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1	The Importance of Pediatric Scoring Systems of Multiorgan	
2	Failure in Intensive Care Unit	
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7 Abstract

Introduction: Use scoring systems facilitates and enables decision making about the appropriate therapeutic treatment (right evaluation and classification of the patient group at 9 high risk), which can also increase the likelihood of survival rationalize a decision on the need 10 and intensity of therapy. Aims: To analyze the Pediatric Logistics Organ Dysfunction Scoring 11 system (PELOD) and Pediatric Risk Score of Mortality (PRISM), in the surgical intensive 12 care unit (ICU) of tertiary pediatric medical facility. Methods: The study included a 90 13 patients aged 0-18 years, in the period of three years. To analyze parameters of the PELOD 14 and PRISM score. In the analysis were used statistical data about predictors of mortality: 15 Receiver Operating Characteristics (ROC) curve and Hosmer-Lemeshow goodness of fit test 16 (HL-GOF). 17

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19 Index terms— pediatric scoring systems, multiple organ dysfunction syndrome-MODS, intensive care unit.

20 1 Introduction

vsfunction and organ failure in the sepsis is very common and serious complication of the most serious ill 21 patients. Research on various factors in explanation of sepsis occurrence, imposed a concept that was accepted 22 at the International Conference on definitions of sepsis from 2001. The diagnosis of sepsis is based on defined 23 24 criteria Association Consensus Conference Chest Physicians and Intensivists (ACCP / SCCM) [1,2] Multiorgan 25 dysfunction syndrome (Multiple Organ Dysfunction Syndrome-MODS) is the most common cause of death in the pediatric intensive care units, with frequency range of 26-50% [3,4]. In adult patients, mortality due to MODS 26 is of a similar value [5], according to Bilevicius and associates data the level of mortality reaches 85% [6]. It is 27 believed that the high mortality is a direct result of the progression of organ system failure [7,8] because a direct 28 link has been proved between mortality and the number of affected organ systems, as well as between mortality 29 and the severity of their dysfunction [9,10]. Wilkinson, Proulx and associates also point out in their studies that 30 the mortality caused by MODS directly depends on the number of affected organ systems [11]. 31

Different scoring systems for the estimate of severity of illness in intensive care units emerged from the gaining 32 of clinical experiences, primarily as a response to a question on the efficiency and quality of a treatment. In the 33 last decade scoring system has developed on the basis of results of multicenter studies. A separate category for 34 35 the estimate of the severity of illness are so-called score table which make it possible to statistical calculate the 36 probability of survival (PS-Probability of Survival) and the probability of dying (PM-Probability of Mortality) 37 [12]. The ideal scoring system does not exist, but a good score definitely has to meet several basic requirements: 38 first of all, the system must be simple, mathematically consistent, research results should have high sensitivity and specificity, and environmental factors should not affect the tests which make point system [13]. 39

The largest number of scores that are now used in intensive care units are primarily related to the adult population. Threfore, the pediatric scores that are used in clinical practice, usually resulting from the preexisting scores for adult patients. However, the specific physiology of pediatric patients has imposed a need to establish scores that just respect these facts. These are primarily characteristic pulse and systolic pressure caused by age, specific dynamics of water and electrolyte metabolism with an increased tendency towards metabolic acidosis, a relatively small amount of circulating volume, the immaturity of immune system and the difficulty in the maintaining of body temperature. a) Pediatric Risk Score of Mortality (PRISM) PRISM score is used

in age from the newborn to adolescence and shows the seriousness of the illness on the basis of disorders of the

observed physiological and clinical parameters, with the additional verification of pathological findings in special

49 laboratory tests. This score, however, did not appear to be useful enough with premature babies [14]. There are

50 several versions of this scoring system which was first applied in clinical practice under the name the physiological 51 stability index (Physiologic Stability Index-PSI). Originally, 24 physiological parameters were followed by this

stability index (Physiologic Stability Index-PSI). Originally, 24 physiological parameters were followed by this score [15,16]. It was published in the literature 1986, as a dynamic assessment of the patients condition [17].

