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TRISS, NTRISS AND ASCOT VALIDATION IN SEVERE TRAUMA POPULATION ADMITTED IN MOLDOVIAN TRAUMA CENTER

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ПЕРЕВІРКА TRISS, NTRISS ТА ASCOT У ПОПУЛЯЦІЇ З ВАЖКИМИ ТРАВМАМИ, ЩО НАДХОДЯТЬ ДО ТРАВМАТОЛОГІЧНОГО ЦЕНТРУ МОЛДОВИ

Арнаут О., Грабовщий І., Балтага Р., Шандру С.

Вступ. Відповідно до останніх статистичних даних із різних країн травма належить до числа провідних причин смерті зі зростаючим внеском у загальний рівень смертності. Можливість прогнозувати й передбачити ймовірні ускладнення може значно збільшити виживаність після травми. Це можливо шляхом аналізу різних клінічних параметрів пацієнтів із травмами та виявлення тих, які мають високу прогностичну силу. Результати були використані для визначення різних оцінок травматичності. На цей час існує багато шкал, розроблених з урахуванням анатомічних, фізіологічних або змішаних критеріїв. Вони були розроблені з огляду на особливості медичних систем різних країн і багато в чому відрізняються одна від одної, у тому числі й від молдавської. Отже, потрібно знайти оптимальну шкалу оцінювання для щоденного використання в різних умовах для цільової популяції поточного дослідження.

Мета та завдання. Валідація та порівняльний аналіз найпоширеніших змішаних оцінок травматичності в умовах травмпункту Республіки Молдова.

Методи. У поточному ретроспективному аналітичному дослідженні було проаналізовано дані 2651 пацієнта з важкою травмою, яких було послідовно госпіталізовано у травматологічний центр Молдови в період із січня 2013 р. по листопад 2018 р. Джерелом інформації слугувала електронна база даних IMU без персональної інформації. Критерії включення та виключення були дотримані. Вони були розраховані за шкалами ASCOT, TRISS і NTRISS для оцінки виживаності пацієнтів. Результати прогнозу порівнювали та статистично аналізували за допомогою логістичної регресії.

Результати. Порівняння змішаних оцінок, включених у дослідження, показало, що шкала NTRISS мала максимальний коефіцієнт детермінації порівняно з TRISS і ASCOT, усі моделі мали калібрувальні індикатори, які потребують покращення, критерієм є значимість тесту.

Висновок. У цій статті перевірено три загальні змішані прогностичні моделі. З них шкала NTRISS має оптимальні характеристики з точки зору детермінації / розрізнення і може бути рекомендована для щоденного використання в умовах травмпункту Республіки Молдова.

Ключові слова: травма, прогностична модель виживання.

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TRISS, NTRISS AND ASCOT VALIDATION IN SEVERE TRAUMA POPULATION ADMITTED IN MOLDOVIAN TRAUMA CENTER

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Introduction. Recent statistical data from different countries places the trauma among the leading causes of death with increasing contribution to the overall mortality rate. The possibility to predict and to anticipate the eventual complications could significantly increase trauma survival rate. This is possible by analyzing different clinical parameters of trauma patients and identifying those with high predictive power. The results were used to concept different traumatic scores. Nowadays, there are a lot of scores elaborated considering anatomical, physiological or mixed criteria. They were developed considering the particularities of distinct medical systems from different countries. They could differ in many aspects from each other, inclusively, from the Moldavian one. Thus, it is necessary to find the optimal score for daily use in distinct conditions for target population of current study.

Purpose and task. Validation and comparative evaluation of the most common mixed traumatic scores in conditions of a trauma center from Republic of Moldova.

Methods. In the current retrospective analytical research, was analyzed the data of 2651 severe trauma patient's consecutive admitted in Moldavian trauma center in period between January 2013 – November 2018. The source for information was the electronic database of IMU with no personal information. The inclusion and exclusion criteria were respected. They were calculated ASCOT, TRISS and NTRISS scores to assess patient's survival rate. The prediction results were compared and statistically analyzed by logistic regression.

