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Survival predictive models in severe trauma patients' transportation within Moldovan medical system

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Abstract

Background: Trauma remains an unresolved medical problem and its severity often requires the transfer of patients to specialized trauma institutions (centers). The elaboration of the predictive models represents an effective tool for improving the prognosis of the transported patients by optimizing the management of the trauma and/or improving the national interhospital transfer system. The survival probability predictive models in severe trauma were proposed in this pilot research.

Material and methods: Data were collected from 39 patients with severe trauma (NISS > 15) transported to the Emergency Medicine Institute (EMI), Chisinau, the Republic of Moldova, from district hospitals. These data were statistically processed using multivariate logistic regression where NISS, MPMoIII, age and biological gender were considered as covariates.

Results: There were developed three predictive models: based on the estimation of anatomical lesions (NISS), based on physiologic parameters estimation and conditions during/immediately after hospital admission (MPMoIII) and their combination (NISS + MPMoIII). The last of these showed significance only after the resampling, the characteristics of the model being superior (the coefficient of determination over 0.8, the sensitivity and the specificity over 80%) compared to the first two taken separately. Age and biological gender were insignificant and were not included in the equations.

Conclusions: Developed models are perspective (especially a combined one) in predicting survival rate of severe trauma patients transported to EMI from district hospitals. At the same time, taking into account the particularities and limitations related to the pilot study, the models can be recommended for use in clinical practice after validation procedure only.

Key words: severe trauma, predictive models, interhospital transportation.

Introduction

Trauma remains an unresolved medical problem. According to data from the literature, traumatic lesions occupy the third place in the overall structure of the lethality and are the first cause of death in the category of patients between the ages of 1 and 44 years [1]. The mentioned trends are also characteristic for the Republic of Moldova. According to the data of the National Management Center of the National Agency of Public Health for the period 2008-2017, traumas are placed on the fourth place, constituting 8.1% (36889 cases) of all the death cases registered after the diseases of the circulatory system (61%, 226195 of cases), tumors (15.8%, 58518 cases) and diseases of the digestive system (10%, 36889 cases). The analysis of the lethality structure by age shows that in the first year of life the traumas are placed second (30.3%) after the diseases of the respiratory system (57.9%). Subsequently, as the age progresses, the rate of deaths caused by trauma increases and reaches maximum values at 18 years (81.3%), after which it is decreasing, predominating until the age of 45 years (27.2%) compared to other causes of death, continuing to decrease to zero at old age [2].

Often, patients with trauma are admitted to a medical institution and subsequently, for different reasons, require transfer to the trauma center, sometimes being in a serious or critical condition during transfer. On the one hand, transporting patients from one institution to another represents an increased risk for complications and even death. On the other hand, the transfer of patients to specialized institutions has benefic effects for patients. But, unfortunately, currently for patients with severe trauma are not unanimously accepted criteria for the need, the right time, and the mode of transport between two medical institutions [3, 4, 5].

One of the criteria to determine the tactics for transferring to a specialized institution is to determine the severity of the injuries and the prognosis of the patient's condition. These are crucial for trauma management. Currently, two approaches need to be considered in order to mark patients at high risk of complications, including death. The first is the use of terms such as "severe trauma", "major trauma" and "polytrauma". The analysis of the number of records / documents in the Web of Science database in 2016 highlighted 24441, 19471 and 2813 records for these notions, respectively. The terms "severe trauma" and "major trauma" are very close, interchangeable, but the criteria are not well established, the critical value of ISS (Injury Severity Score) or NISS (New Injury Severity Score) varies in different studies at the level of 16-17 points [6, 7, 8]. Polytrauma is one of the most complicated and unexplored categories of trauma, being a restricted notion compared to severe trauma or major trauma. According to the Berlin definition, polytrauma is defined as lesion of at least two regions of the body, assessed by AIS (Abbreviated Injury Scale) with score ≥ 3 and presence of at least one of the 5 physiological parameters (systolic pressure ≤ 90 mmHg, GCS ≤ 8, acidosis, coagulopathy and age ≥70 years [9]. This approach has as a disadvantage – the lack of the possibility of individualizing the management of a patient with traumatic lesions arising from the particularities of their evolution, the circumstances of the trauma, etc. As a result, the most severe patients within each group cannot be identified and there are no indications of the probability of survival/death, of developing complications, which of the parameters/variables are effective in determining the treatment results, which of the examined factors would have the greatest influence, which of the patients requires admission in Intensive Care Unit or how rational it is to benefit from a procedure, etc.