⁵³ Pollack and his collaborators published a new version of the score in 1988, giving it the final name Pediatric

54 Risk of Mortality (PRISM). This point system was by then named PRISM II score by some intensivists, which 55 definitely separated it from the initial PSI scoring system, which was also defined as PRISM I score. PRISM II

so definitely separated it from the initial 151 scoring system, which was also defined as 11tibit 1 score. 11tibit 1 scoring system included 14 parameters, and its dynamic estimation according to the daily analysis type was first

shown in 1991's [18]. Score values in the range of 0-76. Table 1 shows the parameters that make the PRISM II
 score. b) Paediatric Logistic Organ Dysfunction score (PELOD)

The scoring system which is applied to the dysfunction of various organs in the pediatric age group was described in detail by Leteurtre in 1999. The score included the evaluation of the condition of the six organ systems (cardiovascular, respiratory, hepatic, renal, hematological and central nervous), and the possible existence of the dysfunction some of the selected organ systems. This score is also part of the dynamic scores, because it means a daily record of 12 observed parameters of organ dysfunction [3]. In addition, physiological parameters that are dependent on the age of patients (neonatal, infant, toddler, school age and adolescents) are continuously

⁶⁵ recorded [19,20]. Table 2 gives the parameters of PELOD score.

⁶⁶ 2 II.

67 **3** Aims

Analyzing the clinical value of pediatric scoring systems, Pediatric logistics organ dysfunction score (PELOD) and Pediatric Risk score of Mortality (PRISM), in the presence of sepsis accompanied by multiple organ dysfunction

⁷⁰ syndrome (MODS) in the surgical intensive care unit of tertiary pediatric hospital.

71 **4 III.**

$_{72}$ 5 Methods

73 The study was conducted at the Intensive Therapy of Pediatric Surgery Clinic in Novi Sad in the period of 36 74 months. The method of random selection was applied, and it included 90 patients who were previously treated 75 surgically or primarily located in the intensive care unit.

On the basis of the results of analyzed scoring systems and their completed correlation with the expected and actual (real) mortality, checking out of the prognostic reliability of the examined systems carried out. The study data are numerical and they were analyzed by standard procedures of descriptive and comparative statistics. ROC (Receiver Operating Characteristics) analysis was also used in the evaluation of score value for predicting of hospital mortality. Lemeshov Hosmer goodness of fit test was also used in the evaluation of the expected and actual (real) mortality and it present the measure of the degree of calibration. [21,22,23].

82 IV.

6 Results

The study included 90 patients aged 0-18 years treated at the Pediatric Surgery Clinic in Novi Sad, in the Intensive 84 Care Unit. The average annual number of patients hospitalized in the intensive care unit of the Pediatric Surgery 85 Clinic was 195, with a reported mortality of 8.8%. Out of the total number of patients, in 10% of patients MODS 86 have developed, with a mortality rate of 62%. In the group of newborn babies there were total of 39 examined 87 patients (43.3%). The group of infants had a total of 10 examined patients (11.1%). In the group of patients over 88 12 months there were 41 patients (45.5%). The gender distribution in the study was equal: 42 female subjects 89 (46.6%) and 48 males (53.3%). The average length of stay patients in the ICU for the total number of patients 90 was 10.3 days. With patients with lethal results 18.6 days, and in cured patients 8.2 days. By the analysis of 91 outcome, 72 patients (80%) survived, and death outcome was noted in 18 (20%) patients. 92

⁹³ 7 a) PRISM score

For the total number of examined patients, the mean PRISM score was 10.0. The mean value of the PRISM score in the group of patients with favorable outcome was 8, and with patients with lethal results 18.

⁹⁶ 8 b) PELOD score

 $_{97}$ $\,$ For the total number of examined patients mean PELOD score value were 9.5 The mean PELOD score value in

the group with favorable outcome was 7.7. In the group with lethal outcome it was 17.7.

⁹⁹ 9 c) The results of ROC analysis

The showing of PRISM score values using ROC curve (Figure ??). In area under the curve in our results for the
 PRISM score was 0.8306, which indicates a very good prediction of PRISM score in relation to the final outcome.
 which also proves a good prediction of PELOD score in relation to the final outcome.

¹⁰³ The prediction of outcome based on the PRISM score value using logistic regression

Based on the PRISM score value, using the Hosmer-Lemeshov goodness-of-fit test, the predicted mortality was compared to the current. (Table 3).

106 Predicting outcomes based on the PELOD score value using logistic regression

¹⁰⁷ The table 4 shows the probability of lethal outcome based on the of PELOD score values and using logistic ¹⁰⁸ regression. (Table 4).

109 Table 5 gives a collective survey of the examined scores and their comparisons. Hosmer-Lemeshov GOF, ROC

curve and standard error tests were valued. Based on the comparison of the examined scores better calibration results were obtained for PELOD score, while the results of discrimination with the ROC curve indicates greater reliability PRISM score, using the statistical method.(Table 5).