Results. The comparison of the mixed scores included in the research showed that the NTRISS score showed a maximum coefficient of determination compared to TRISS and ASCOT, all models having calibration indicators that need improvement, the criteria being the significance of the test.

Conclusion. In this article, three common mixed predictive models were validated. Of these, NTRISS has optimal characteristics in terms of determination/discrimination and could be recommended for daily use in conditions of a trauma center from Republic of Moldova.

Key words: trauma, survival predictive model.

Introduction. According to the World Health Organization (WHO), tens of millions of people are traumatized each year, and 5 million people die from traumatic injuries

(9% of all deaths), which is about 1.7 times more than the amount of deaths caused by HIV/AIDS, tuberculosis and malaria, accounting for 16% of all disabilities caused by traumatic injuries [1]. Data from the US National Center for Injury Prevention and Control places trauma as the leading cause of death among people aged 1 to 44 [2], with trauma ranking third in the overall structure of lethality, after circulatory system diseases and neoplasms.

In the near future, a negative dynamic is forecast in the sense of increasing death rates due to trauma. In 2030, according to WHO calculations, in the general structure of lethality, road accidents will be placed on the 7th place (in 2012 the 9th place), suicides on the 16th place (in 2012 the 15th place) and catatraumas on the 17th place (in 2012 the 21st place) [1]. This trend has been confirmed in other similar research. For example, a study that looked at the causes of death in the United States from 2000-2011 found that the death rate from circulatory system diseases and neoplasms was declining and that from trauma was rising. The same study also showed that the rate of fatal injuries was 22.8% higher in 2010 compared to 2000, while the population increased by only 9.7% [3].

The Republic of Moldova, having some peculiarities, is not an exception, trauma being a serious problem. According to data from the Statistical Database of Moldova, in the period 2009–2018, injuries were the leading cause of death for the age of 1–44 years, which corresponds to world data and is valid for both raw and standardized data by age and biological gender. The argument for the standardization procedure served the changes in the population structure. One of the indicators was the progressive increase of the aging coefficient (number of people aged 60 and over per 100) from 14 in 2009 to 18.4 in 2018. For ages between 0 and 1-year, traumatic injuries were the second cause of death, after respiratory diseases for both raw and standardized data. Analysis of the general structure of lethality shows that traumas are ranked fourth after circulatory system diseases, tumors and digestive system diseases [4].

The use of predictive scores has a maximum efficiency when they are adjusted to the realities of the medical system in which they will be used. Thus, the validation of the usual traumatic scores (models) is seen as absolutely necessary until their use for a certain population or medical system, different from the one in which they were conceived. This method offers the possibility to correct the coefficients in the regression equation with their adjustment to the current situation and can significantly increase the accuracy of the forecast. Such a procedure for the usual traumatic scores was not performed for the population of patients in the Moldovan medical system, so they cannot show their maximum utility. The resulting prediction deviations may induce some problems in their use by medical staff at different stages, including ICU conditions. Studies in this direction started some time ago. As patients were added to the study groups, the results were checked periodically. Some of the preliminary data have been published recently [5]. According to them, from the very beginning, the ASCOT score was characterized by the maximum predictive power among patients in the preliminary analyzed groups. This article contains complementary information on the validation of routine predictive models for the population of patients with severe trauma within the Clinic of Anesthesiology and Resuscitation Institute of Emergency Medicine (IMU) – Trauma Center of the Republic of Moldova.

Purpose and task. The purpose of this study is to minimize prediction errors resulting from the arbitrary use of traumatic scores caused by the lack of validation of such scores and their adjustment to the particularities of the medical system in the Republic of Moldova. Also, the results presented tend to attract attention and motivate specialists from other medical centers to follow the same strategy for the institutions in which they operate.

