леваниями экстрапирамидной нервной системы, эпилепсией и другими пароксизмальными заболеваниями нервной системы на амбулаторном этапе» [Order of the Ministry of Health of the Chelyabinsk Region of December 8, 2016 No. 2079 "On the procedure for routing neurological patients suffering from multiple sclerosis, diseases of the extrapyramidal nervous system, epilepsy and other paroxysmal diseases of the nervous system at the outpatient stage" https://docs.cntd.ru › document (In Russ.).]

9. Приказ Минздрава России от 20.12.2012г. №1228н «Об утверждении стандарта медицинской помощи при болезни Альцгеймера» [Order of the Ministry of Health of Russia dated 12/20/2012. No. 1228n "On approval of the standard of care for Alzheimer's disease" (In Russ.).]

10. Приказ о маршрутизации МЗ РС(Я) за № 01-07/184 от 14.02.2019 «О порядке маршрутизации больных неврологического профиля, страдающих нейродегенеративными заболеваниями, на амбулаторно-поликлиническом и госпитальном этапах» [Order on routing of the Ministry of Health of the Republic of Sakha (Yakutia) No. 01-07 / 184 dated February 14, 2019 "On the procedure for routing neurological patients suffering from neurodegenerative diseases at the outpatient and hospital stages" https://minzdrav.sakha.gov.ru (In Russ.).]

11. Сухомясова А.Л. Аутосомно-доминантная миотоническая дистрофия в Республике Саха (Якутия): автореф. дис.канд.мед.наук /А.Л. Сухомясова. - Томск, 2005.- 22 с [Sukhomyasova A.L. Autosomal dominant myotonic dystrophy in the Republic of Sakha (Yakutia) *Abst. dis. cand. med. sciences*. 2005; 22 (In Russ.).]

12. Эпидемиология болезни Паркинсона в Республике Саха (Якутия) /Т.Е.Попова, А.А.Таппахов, Т.Я.Николаева, Л.Т.Оконешникова и др. [Popova T.E, Tappakhov A.A., Nikolaeva T.Ya.,.Okoneshnikova L.T et al. Epidemiology of Parkinson's disease in the Republic of Sakha (Yakutia). 2017; 3 (59): 98-101 (In Russ.).]

13. Genetic fitness and selection intensity in apopulation affected with high-incidence spinocerebellar ataxia type 1 / F.A. Platonov, K. Tyryshkin,D.G. Tikhonov [et al.] *Neurogenetics.* 2016; 17(3): 179-185. doi: 10.1007/s10048-016-0481-5

14. Lane C.A., Hardy J., Schott J. M. Alzheimer's disease / *Eur J Neurol Review*.-2018; 25 (1): 59-70. DOI: 10.1111 /ene.13439.Epub 2017 Oct 19.

HEALTHY LIFESTYLE. PREVENTION

O.G. Sivkov, A.O. Sivkov, I.N. Leiderman

PREDICTION OF NEGATIVE CLINICAL OUTCOME OF CRITICAL CONDITION USING THE APACHE-II, SOFA, NRS-2002 SCALES

DOI 10.25789/YMJ.2021.75.14

УДК 616-036.81

During the first 24 hrs of patient's admission to ICU, it is essential to perform a negative outcome screening, which can be done using acute physiology severity scales - APACHE-II and SOFA. It is known that these scales do not include nutritional insufficiency assessment, which itself affects survivability of critically ill patients. The model that uses three scales: assessment of pathophysiological changes - APACHE-II, intensity of multiple organ failure – SOFA, and assessment of nutritional insufficiency risk - NRS-2002, reliably improves the accuracy of the negative outcome prognosis in an ICU patient compared to their individual application.

Keywords: APACHE II, SOFA, NRS-2002, critically ill patients, predictors, mortality.