113 V.

114 **10** Discussion

In recent years, the complexity of intensive treatment need for more objective assessment of weight status of patients and their ultimate prognosis. Using of scoring systems, it is possible to not only predict the final outcome, but also to compare groups of patients within one health facility or among multiple institutions.

In our study, the average number of patients hospitalized in the intensive care unit of the Pediatric Surgery 118 Clinic at the annual level was 195, with recorded mortality of 8.8%. MODS developed in 10% with a mortality 119 rate of 62%. In our study, despite the relatively low incidence of MODS, mortality rate is high. Data from 120 the literature for the pediatric population are very often different, mostly because in some pediatric intensive 121 units both pediatric and surgical patients are treated together. The data of Tantalean and associates suggest 122 that the frequency of MODS in the intensive care unit is 25% and mortality from 26-50% [4]. Proux states 123 that the frequency of MODS was recorded from 11-27% [9], and Wilkinson gives data on mortality of 54% [11]. 124 The analysis of the study results considering patients age, showed that nearly half of examined patients belong 125 to the group of infants (43.3%). According to published data from the USA, age is a significant factor in the 126 epidemiology of sepsis. It is thought that children up to one year, especially newborns, are the patients with 127 the significantly greatest risk of sepsis development, with even up to 10 times more bigger risk compared to the 128 129 other categories of pediatric patients [8]. The total number of participants, males and females was almost equal: 46.6% female and 53.3% males. Watson and associates, in their epidemiological study of sepsis in the pediatric 130 131 age, indicate that boys under 10 years occur more frequently than girls, but there is not a significant difference in their recording mortality [10]. When it comes to the final outcome of treatment, no gender predisposing is 132 133 noticed in the analyzed literature.

For the total number of observed patients, the mean PRISM score value was 10.0. The mean PRISM score 134 135 value in the group of observed patients with favorable outcome was 8, and with lethal outcome it was 18. In our study, PRISM score values over 10 indicated a possible unfavorable outcome. Different from this, Tantalean 136 and associates, in their study, with patients with lethal outcome, got results which showed the average values 137 of PRISM score of 22.07, but also relatively high mean values of PRISM score even with patients who survived 138 [4]. For the total number of the observed patients, the results of mean values of PELOD score were 9.5. In our 139 survey, the mean value of PELOD score in the group with favorable outcome of treatment was 7.7, whereas in 140 the group with lethal outcome it was 17.7. In Leteurtre and associates study, the mean value of PELOD score 141 142 in patients with favorable outcome was 9.4, whereas in the group with lethal outcome mean scores were 31.0 PELOD (3). For both point systems, according to the literature data, values are significantly higher for the 143 observed patients with lethal outcome. Considering the difference of our results compared to the literature data, 144 the obtained results suggest the need for analysis on a greater number of the observed patients. 145

By using the ROC curve the values of the area under the curve were obtained for the Pediatric risk of mortality 146 score (PRISM) which were 0.8306, whereas for the Pediatric logistic organ dysfunction score (PELOD) the values 147 of area under the curve were 0.7967. These results show that by the use of PRISM and PELOD numerical system 148 it is possible to achieve high reliability and safety is satisfying certainty in prediction of the final outcome of 149 treatment. Both scores meet the ROC criteria for a good prediction, which means that the value of the area 150 under the curve is higher than 0.70. A similar survey, with the help of ROC curve was carried out by A. Thurkal, 151 where the validity of PRISM score was verified by the values of ROC curve 0.80 [24]. Singhal et associates by the 152 determining of mortality prediction using the PRISM score received a value of discrimination with the ROC curve 153 154 0.72 which indicates a satisfactory value of prediction [25]. Moreno and associates in their multicenter study, got a discrimination value of PELOD score of 0.91 ??26]. score (ROC 0.93) [28]. Regardless of the different 155 values of the results obtained by different researchers, it is clear that both point systems show strong reliability 156 in the assessment of the final outcome prediction A calibration degree was established by Hosmer-Lemeshov 157 goodness-of-fit test. When Hosmer-Lemeshov goodnes-of-fit test (HL GOF) was applied in the prediction of a 158 treatment outcome, based on the results of PRISM score, the values were 2.913 with the risk factor p = 0.405. 159 Assessment of treatment outcomes based on the results PELOD score, applying this test the values of 0.609 with 160