Methods. The actual retrospective analytical research had the aim to improve the identification and prediction for severe trauma patients from Moldavian medical system. Nicolae Testemițanu State University of Medicine and Pharmacy (Chisinau, Republic of Moldova) ethical committee approved the design of study (Protocol 33/46 from 16.12.2016). There were considered 2651 severe trauma patients consecutive admitted in Moldavian trauma center ICU, Chisinau, Republic of Moldova (period January 2013 – November 2018). The source for information was the electronic database of IMU with no personal information as first and second names, addresses, personal ID number, phone number etc. The inclusion criteria were admission in ICU from IMU in first 24 hour after traumatic event, severe trauma (Injury Severity Score (ISS) ≥ 15 [6]), age ≥ 18 and blunt injury. The exclusion criteria were the age < 18, repetitive admission, burns, penetrating injury, incomplete data for trauma scores estimation or unusual analyzed variables values determined in preliminary dataset analysis, patients transferred to other institutions and mental disorders (senile or other deliriums) as reason for admission in ICU. The criteria for trauma severity was the survival probability. It was estimated for each patient, using three mixt traumatic scores: TRISS NTRISS and ASCOT. The AIS component for NTRISS and TRISS evaluation as Abbreviated Injury Scale (AIS) estimation for ASCOT the 2015 edition (last edition) of AIS vocabulary were used [7]. The coefficients for models' equations were estimated especially for examined population, this means validation of these traumatic scores and second, the models were compared in order to identify the most accurate score for survival rate prediction in ICU severe trauma population from Moldavian trauma center. The models without gender and age were adjusted for these parameters. In addition, the obtained tested scores' coefficients were used to generate the equation to estimate the severe trauma survival probability from IMU ICU. Also, odds ratio (OR) and 95% confidence interval (95% CI) for OR were calculated. To validate and to compare the models, logistic regression technique was used. For each model were estimated the following characteristics – determination coefficient (Nagelkerke R Square), calibration (Hosmer– Lemeshow test) and discrimination abilities (surface under the ROC curve). Considering the number of developed models (three), the problem of multiple comparisons problem was solved by Bonferroni correction – the significance level of the models (α) being equal to .05 / number of developed models (α = .05/3 = .017).

For validation, three scores were selected from the variety of mixed predictive models that are most often used in clinical practice – TRISS, NTRISS and ASCOT [8]. After that, a comparative evaluation of the validated models was performed in order to highlight an optimal model from the perspective of determination, calibration and discrimination. The data obtained will be the basis for arguing the use in clinical practice of ICU of IMSP IMU until the identification of other possible alternative models that will be proposed in the future for more detailed assessment of the condition of a patient with severe trauma.

Null hypotheses that postulate that the scores do not have the ability to predict the probability of survival in patients with severe trauma better than a model based on only one constant have been made. Respectively, alternative hypotheses assume that scores can predict the outcome of treatment better than a model that is based only on a constant. Next, the features of each of the analyzed scores will be described.

Results and Discussions. The TRISS score was shown to be able to predict the outcome of treatment (survival / death) by rejecting the null hypothesis (Omnibus Test of Model Coefficients ($\chi 2$ = 680,570, df = 3, p <0.001). the following characteristics of the examined model: The determination indicator, Nagelkerke R Square, had the value of 0.371 (37.1%), i.e. almost a third of the dispersion of the variable of interest was explained by the covariates from the validated model.

The calibration indicator (Hosmer – Lemeshow test) showed a significant value, $\chi 2$ = 16,864, df = 8, p = 0.032, but it needs optimization, because the score does not predict efficient results on the full range of possible scores.

The discrimination indicators of the classification table, namely specificity and sensitivity were equal to 59.8% and 87.6% respectively, the summary percentage (overall) being estimated at 79.7%. The results correspond to cut-off point 0.6 (Figure 1).