Introduction. Evaluation of patient's condition severity in an intensive care unit (ICU) is an essential task in the work of a resuscitator. Identification of patients with a high risk of developing a negative outcome at early stages of intensive care provides an opportunity for timely adjustment of the diagnostic and treatment process. Different comprehensive prognostic scales are used to address this issue. The most popular scales are APACHE-II that reflects pathophysiological changes in the patient's organism at admission and serves to predict a disease outcome, and SOFA that allows tracing the dynamics of the multiple organ dysfunction syndrome [1,2]. Numerous studies have proven that critically ill patients with nutritional insufficiency (NI) stay longer in ICU and hospital, and demonstrate a higher mortality rate [3]. The drawbacks of these scales include the fact that they do not consider patient's protein-energy metabolism and nutritional status – the risk of NI. One of the most convenient and frequently used, in the world practice, scale assessing the risk of NI is Nutritional Risk Screening 2002 (NRS-2002), which is recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) [4]. It can be applied to all inpatients including those treated in ICU [4]. The NRS-2002 score helps identifying NI patients and serves a lethal outcome predictor in critically ill patients [5]. The meta-analysis assessing usefulness of NRS 2002 as a predictor of postoperative outcomes in the abdominal surgery included 11 studies in total. Postoperative complications developed much more frequently in the risk-group patients (the odds ratio (OR) - 3.13, p <0.00001). Mortality was also significantly higher in patients having a higher risk score according to NRS 2002 (OR – 3.61, p <0.009) [6].

Absence, in the available literature, of information on how the prognostic value of APACHE-II and SOFA scores will change if the risk of developing NI assessed by the NRS-2002 score will be taken into account, makes our study relevant.

Purpose of the study: to assess the informative value of the model predicting a negative outcome in ICU patients through combined application of APACHE-II, SOFA, and NRS-2002 scores.

Materials and methods. A prospective single-center study was carried out in ICU of JSC Neftyanik Hospital, Tyumen, in 2012-2017. The inclusion criteria were over 24hrs. in ICU and age between 18 and 80 years. The exclusion criteria were coma and/or impossibility to get answers to questions, shock, moribund state, age older than 80 years of age, pregnancy; moderately ill patients staying in ICU for less than 24 hrs. During the first 24 hours

SIVKOV Oleg G. - PhD, Head of the Anesthesiology and Resuscitation Service of the Tyumen Cardiology Research Center. city of Tyumen http://orcid.org/0000-0002-7694-9293; **SIVKOV Alexey O.** - doctor of the Department of Anesthesiology and Resuscitation of JSC MSCH "Neftyanik", Tyumen.http://orcid.org/0000-0003-3682-2789; **LEIDERMAN Ilya N.** - MD, Professor of the Department of Anesthesiology and Resuscitation of the Almazov Federal State Medical Research Center of the Ministry of Health of the Russian Federation, St. Petersburg http://orcid.org/0000-0001-8519-7145

in ICU, patients were assessed according to APACHE-II, SOFA, and NRS-2002. Questioning was carried out by two resuscitators. The study included 176 patients (89 women and 87 men); of them, 110 subjects (62.5%) were surgical patients and 66 (37.5 %) - therapeutic. The causes for admission to ICU were as follows: an acute surgical pathology - peritonitis (n=34), acute pancreatitis (n=24), intestinal obstruction (n=16), urosepsis (n=9), suppurative-septic diseases of different locations (n=6), gastrointestinal hemorrhage (n=15), thrombosis of major vessels (n=3), pneumothorax (n=1), mediastinitis (n=1); and therapeutic diseases – chronic cardiac insufficiency (n=19), pneumonia (n=17), liver cirrhosis (n=10), delirium (n=4), chronic obstructive lung disease (n=2), anaphylactic shock (n=1), dyscirculatory encephalopathy (n=5), leucosis (n=4), epilepsy (n=1), acute renal failure (n=2), acute exposure to alcohol surrogates (n=2). The patients were split into two groups: the first group included the deceased patients (n=60), the second – the survived patients (n=116). Blood serum C-reactive protein (CRP) was used as a criterion of systemic inflammatory response intensity. The recorded demographic information included gender and age; body mass index (BMI) was calculated, too. Patients' characterization is shown in table 1.

