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The validation of New Injury Severity Score for severe and critical trauma patients

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Abstract

Background: Considerable part of traumatized patients has criteria for severe/critical trauma. There is no international consensus concerning the most accurate traumatic scores. Their utilization in Moldova requires optimization. This article's goal is to validate the predictive ability of New Injury Severity Score (NISS) in sever/critical trauma patients admitted in Moldovan trauma center.
Material and methods: The retrospective cohort study, trauma patients (n=476) were admitted to Intensive Care Unit (ICU). The cohort was divided into severe (NISS > 15) and critical (NISS > 24) traumas. To achieve the aim, the multivariate logistic regression was used. The results were adjusted to gender, age and the mechanical ventilation use.
Results: Severe trauma model had an acceptable determination coefficient (Nagelkerke R Square=0.541). The calibration was poor (Hosmer-Lemeshow test, χ^2=17.430, df=8, p=0.026). The discrimination parameters, sensibility and specificity, were 85.9% and 85.1%. The determination coefficient for critical trauma model was 0.568, the calibration ability being normal (χ^2=7.249, df=8, p=0.510). The sensibility and specificity were 70.9% and 94.7%, respectively.
Conclusions: In this study, were proposed two mathematical models that validated NISS as an instrument to predict the outcomes in sever/critical trauma patients admitted in Moldovan trauma center. In general, the model's characteristics (determination, calibration and discrimination) could be appreciated as good ones with some limitations. Taking into account the advantages and disadvantages, both models could be recommended for daily practice usage in condition of ICU from Emergency Medicine Institute.
Key words: new injury severity score, severe trauma, critical trauma, score validation.

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Introduction

Trauma remains medical, social and economic problem being the main worldwide cause of death for the patients younger than 40 years [1]. In addition, while the death rate from oncological and cardiac diseases has favorable trend, the death rate from trauma is rising faster than the parallel population increase. This is a sign that, in the long perspectives, probably, the trauma will prevail in general lethality structure [2].

The trauma structure analysis has shown that considerable part of traumatized patients, almost 40%, has criteria for severe or critical trauma. These two categories of trauma require treatment in the intensive care unit (ICU) department considering the increased risk of complications and death. The trauma completes condition for severe if NISS (New Injury Severity Score) > 15, and when NISS > 24, the trauma is classified as critical [3, 4]. Taking into account the risks, it is crucial to estimate the trauma's lesions severity. Unfortunately, today, there is no international consensus on what kind of scores or algorithms of trauma assessment are optimal. As a consequence, different medical systems use different scores [5, 6], considering particularities of these systems, of demographic structure or sometimes geographical factors [7].

The rational (optimal) utilization of the traumatic scores in the Republic of Moldova remains a serious problem. Because of that, at the patient's evaluation there are some disagreements on the prediction, different scores often estimating the outcomes completely different. According to the open resources at least, RTS (Revised Trauma Score), AIS (Abbreviated Injury Score) and ISS (Injury Severity Score) algorithms have been used, all these models having no any statistical validation [8]. The same statement is avai-lable for Acute Physiology, Age, Chronic Health Evaluation II score (APACHE II), used by the anesthesiologists to predict mortality rate for critical patients in ICU condition [9] and A Severity Characterization of Trauma (ASCOT) used for patients with associated trauma and Traumatic Brain Injury (TBI) lesions [10]. There are only two validated trauma scores. Both, the MPMoIII (Mortality Probability Admission Model) and NISS were tested for survival prediction in severe trauma patients (criteria being NISS > 15) transferred from regional hospitals to Emergency Medicine Institute (EMI). These models were used in a pilot research with relatively reduced number of respondents and, of course, the accuracy of coefficient needs improvement, results being extrapolated on the specific category of trauma patients and as a result cannot be used for patients admitted directly in EMI [11].

The described problems need solution. This can be done using the strategy, described above [12]. It is based on three main elements – revision of potential models, their adaptation or alternative model/models ela-boration and, finally, comparative evaluation. The first element was performed and the main existing trauma scoring systems were revised to highlight the potential scoring systems that in perspective can be validated in the Moldovan medical system. Totally, we have analyzed 33 potential mo-dels divided into three main groups: anatomical, physiological and mixed.