For the predictive model based on the TRISS score, the area under the ROC Curve was 0.823, with a 95% confidence interval between 0.804 and 0.843 and with a significant difference from the value 0.5 (p <0.001) (Table 1). The model included the constant (B = -3.781), the ISS value (B = -0.091), the age in binary form ≥ 55 years or < 55 years (B = -1.334) and the RTS value (B = 0.982), the coefficients having the respective signs in front (Table 1, section a) – age and ISS negative signs, RTS positive. Analysis of stability by resampling, bootstrapping method (1000 samples), TRISS validated model for the probability of survival in severe trauma showed that the coefficients are stable, the argument being their meanings, small amplitude of confidence intervals and unchanged signs (Table 1, section b).

```
             Observed Groups and Predicted Probabilities

     320 +                                                                                                    +
         I                                                                                                    I
         I                                                                                                    I
F        I                                                                                                    I
R    240 +                                                                                                    +
E        I                                                                                                    I
Q        I                                                                                               S    I
U        I                                                                                               S    I
E    160 +                                                                                               S    +
N        I                                                                                     S       S S    I
C        I                                                                                     S  S  S S S    I
Y        I                                                                                     S  S  SSS S    I
      80 +                                                                           S        SS  SS SSS S    +
         I                                                                  S S    S S  S   S SS  SS SSS S    I
         I                         S                  S S       S S         S D    SSSS S SSS SS  SS SSS S    I
         ID           D     S    D D       SDS    S  SDDDDD    SDSDS DSS S SDSDD   SDSS D DSSSSSS DDSSSD SS   I
Predicted ---------+---------+---------+---------+---------+---------+---------+---------+---------+----------
  Prob:   0        ,1        ,2        ,3        ,4        ,5        ,6        ,7        ,8        ,9         1
  Group:  DDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS

          Predicted Probability is of Membership for Supravietuire