a risk factor p = 0.434. Leteurtre and associates in their multicenter study showed the values of PELOD score 161 calibration using HL-HL GOF ?2 = 4.03 with the risk factor p = 0.54 [3]. V.F. Martha survey similarly suggests 162 the use of PRISM score, because the calibration values PRISM score are 2-HL = 9.23 with the value of p = 0.10, 163 [29]. The analysis of PELOD score, Pedro Garcia and associates in two pediatric intensive unit, according to its 164 statistical results indicated very poor calibration values (?2-HL = 72.3, with risk values p lower than 0.001) [28]. 165 Considering the difference in our results compared to literature data, where the calibration values, using HL-GOF 166 test indicated good reliability in the prediction assessment of the final outcome of treatment with both point 167 systems, but with slightly better results for PELOD score, the obtained results indicate the need for analysis 168 to be carried out on a larger number of subjects. Costa and associates in their retrospective cohort study, got 169 results in a period of one year, at a general tertiary pediatric intensive care unit. The pediatric risk of mortality 170 score (PRISM) showed adequate discriminatory capacity and thus constitutes a useful tool for the assessment of 171 prognosis for pediatric patients admitted to a tertiary pediatric intensive care units [29]. 172

173 **11 VI.**

174 **12** Conclusion

The average number of hospitalized patients in Intensive Care Unit of the Pediatric Surgery Clinic, annually was 195, with an average mortality of 8.8%. The reported incidence of multiple organ dysfunction syndrome (MODS) 177 in the intensive care unit in the study was 10%, with a mortality of 62%. Most at-risk for the development of 178 severe sepsis were neonates.

For the total number of respondents, the median PRISM score was 10.0. The mean value of PRISM score in the group of patients with favorable outcome was 8, and with lethal results 18. The results were obtained for the mean values of PELOD score of 9.5 for the total number of respondents. In our study, the median PELOD score in the group with favorable outcome of treatment was 7.7, whereas in the group with lethal results mean was 17.7. Based on these results, it was confirmed that the higher values of the PRISM score and PELOD directly related to an unfavorable outcome. In addition, this study confirms that both scores reliably reported and described the clinical condition of patients analyzed.

Using ROC curves the values of area under the curve were obtained for the pediatric risk of mortality score (PRISM) of 0.8306, while for the pediatric logistic organ dysfunction score (PELOD) values of area under the curve 0.7967. These results indicate that the application of the PRISM and PELOD numerical system achieves high reliability and satisfactory safety in predicting the outcome of treatment.

Using Hosmer-Lemeshov goodnes-of-fit test in the assessment the outcome, based on the results of PRISM score, the values of risk factors p = .405. Assessment of treatment outcomes based on the results PELOD score, applying this test the values of the likelihood ratio p = 0.434were obtained. Results of the application Hosmer-Lemeshov goodnes-of-fit test indicate that it is possible to predict the outcome in the regression model. The study results show that both scores, based on statistical methods of discrimination (ROC curve) and calibration (HL-GOF test) reliably show and describe the clinical condition of patients analyzed.

Daily use and use of numeric system is needed to achieve full effectiveness of the therapy. Initial assessment, daily monitoring and reliable prediction of the final outcome of the application of pediatric scoring systems allow to raise efficiency and rationalization of work in an intensive care unit.

Previous clinical trials need to be upgraded through a multi-center study, with the aim of finding, as more reliable parameters, as new scoring systems to predict the outcome of treatment for multiple organ dysfunction in the pediatric age.

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Figure 1: F

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PARAMETER Systolic pressure(mmHg)

2014 Diastolic (mmHg) pressure Year Heart rate/min Breathing frequency/min Pa O 2 /Fi O 2 Pa CO 2 (mmHg) GCS Pupil reaction PT/PTT Total b Volume XIV Issue II Version I () Calcium (µmol/l) Glu-Medical Re- $\cos a (mg/dl)$ search Global Bicarbonates (µmol/l) Jour- nal of

Figure 2: Table 1 :

 $\mathbf{2}$

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Figure 3: Table 2 :

3

Actual result (number of patients)

Figure 4: Table 3 :

 $\mathbf{4}$

Actual result (number of patients)

Figure 5: Table 4 :

 $\mathbf{5}$

The values of tests	PRISM	PELOD
H-L GOF test x 2 (p)	2,913 (p=0,405)	0,609 (p=0,434)
Area of ROC curve-AUC (CI	0,8306	0,7967
95%) Standard error AUC	0,062	0,066

Figure 6: Table 5 :

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