,9% in SPAD and control, respectively (χ^2=7,445; df=2; p=0.025).

4. Conclusions

An improved HDF technique using 2% albumin in patients with ALF and ACLF made it possible to achieve stable regression of disease in 86.8% of cases. At the same time, good results of applying the proposed methodology of 2% albumin SPAD-therapy were noted in the absence of

initial manifestations of hepatorenal syndrome in patients with a creatinine index of less than 100 μmol/L.

REFERENCES

[1] García Martínez JJ, Bendjelid K. Artificial liver support systems: what is new over the last decade? Ann Intensive Care. 2018; 8(1): 109. Published 2018 Nov 15. doi: 10.1186/s13613-018-0453-z.

[2] Grek A, Arasi L. Acute Liver Failure. AACN Adv Crit Care. 2016; 27(4): 420-429. doi: 10.4037/aacnacc2016324.

[3] Naghavi M, Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017; 390(10100): 1151–1210. doi: 10.1016/S0140-6736(17)32152-9.

[4] Larsen FS. Artificial liver support in acute and acute-on-chronic liver failure. Curr Opin Crit Care. 2019; 25(2): 187-191. doi: 10.1097/MCC.0000000000000584.

[5] García Martínez JJ, Bendjelid K. Artificial liver support systems: what is new over the last decade? Ann Intensive Care. 2018; 8(1): 109. Published 2018 Nov 15. doi: 10.1186/s13613-018-0453-z.

[6] Villarreal JA, Sussman NL. Extracorporeal Liver Support in Patients with Acute Liver Failure. Tex Heart Inst J. 2019; 46(1): 67-68. Published 2019 Feb 1. doi: 10.14503/THIJ-18-6744.

[7] Wiesmann T, Hoenl D, Wulf H, Irqsusi M. Extracorporeal liver support: trending epidemiology and mortality - a nationwide database analysis 2007-2015. BMC Gastroenterol. 2019; 19(1): 160. Published 2019 Sep 3. doi: 10.1186/s12876-019-1077-y.

[8] MacDonald AJ, Karvellas CJ. Emerging Role of Extracorporeal Support in Acute and Acute-on-Chronic Liver Failure: Recent Developments. Semin Respir Crit Care Med. 2018; 39(5): 625 - 634. doi: 10.1055/s-0038-1675334.

[9] He YT, Qi YN, Zhang BQ, Li JB, Bao J. Bioartificial liver support systems for acute liver failure: A systematic review and meta-analysis of the clinical and preclinical literature. World J Gastroenterol. 2019; 25(27): 3634-3648. doi: 10.3748/wjg.v25.i27.3634.