          The Cut Value is ,60
          Symbols: D - Deces
                   S - Supravietuire
          Each Symbol Represents 20 Cases.
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Fig. 1. Classification chart for the predictive model of the probability of survival in patients with severe trauma based on the TRISS score

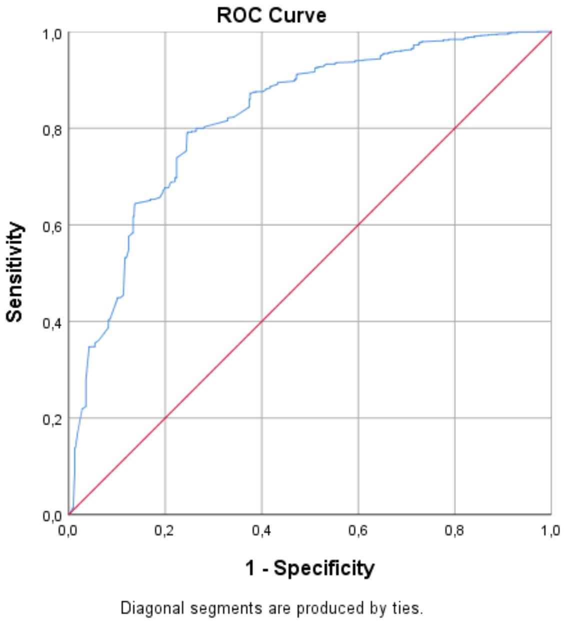

Fig. 2. ROC curve of the predictive model for the predictive model of the probability of survival in patients with severe trauma based on the TRISS score

Considering the mentioned coefficients, the validated model has the following mathematical expression:

$$p = \frac{1}{1+e^{-(-3.781-0.091*\text{valoarea ISS}-1.334*\text{Vârsta}\geq 55+0.982*\text{RTS})}} \quad \text{(formula 1)},$$

where p – the probability of death in severe trauma;
e (exponent) – constant equal with 2.71828.

The components of the TRISS score were analyzed in detail and showed the following characteristics. The RTS value showed a positive association with the probability of survival (OR = 2,670 (95% CI 2,371, 3,007)) which means that a difference of one unit in the RTS score changes the prognosis more than 2.5 times, the confidence interval being narrow. It is important to note that the adjustment to age and severity of lesions after ISS did not change the form of RTS associations with the variable of interest. At the same time, age in binary form (above or below 55 years) showed a negative association (OR = 0.264 (95% CI 0.210, 0.331)) – the effect estimated approximately four times – if the patient is over 55 years of age, the chances of survival are reduced by that amount. The ISS score values, obviously, showed negative correlations with the treatment results (OR = 0.913 (95% CI 0.898, 0.929)), the odds ratio being similar to the value from the previously univariate analysis performed to validate this score.

The NTRISS score, which uses NISS instead of ISS, similar to TRISS, showed the ability to predict the outcome of treatment of a patient with severe trauma, the null hypothesis being rejected (Omnibus Test of Model Coefficients ($\chi 2 = 965{,}427$, df = 3, $p < 0.001$)). Subsequent analysis showed the following characteristics of the validated model. The determination indicator, Nagelkerke R Square, was higher compared to TRISS – 0.496

Table 1

Variables in the equation from the final predictive model of the probability of survival in patients with severe trauma based on the TRISS score a. Coefficients in the model

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
ISS, points	-.091	.008	116.365	1	.000	.913	.898	.929
Age, ≥ 55 years	-1.334	.116	131.213	1	.000	.264	.210	.331
RTS	.982	.061	262.896	1	.000	2.670	2.371	3.007
Constant	-3.781	.454	69.447	1	.000	.023		

b. Bootstrap resampling results for variables included in the model

	B	Bias	S.E.	Sig.	95% Confidence Interval for B	
					Lower	Upper
ISS, points	-.091	-.001	.010	.001	-.111	-.073
Age, ≥ 55 years	-1.334	-.002	.115	.001	-1.563	-1.096