In this list of scores for trauma patient evaluation, the ISS and NISS, mentioned above, derivate from AIS, are the most popular anatomical scores being widely used in different medical systems. To estimate ISS, we have to use the following formula: $ISS = AIS_1^2 + AIS_2^2 + AIS_3^2$, where AIS_1, AIS_2, AIS_3 are the highest AIS values present in six topographic regions [5]. NISS in comparison with ISS, estimates trauma severity taking into account three maximal values of AIS, without taking into account the lesion's localization [6]. For example, in case of trauma when $AIS_{abdomen} = 2$, $AIS_{head\ and\ neck} = 3$, $AIS_{head\ and\ neck} = 3$ and $AIS_{limbs} = 5$, the NISS value will be higher ($NISS=5^2 + 3^2 + 3^2 = 43$) in comparison with ISS ($ISS=5^2 + 3^2 + 2^2 = 38$). Both, the ISS and NISS can vary from 0 up to 75. In condition if there is a topographical region with AIS = 6, ISS or NISS automatically is considered equal to 75. A meta-analysis shows similar sensibility and specificity of NISS and ISS mortality prediction in trauma patients [13]. We suppose that this result can be explained by insufficient determination coefficient in equations that use NISS or ISS. At the same time, there are data that the NISS is more precise, especially for patients with multiple injuries [14].

This article's goal is to validate the NISS as an instrument to predict the outcomes in sever/critical trauma patients admitted in Moldovan trauma center in order to use it for survival prediction. The validation has two elements – the confirmation of predictive power and adaptation of NISS regression coefficients for sever and critical trauma patients admitted in ICU, EMI of Chisinau, the Republic of Moldova.

Material and methods

The retrospective cohort study was performed. The injured patients (n = 467) were admitted in acute trauma period (the first 72 hours after impact) to ICU of EMI, Chisinau, the Republic of Moldova. The severity of lesions was appreciated using the NISS (AIS 2015), criteria for severe trauma being the value over the 15 points (n = 467 patients), the cut-off for critical trauma was considered the NISS value over the 24 points (n = 225 patients). Taking into account particularities related to the patients with mental disorders (psychoses) as the reason for admission to ICU, these ones were not considered in this research.

Statistical analysis

Descriptive statistics had the following components. The continuous data were represented using the central tendency indicators (mean, median) and dispersion parameters (standard deviation, interquartile range). To describe the dichotomous data have been used the frequencies and proportions. To analyze the precision of obtained data the 95% confidence intervals were estimated. To achieve the aim of this research, taking into account that the outcome (death/survival) depends on a variety of factors and it represents a dichotomous variable, the multivariate logistic regression procedure was used. The results were adjusted to gender, age and the mechanical ventilation (MV) use. In order to match the regression analysis conditions the data was tested for multicollinearity. The potential model was characterized using determination (*Nagelkerke R Square*), calibration (*Hosmer-Lemeshow test*) and discrimination (*sensibility, specificity, mean validation, ROC curve and classification graph, cut-off* modification) parameters. In addition, the proposed models stability analysis was performed (resampling using *bootstrapping*). According to literature data, we expected better discrimination and calibration in critical vs severe trauma patients [4].

Results

According to the table 1 data, becomes evident the prevalence of males in both cohorts, the proportion being similar (70.2% for severe and 72% for critical trauma, 95% CI having approximately the same range, 65.9, 74.2 and 65.8, 77.5, respectively). Similar affirmation is valid for age variable (median 43 vs 44, interquartile range being 26 and 24, respectively for severe and critical trauma).

Intrahospital lethality was estimated at level 13.7% (CI 95% 10.9, 17.1) and 24.4% (CI 95% 19.3, 30.5), evidently predominating in critical trauma patients. It is important to mention that CI 95% are not large and there is no any intersection between them. This is a sign for significant differences in outcomes for these two cohorts and the lethality in critical trauma is twice higher (OR=2.04, CI 95% 1.36, 3.05).

The NISS variable, without any doubts, is significantly higher in critical trauma patients (mean=43, 95% CI 40.8, 45.2 for critical and mean=26.6, 95% CI 25.6, 27.6 for severe trauma patients). Regarding MV, it can be concluded that, in condition of critical trauma, the proportion of alternative approach is similar with traditional one that is not characteristic for severe trauma patients (39% vs 61%), (tab. 1).