The raw data obtained were processed using the SPSS software package. Normality of distribution was checked by the Shapiro-Wilk test. The findings are given as the mean and mean square deviation M±σ or as the median and quartiles Me, [Q25; Q75]. The prognostic value of scores was assessed using the logit regression technique. To establish the separation power, ROC analysis was undertaken. Nigel Kirk's determination coefficient was calculated. The null hypothesis was discarded at p<.05.

Results and discussion. In our study we observed statistically significant inter-group differences (table 1) for APACHE-II, SOFA, and NRS-2002 scales. The score according to all three scales was higher in patients of the first group, in which BMI and blood plasma CRP were higher, too. No statistically significant differences were noted in the therapeutic group while among the surgical patients the number of survived patients was statistically significantly greater. One can see from table 2 that the patients of the first group stayed in hospital statistically significantly longer and stayed on mechanical lung ventilation (MLV) for a longer period of time.

Logit regression identified indices in-

Table 1

Clinical and Laboratory Characteristics of Patients in the Compared Groups

Index	Group I (n=60)	Group II (n=116)	p
Age, (years)	62.7±18.8	59±16.4	0.16[d]
Gender, (male, %)	64.4	35.6	0.05[f]
Body Mass Index, (kg/m$^{2)}$	24 [21.4;27.7]	26 [23.3;30.2]	0.009[e]
APACHE-II[a], (score)	15 [12;20]	9 [5;13]	<0.001[e]
SOFA[b], (score)	4 [3;7]	2 [1;3.75]	<0.001[e]
NRS-2002[c], (score)	5 [4;6]	3 [2;5]	<0.001[e]
C-reactive protein, (mg/L)	94.1 [44.2;181.5]	60.4 [11;166]	0.045[e]
Therapeutic patients, %	51.5	48.5	0.35[f]
Surgical patients, %	23.6	78.4	<0.001[f]

Note: a – Acute Physiology and Chronic Health Evaluation; b – Sequential Organ Failure Assessment; c – Nutritional Risk Screening 2002, d – Student's t-test, e – Kruskall-Wallis h-test, f – Pearson's chi-squared test.

Table 2

Duration of Treatment in ICU and Duration of Mechanical Lung Ventilation in the Compared Groups

Parameter	Group I (n=56)	Group II (n=120)	p
Bed-days in ICU, days	5.6±4.7	4.6±4.2	0.3
Bed-days in hospital, days	5 [3;9]	10 [7;15.75]	<0.001
Bed-days on MLV, days	3 [1;4]	1 [0;1]	<0.001

Table 3

Predictive Value of Scales and Some Indices in respect of the Risk of Lethal Outcome (Logit Regression)

Index	Odds Ratio (OR)	95% CI	p=
Age, (years)	1.01	0.99-1.03	0.16
Body Mass Index, (kg/m$^{2)}$	0.92	0.87-0.98	0.055
APACHE II, (score)	1.2	1.12-1.27	<0.001
SOFA, (score)	1.4	1.2-1.6	<0.001
NRS-2002, (score)	1.7	1.38-2.21	<0.001
C-reactive protein, (mg/L)	1	0.99-1	0.18

Note. Table 3, 5 CI - confidence interval.

Table 4

ROC Analysis of the Predictive Value of APACHE-II, SOFA, and NRS-2002

Index	AUC	p	COV	Sensitivity, %	Specificity, %
APACHE-II, score	81.5	<0.001	>13.5	74	74.5
SOFA, score	79.7	<0.001	>2.5	71.7	72.6
NRS-2002, score	73.7	<0.001	>3.5	89.1	50.9

Note. AUC-area under curve, COV-cut-off value.

dependently influencing the risk of lethal outcome – APACHE-II, SOFA, and NRS-2002 scores (table 3). Age, CRP and BMI did not display a separation power in respect of the risk of lethal outcome in ICU patients (table 3)

To analyze the quality of models, ROC analysis was carried out; its results are given in table 4.