RTS	.982	.003	.067	.001	.855	1.114
Constant	-3.781	-.004	.509	.001	-4.798	-2.780

(49.6%), which means that almost half of the dispersion of the variable of interest (survival / death) was explained by the covariates of the validated NTRISS model. The calibration indicator (Hosmer – Lemeshow test) showed a significant value, $\chi 2 = 61{,}793$, df = 8, $p < 0.001$ – a calibration indicator that requires optimization, i.e. the score does not predict the results efficiently over the entire range of possible score values – no it is

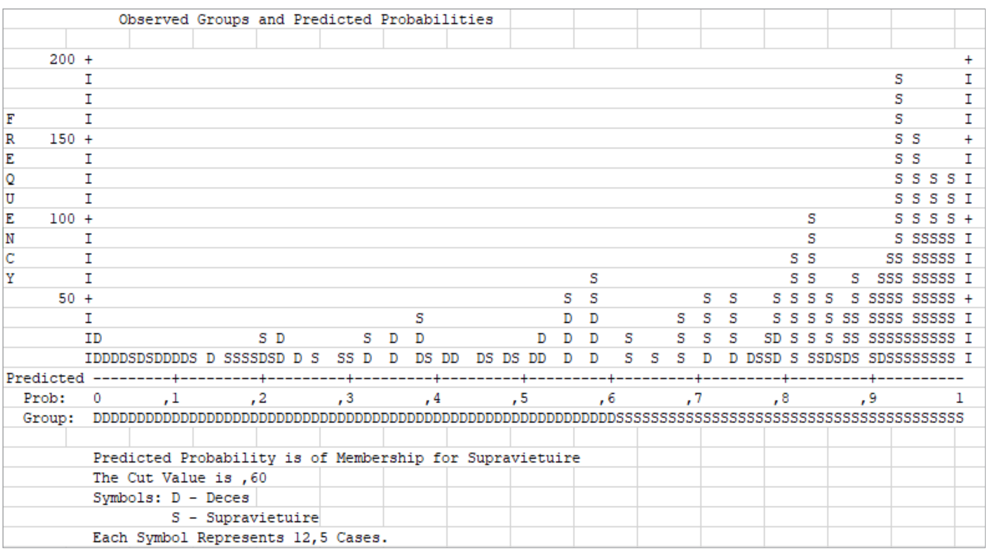

Fig. 3. Classification chart for the predictive model of the probability of survival in patients with severe trauma based on the NTRISS score

possible to stratify the risk of death. At the same time, the model predicts the patient's chances of dying or not quite well compared to other models presented.

The discrimination indicators in the classification table, namely specificity and sensitivity were equal to 74.4% and 89.1% respectively, the summary (global) percentage was estimated at 85.0%. The results were obtained after optimization by changing the critical point to 0.6 instead of the standard 0.5 (Figure 3).

The area under the ROC Curve, for the predictive model based on the NTRISS score, was 0.881, with 95% confidence interval (0.865, 0.896) and with a significant difference from the value 0.5 ($p < 0.001$) (Fig. 4). The model included the constant (B = -1.496), the NISS value (B = -0.138), the age similar to TRISS (B = -1.496) and the RTS value (B = 0.869), the coefficients having the appropriate sign in front (Table 2, section a). The stability analysis by resampling the model developed for the probability of survival in severe trauma, the bootstrapping method (per 1000 samples), showed that the coefficients are stable, the argument being their significance, the small amplitude of the confidence intervals and keeping the signs in front of the coefficients. logistics (Table 2, section b).

Considering the mentioned coefficients, the developed model has the following mathematical expression:

$$p = \frac{1}{1+e^{-(-1.496-0.138*\text{valoarea NISS}-1.496*\text{Vârsta}\geq 55+0.869*\text{RTS})}} \text{ (formula 2),}$$

where p – the probability of death in severe trauma;
e (exponent) – constant equal with 2.71828.

The components of the NTRISS score showed the following features. The RTS value, as for TRISS, showed a positive association with the probability of survival (OR = 2,384

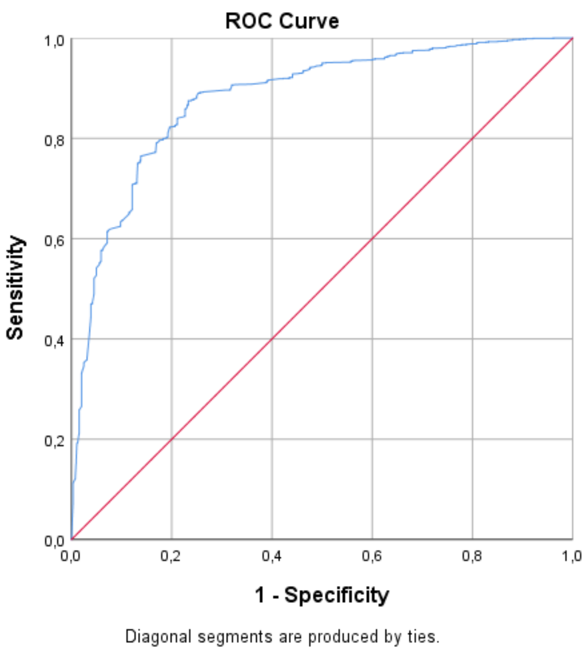

Fig. 4. ROC curve of the predictive model for the predictive model of the probability of survival in patients with severe trauma based on the NTRISS score

Table 2

Variables in the equation from the final predictive model of the probability of survival in patients with severe trauma based on the NTRISS score a. Coefficients in the model

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Age, ≥ 55 years	-1.496	.128	135.845	1	.000	.224	.174	.288