The predictive model for primary outcome (death/survival) in severe trauma

First, for the patients that meet criteria for severe trauma, were formulated the hypotheses as follows. *The null hypothesis* – the covariates included in the model (gender, age, NISS, MV) are not able to predict the death's probability in severe trauma patients better than a model that includes only the constant. *The alternative hypothesis* – at least one variable is able to predict the death's probability in severe trauma patients better than a model that includes only the constant.

Table 1

Descriptive statistics for severe (a) and critical (b) trauma patients

		Mean (Standard Deviation)/ Count (%)	95% Confident interval Lower limit, Upper limit	Median (Interquartile Range)
a. Severe trauma patients (NISS > 15)				
Gender	**Female**	139 (29.8%)	25.8, 34	
	Male	328 (70.2%)	65.9, 74.2	
Age, years		42 (17)	40.5, 43.5	42 (26)
NISS, points		26.6 (11.5)	25.6, 27.6	23 (15)
Mechanical ventilation	**Traditional**	285 (61%)	56.5, 65.3	
	Prophylactical	182 (39%)	34.7, 43.5	
Outcome	**Survival**	403 (86.3%)	82.9, 89.1	
	Death	64 (13.7%)	10.9, 17.1	
b.	**Critical trauma patients (NISS > 24)**			
Gender	**Female**	63 (28%)	22.5, 34.2	
	Male	162 (72%)	65.8, 77.5	
Age, years		43 (17)	40.8, 45.2	44 (24)
NISS, points		36 (10)	34.7, 37.3	34 (14)
Mechanical ventilation	**Traditional**	117 (52%)	45.5, 58.5	
	Prophylactical	108 (48%)	41.6, 54.5	
Outcome	**Survival**	170 (75.6%)	69.5, 80.7	
	Death	55 (24.4%)	19.3, 30.5	

The null hypothesis was rejected (*Omnibus Test of Model Coefficients* (χ^2 = 165.044, df=3, p<0.001, significance being 0.05/2 = 0.025) that means that at least one variable is able to predict the outcome, the elaborated model having the following characteristics. Determination coefficient, *Nagelkerke R Square* = 0.541 (54.1%). This result can be considered as acceptable one, but anyway it can be improved. The calibration ability was poor, *Hosmer-Lemeshow test* being significant (χ^2 = 17.430, df=8, p=0.026). The discrimination parameters, sensibility and specificity, according to the classification table, were 85.9% (55 dead patients out of 64) and 85.1% (343 survived patients out of 403), respectively, overall percentage being estimated at 85.2% (cut-off=0.13, fig. 1). Analysis of classification graph can reveal the overfitting problem.