The largest area under the ROC curve was found in APACHE-II scale (table 4). All models were statistically significant (p<0.001). APACHE-II demonstrates a very good quality of the model while SOFA and NRS-2002 – just good. The best correlation of sensitivity and specificity was found in APACHE-II. When the score is APACHE-II>13.5 or SOFA>2.5, or NRS-2002>3.5, a high risk of lethal outcome development is surmised (table 4). To establish the model featuring the best predictive value, combinations of scores according to all three scales were made (table 5).

The resultant models were statistically significant (p<0.001). Based on regression coefficients' values, APACHE-II, SOFA, and NRS-2002 are directly related to the lethal outcome probability. The best area under the ROC curve was observed in the model that accounted scores of all three scales together – APACHE-II, SOFA, and NRS-2002 (p<0.001). According to Nigel Kirk's determination coefficient, the model takes into consideration 40% of factors determining the lethal outcome probability. Its diagnostic efficacy amounted to 74%, its sensitivity being 83.6% and specificity - 55%. The advantage of this study is that when the scores of all three scales are used, it improves the accuracy of prognosis that can be calculated by a binary logit regression formula.

Table 5

ROC Analysis of the Predictive Value of Models of Combined Application of APACHE-II, SOFA, and NRS-2002 Scales

Index	AUCd	Sensitivity, %	Specificity, %	95% CI	p
APACHE II+SOFA	84.6	82.6	74.5	0.78-0.91	<0.001
APACHE II+ NRS-2002	83.3	78.3	74.5	0.77-0.89	<0.001
SOFA+NRS-2002	84.6	78.3	71.3	0.78-0.9	<0.001
APACHE II+ SOFA+ NRS-2002	86.4	84.8	70.8	0.80-0.92	<0.001

Note. AUC – area under curve, CI – confidence interval.

$$p = \frac{1}{(1+e^{-z})} \times 100,$$

where p is the probability of occurrence of an outcome, units; z is the logit function power exponent, e – is the Euler's number (≈2.718).

$$z = -4{,}3 + 0{,}97 \times X_{Apache\ II} + \\ + 0{,}2 \times X_{Sofa} + 0{,}41 \times X_{NRS-2002},$$

where X is independent indices (scores).

Conclusion. Each of the APACHE-II, SOFA, and NRS-2002 scales separately is an independent predictor of a negative outcome in critically ill patients, and their scores can be used as a prognostic criterion. Their combined use improves the accuracy of the negative outcome prognosis in ICU patients.

Reference

1. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985; 13(10):818-29. PMID: 3928249.

2. Vincent J.L., Moreno R., Takala J., Willatts S. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med.* 1996; 22: 707–710. doi: 10.1007/BF01709751.

3. Hiura G, Lebwohl B, Seres DS. Malnutrition Diagnosis in Critically Ill Patients Using 2012 Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition Standardized Diagnostic Characteristics Is Associated With Longer Hospital and Intensive Care Unit Length of Stay and Increased In-Hospital Mortality. *JPEN J Parenter Enteral Nutr.* 2020; 44(2): 256-264. doi: 10.1002/jpen.1599.

4. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z; Ad Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *ClinNutr.* 2003; 22(3): 321-357. doi: 10.1016/s0261-5614(02)00214-5.

5. Marchetti J, Reis AMD, Santos AFD, Franzosi OS, Luft VC, Steemburgo T. High nutritional risk is associated with unfavorable outcomes in patients admitted to an intensive care unit. *Rev Bras Ter Intensiva.* 2019; 31 (3): 326-332. doi: 10.5935/0103-507X.20190041.

6. Ratnayake CB, Loveday BP, Shrikhande SV, Windsor JA, Pandanaboyana S.Impact of preoperative sarcopenia on postoperative outcomes following pancreatic resection: a systematic review and meta-analysis. *Pancreatology* 2018;18:996e1004.