RTS	.869	.064	187.026	1	.000	2.384	2.105	2.700
NISS, points	-.138	.008	308.408	1	.000	.871	.858	.885
Constant	-1.543	.479	10.387	1	.001	.214		

b. Bootstrap resampling results for variables included in the model

	B	Bias	S.E.	Sig.	95% Confidence Interval for B	
					Lower	Upper
Age, ≥ 55 years	-1.496	-.006	.126	.001	-1.770	-1.259
RTS	.869	.006	.070	.001	.742	1.012
NISS, points	-.138	.000	.009	.001	-.157	-.122
Constant	-1.543	-.034	.531	.007	-2.674	-.487

(95% CI 2,105, 2,700)), adjustment to NISS and age showed a tendency to reduce the impact of RTS. The difference with one point changes the prognosis more than 2 times, the confidence interval being narrower than the odds ratio within the TRISS score. At the same time, age used as a predictor in binary form (under or over 55 years) showed a negative association (OR = 0.224 (95% CI 0.174, 0.288)) – is associated with reduced survival about five times. The values of the NISS score, obviously, were negatively correlated with the treatment results (OR = 0.871 (95% CI 0.858, 0.885)), the chance ratio being similar to the value from the univariate analysis performed during the validation.

The ASCOT score, as well as the NTRISS and TRISS scores, showed the ability to predict the outcome of treatment, the null hypothesis being rejected (Omnibus Test of Model Coefficients ($\chi 2$ = 538,483, df = 1, p <0.001).) Subsequent analysis showed the following characteristics of validated model.

The determination indicator, Nagelkerke R Square, showed 0.302 (30.2%). This tells us that almost a third of the dispersion of the variable of interest (survival / death) was explained by the covariates in the validated ASCOT score.

The calibration indicator (Hosmer – Lemeshow test) showed a significant value, $\chi 2$ = 22,353, df = 8, p <0.004 – a calibration indicator that requires optimization, i.e. the score is not as efficient on the full range of possible scores – result characteristic for all mixed models.

The discrimination indicators in the classification table, namely specificity and sensitivity, were equal to 41.6% and 93.5% respectively, the summary (global) percentage being 78.8%. The results were obtained at the critical point 0.5, the optimization by modifying them being inefficient (Fig. 5).

The area under the ROC curve, for the predictive model based on the ASCOT score, was 0.787, with 95% confidence interval (0.766, 0.809) and with a significant difference compared to the value 0.5 (p <0.001) (Fig. 6). The model included the constant (B = -1.249) and the value of the ASCOT score (B = 0.894) (Table 3, section a). The analy-

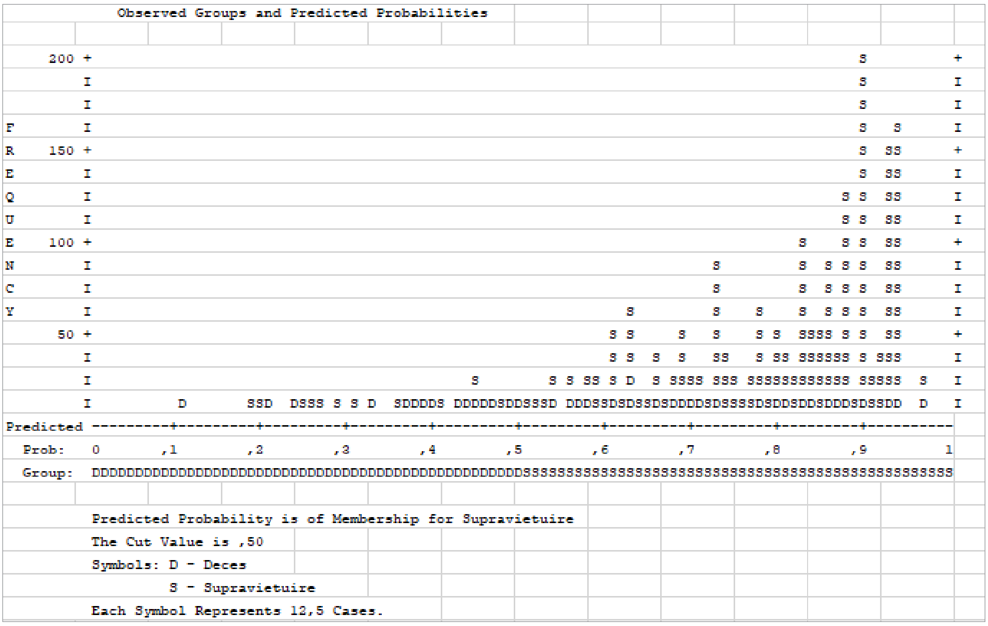

Fig. 5. Classification chart for the predictive model of the probability of survival in patients with severe trauma based on the ASCOT score

sis of the stability of the model elaborated by resampling, the bootstrapping method (1000 samples), showed that the coefficients are stable, the argument being the significance, the small amplitude of the confidence intervals and the keeping of the signs in front of the coefficients in the equation (Table 3, section b).