Area under the Receiver Operating Characteristics

```
             Observed Groups and Predicted Probabilities

     160 +                                                                                                    +
         I                                                                                                    I
         I                                                                                                    I
F        I                                                                                                    I
R    120 +                                                                                                    +
E        IS                                                                                                   I
Q        IS                                                                                                   I
U        IS                                                                                                   I
E     80 +S                                                                                                   +
N        IS                                                                                                   I
C        ISS                                                                                                  I
Y        ISSS                                                                                                 I
      40 +SSS                                                                                                 +
         ISSSS                                                                                                I
         ISSSSSS                                                                                              I
         ISSSSSSSSSSSS D      D                                                                               I
Predicted ---------+---------+---------+---------+---------+---------+---------+---------+---------+----------
  Prob:   0       ,1        ,2        ,3        ,4        ,5        ,6        ,7        ,8        ,9         1
  Group:  SSSSSSSSSSSSSDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDD

          Predicted Probability in the quantity of dead
          The Cut-off Value is ,13
          Symbols: S - Survival
                   D - Dead
          Each Symbol Represents 10 Cases.
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Fig. 1. Classification graph for severe trauma prediction model.

Table 2

Variables in equation of severe trauma. Initial model (a), final model (b) and after resampling (c)

a. Model before the Gender elimination

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Gender	.062	.406	.023	1	.879	1.064	.480	2.357
Age, years	.050	.012	18.441	1	.000	1.052	1.028	1.076
NISS, points	.156	.018	76.982	1	.000	1.169	1.129	1.210
MV	-1.335	.432	9.533	1	.002	.263	.113	.614
Constant	-8.807	1.021	74.443	1	.000	.000		

Variable(s) entered on step 1: NISS, Age, MV, Gender

b. Model after the Gender elimination (final model)

	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Age, years	.050	.012	18.677	1	.000	1.051	1.028	1.075
NISS, points	.156	.018	77.132	1	.000	1.169	1.129	1.210
MV	-1.328	.430	9.549	1	.002	.265	.114	.615
Constant	-8.755	.960	83.249	1	.000	.000		

Variable(s) entered on step 2: NISS, Age, MV

c. Bootstrap for Variables in the Equation

	B	Bias	S.E.	Sig.	95% Confidence Interval for B	
					Lower	Upper
Age, years	.050	.002	.012	.001	.029	.078
NISS, points	.156	.005	.021	.001	.124	.206
MV	-1.328	-.056	.488	.004	-2.440	-.489
Constant	-8.755	-.278	1.038	.001	-11.364	-7.226

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

(ROC) curve for severe trauma model was estimated at 0.907 (95%CI 0.862, 0.952) being significant compared with 0.5 value (p<0.001), (fig. 2).

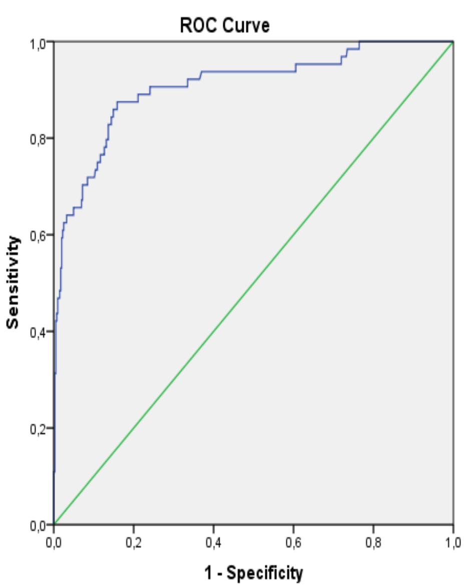

Fig. 2. ROC curve for severe trauma patients mortality predictive model.

Taking into account the data from table 2, the proposed (final) predictive model has the following formula:

$p = 1/(1+e^{8.775 - NISS * 0.156 - Age * 0.05 + MV * 1.335})$ (formula 1),

where

p – probability of death in severe trauma

e (exponent) – constant equal to 2.71828

The final model includes the constant (B = -8.755), NISS (B = 0.156), Age (B =0.050) and MV (B = -.1.335) as efficient variables. Gender did not achieve the significance (p=.879). Moreover, after the elimination of this variable (tab. 2a and tab. 2b), the regression's coefficient, the Odds Ratio (OR) and the confidence intervals were without significant changes.

According to the obtained data, the most important covariate was NISS (determination coefficient .424), followed by Age (approximately 9%) and MV (3%). The quantitative expression of positive relationships of NISS and Age on the one hand and the primary outcome on the other hand (positive regression coefficients and OR more than 1, confident intervals being relatively narrow) allows to modulate different situations as follows. For example, if in ICU, we meet two similar patients according to NISS and MV criteria, having only one year age difference, the death probability is 5% higher (95% CI 2.8. 7.5) for the older patient. In the same way, the only one NISS point difference can increase

```
             Observed Groups and Predicted Probabilities

      32 +                                                                                                     +
         I                                                                                                     I
         I                                                                                                     I
F        I                                                                                                     I
R     24 +                                                                                                     +
E        I S                                                                                                   I
Q        I SS                                                                                                  I
U        IDSS                                                                                                  I
E     16 +SSS                                                                                                  +
N        ISSS D                                                                                                I
C        ISSSSS                                                                                                I
Y        ISSSSS                                                                                                I
       8 +SSSSSSSSD                                                                                            +
         ISSSSSSSSSS          D                                                                                I
         ISSSSSSSSSSSD SDS S  DD        S                                D                    D          D D  I
         ISSSSSSSSSSSSSSSSSSSSSSSS SS SSSSS S S SSS SD SSDD S  DS S  SDD S D  D    D S D   DSDD D  DDDDDDS D DI
Predicted ---------+---------+---------+---------+---------+---------+---------+---------+---------+----------
  Prob:   0        ,1        ,2        ,3        ,4        ,5        ,6        ,7        ,8        ,9        1
  Group:  SSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDD

          Predicted Probability in the quantity of dead
          The Cut-off Value is ,47
          Symbols: S - Survival
                   D - Dead
          Each Symbol Represents 10 Cases.
```

Fig. 3. Classification graph for critical trauma prediction model.

the probability of death by 16.9% (95% CI 12.9, 21).

The resampling (bootstrapping, 1000 samples) was used to prove the elaborated model's stability. All parameters were significant, regression coefficients having narrow 95% confidence intervals, these two conditions serving as arguments to consider this model as a stable one (tab. 2c).

Table 3

Variables in equation for critical trauma.
Initial model (a), final model (b) and after resampling (c)

a. Model before the Gender elimination

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Gender	-.065	.483	.018	1	.893	.937	.364	2.414
Age, years	.045	.014	10.526	1	.001	1.046	1.018	1.075
NISS, points	.180	.026	48.722	1	.000	1.197	1.138	1.259
MV	-1.448	.487	8.828	1	.003	.235	.090	.611
Constant	-9.517	1.420	44.940	1	.000	.000		
Variable(s) entered on step 1: NISS, Age, MV, Gender								
b. Model after the Gender elimination (final model)								
Age, years	.046	.014	10.700	1	.001	1.047	1.018	1.075
NISS, points	.180	.026	48.667	1	.000	1.197	1.138	1.260
MV	-1.457	.484	9.068	1	.003	.233	.090	.601
Constant	-9.572	1.363	49.321	1	.000	.000		
Variable(s) entered on step 2: NISS, Age, MV								

d. Bootstrap for Variables in the Equation

	B	Bias	S.E.	Sig.	95% Confidence Interval for B	
					Lower	Upper
Age, years	.046	.001	.015	.002	.019	.082
NISS, points	.180	.009	.032	.001	.134	.258
MV	-1.457	-.094	.565	.003	-2.710	-.553
Constant	-9.572	-.403	1.552	.001	-13.605	-7.578
Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples						

The predictive model for primary outcome (death/survival) in critical trauma

As in condition of severe trauma, for critical trauma patients, were formulated the following hypotheses. *The null hypothesis* – the covariates included in the model (gender, age, NISS, MV) are not able to predict the death's probability in critical trauma patients better than a model that includes only the constant. *The alternative hypothesis* – at least one variable is able to predict the death's probability in critical trauma patients better than a model that includes only the constant.

The null hypothesis was rejected (*Omnibus Test of Model Coefficients* (χ^2 = 107.889, df = 3, p<0.001, significance being 0.05/2 = 0.025) that means that at least one variable is able to predict the probability of death in critical trauma patients. Determination coefficient, *Nagelkerke R Square*, was estimated at 0.568 (56.8%) vs 0.541 (54.1%) in severe trauma. This result can be considered as acceptable but needs improvement. The calibration ability (fidelity results evaluation) was normal, *Hosmer-Lemeshow test* being nonsignificant (χ^2 = 7.249, df = 8, p = 0.510). The discrimination parameters, sensibility and specificity, according to the classification table were 70.9% (39 dead patients out of 55) and 94.7% (161 survived patients out of 170), respectively, overall percentage being estimated at 88.9% (cut-off = 0.47, fig. 3).

Area under the ROC curve for critical trauma model was estimated at 0.905 (95% CI 0.856, 0.954) being significant vs 0.5 value (p<0.001), (fig. 4).

Taking into account the data from table 3, the proposed (final) predictive model for death prediction in critical trauma patient can be converted into the following formula:

$p = 1/(1+e^{9.572 - NISS * 0.180 - Age * 0.46 + MV * 1.457})$ (formula 2), where

p – probability of death in sever trauma

e (exponenta) – constant equal to 2.71828

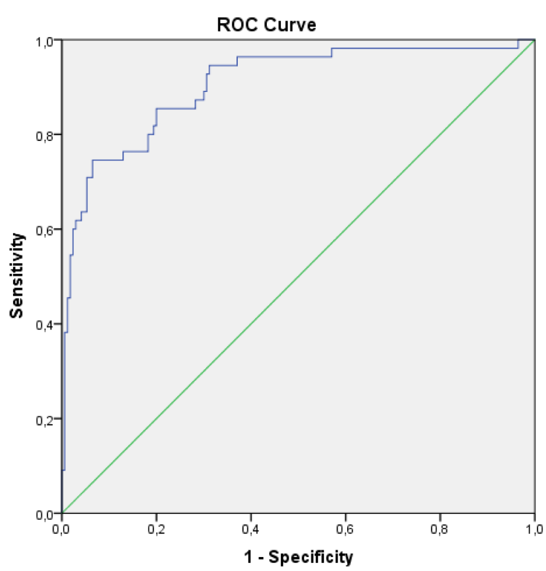

Fig. 4. ROC curve for critical trauma patients mortality predictive model.

The final model includes the constant (B = -9.572), NISS (B = 0.180), Age (B = 0.046) and MV (B = -.1.448) as significant variables, Gender being far from significance range (p = 0.893) without any effects on the regression coefficients, the OR or the confidence intervals (tab. 3a and tab. 3b) as it was mentioned in severe trauma model.

The most powerful covariate (NISS) was able to determine 43.6% of variable dispersion, a result similar with the determination coefficient values of NISS in severe trauma. The effect of Age was estimated at level of 9%, MV having 4.3% instead of 3%.