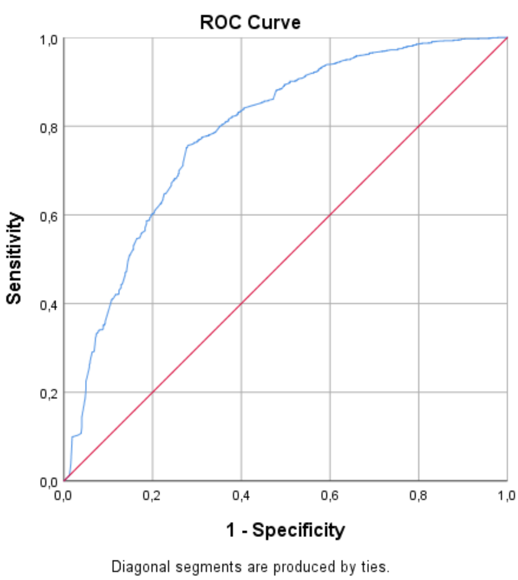

Fig. 6. ROC curve of the predictive model for the predictive model of the probability of survival in patients with severe trauma based on the ASCOT score

Table 3

Variables in the equation from the final predictive model of the probability of survival in patients with severe trauma based on the ASCOT score a. Coefficients in the model

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
ASCOT, points	.894	.046	377.819	1	.000	2.446	2.235	2.677
Constant	-1.249	.119	109.486	1	.000	.287		

b. Bootstrap resampling results for variables included in the model

	B	Bias	S.E.	Sig.	95% Confidence Interval for B	
					Lower	Upper
ASCOT, points	.894	.002	.049	.001	.805	.997
Constant	-1.249	.001	.126	.001	-1.507	-1.008

a. Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Considering the mentioned coefficients, the developed model has the following mathematical expression:

$$p = \frac{1}{1+e^{-(-1.249+0.894*\text{valoarea ASCOT})}} \quad \text{(formula 3)},$$

where p – the probability of death in severe trauma;
e (exponent) – constant equal with 2.71828.

The value of the ASCOT score, having in its composition age, anatomical component and RTS showed a positive association with the probability of survival (OR = 2,446 (95% IC 2,235, 2,677)). The difference with one point changes the practical prognosis 2.5 times, the confidence interval being narrow.

The comparison of the mixed scores included in the research showed that the NTRISS score showed a maximum coefficient of determination (49.6%) compared to TRISS (37.1%) and ASCOT (30.2%), all models having calibration indicators that need improvement, the criteria being the significance of the test. Hosmer – Lemeshow ($\chi2$ = 16,864, df = 8, p = 0.032, $\chi2$ = 61,793, df = 8, p < 0.001 and $\chi2$ = 22,353, df = 8, p < 0.004, respectively). Comparisons of surface values under the ROC curve showed the superiority of the NTRISS score (z = 13,345, p < 0.001 versus TRISS and z = 14,505, p < 0.001 ASCOT score). All this allows to consider NTRISS the optimal score from the list of mixed predictive models, at least from those included in the analysis, which best covers the dispersion of the dependent variable (survival).

Conclusions. In this article, three common mixed predictive models were validated. Of these, NTRISS, consisting of NISS, RTS and age, has a calibration that requires optimization. However, this model showed optimal characteristics in terms of determination / discrimination compared to the validated models and can be considered a reference model (standard) for patients with severe trauma admitted to ICU IMSP IMU. NTRISS can be recommended for implementation and daily use until the development of other alternative models or the validation of other common scores with better characteristics for the studied population.

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