The resampling (bootstrapping) has shown stability; coefficients having significance and narrow 95% confidence intervals (tab. 3c).

Discussion

In this study, were proposed two mathematical models that validated NISS as an instrument to predict the outcomes in sever/critical trauma patients admitted in Moldovan trauma center in order to use it for survival prediction. The validation of trauma scoring scales for different medical systems prior to their practical use represents an efficient instrument with a worldwide use, net result of this process being the regression coefficients correction and optimization [3, 14, 15, 16].

The predictive potential of NISS was proven for both, critical and severe trauma patients. In addition, NISS regression coefficient was adapted to particularities of Moldovan medical system and adjusted to Age and MV strategy. The Gender variable was not significant in both trauma groups, being independent in relation to other variables. The NISS and Age covariates have shown negative effects, having relatively narrow confidence intervals. The MV has had the opposite effect with relatively large confidence intervals.

Taking into account the model's characteristics, logistic regression classified them as significantly better models than aleatory ones. In general, the determination, calibration and discrimination model's parameters could be appreciated as good ones with some following limitations.

Firstly, the research is retrospective that is why there could not be considered all risk factors and potential biomarkers that reduce the evidence level. The perspective group of potential predictors consists of components of proteases/antiproteases system. Among them are cathepsin D and a_2-macroglobulin that have shown their potential to predict the survival rate and Acute Respiratory Distress Syndrome in polytrauma patients [17, 18]. Secondly, evidently, it is not possible to extrapolate the results for all Moldovan medical system hospitals. Thirdly, both models explained less than 60% of dependent variable dispersion, optimal value being over 80%. This fact makes us think that they should be added some other efficient variables that could improve the accuracy of prediction. Fourthly, the poor calibration and potential overfitting for severe trauma model could demand precaution in practical use, other parameters being close to the optimal value [4].

In addition, it is important to mention the reduced NISS determination coefficient values for severe trauma (.424) and critical trauma (.436) vs severe trauma patients transported from regional hospitals (.641) [11]. These differences, about .2 (20%) from dispersion of dependent variable, can be considered as a benefit for patients admitted directly in trauma center because of conversion of the nonchangeable factor (trauma injuries) into potentially changeable. Increasing the ratio of the last one gives us more opportunities to influence the outcomes in order to improve them.

Conclusions

Taking into account the advantages and listed above disadvantages, both models could be recommended for daily practice usage in ICU. The arguments against these models are that they were elaborated for this particular trauma group and do not have alternative validated scores. Also, being incorporated in hospital's informational system the models could be improved in real time by adding the potential efficient variables. In addition, the model's accuracy could be raised by including new severe and critical trauma cases data.

The obtained results determine us to continue the researches in this field. Taking into consideration the experience of this study, the perspective for completely elaborated models is opening, to validate other potential models and to elaborate new scores able to predict the trauma patient's outcomes.

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Ethics approval and consent to participate
The research project was approved by Ethics Committee of *Nicolae Testemitanu* State University of Medicine and Pharmacy (Protocol No 46, 16.12.2016).

Conflict of Interests
No competing interests were disclosed.