Another approach – the use of traumatic scores (NISS, ISS, MPMoIII, ASCOT, TRISS etc.) as well as the development of predictive models, which represent effective tools for solving the mentioned disadvantages. Thus, the predictive models have a potential for improving the prognosis of the transported patients by optimizing the management and/or by improving the interhospital transfer system in the Republic of Moldova [3].

In the pilot research, three predictive models have been proposed and analyzed for estimating the survival probability of patients with severe trauma, transferred from the district hospitals to the EMI through the AVIASAN service.

Material and methods

Analyzing the observation data of the patients admitted to the EMI for 2012, a retrospective pilot study was performed. The study included 39 severely traumatized patients transferred through the AVIASAN service from district hospitals to EMI by the reanimatologic team. The criteria used for severe trauma was the NISS score greater than 15 points [10].

The research project was approved by the ethics committee of the Nicolae Testemitsanu State University of Medicine and Pharmacy.

The elaboration of the predictive models was carried out by the logistic regression analysis, taking into consideration the recommendations for the multivariate analysis. The minimum number of respondents was estimated by the ratio 1:10 (for each covariate included in the model at least 10 respondents) [11].

In addition to NISS, for the determination of patient status, the MPMoIII (Mortality Probability Admission Model) score was used [12]. The age and gender of the respondents were also taken into account. Specifically, these four skills were considered as effective maintenance variables in the predictive models of survival rate for transferred severe trauma patients. Considering the relatively small number of respondents for the mixed model, the resampling was performed by bootstrapping.

Results

Age of the studied group varied from 20 to 74 years (Median 45, interquartile range 32), from which 30 were males evaluated with NISS 16-66 (Median 48, interquartile range10), MPMoIII variated between 17.1 and 91.2 (Median 73.8, interquartile range19) upon admission to IMSP IMU.

Totally, three models were developed: a model based on anatomical lesions (NISS), another model based on the physiological parameters and some patient parameters during/immediately after admission to the hospital (MPMoIII) and the third, mixed one (NISS + MPMoIII), results being adjusted to the age and gender only in the case of the NISS score. Age and biological gender were insignificant and were not included in the final equations.

Model based on the estimation of anatomical lesions (NISS)

For the NISS-based model, the following hypotheses were formulated: *The null hypothesis* - the covariates included in the model cannot predict the probability of survival in severely traumatized transported patients better than a model that is based only on constant. *Alternative hypothesis* – at least a variable can predict the probability of survival in patients with severe trauma better than a model that is based only on constant.

The model presented the following characteristics. *Omnibus Test of Model Coefficients* ($\chi 2$ (df=1) = 23.05 p<0.001). The test was a significant one, which allowed us to reject the null hypothesis and to analyze further, which of the studied covariates is relevant for predicting survival rate in severe trauma. The coefficient of determination, *Nagelkerke R Square*, was estimated at 0.641 (64.1%), which tells us that the variables included in the model (NISS) determine about 2/3 of the dispersion of the examined variable (probability of occurrence of an event). *The Hosmer-Lemeshow test*, ana-

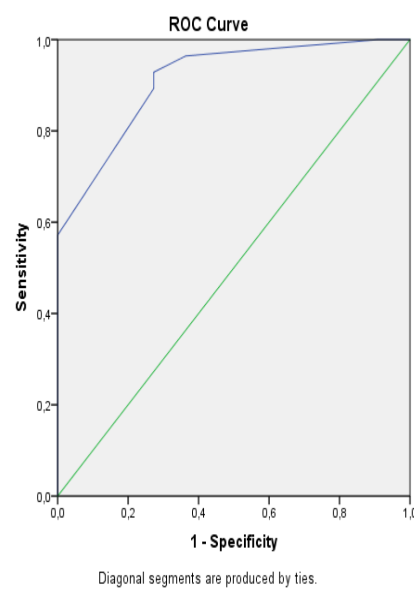

Fig. 1. The ROC curve of the predictive model for the probability of survival in patients transported with severe trauma. SPSS 22 Output.

Table 1

Variables in the equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
NISS	-.369	.128	8.255	1	.004	.692	.538	.889
Constant	18.983	6.405	8.783	1	.003			

Note: Constant – the value of the equation constant; B – the coefficients B; S.E. – standard errors; Wald – Wald statistic; df – degrees of freedom; Sig. – significance threshold; Exp (B) – values for odds ratio; 95% C.I. for EXP (B) – confidence interval for odds ratio.

lyzing the model in terms of the ability to predict positive and negative results, presents the result as insignificant ($\chi2$ (df = 6) = .332, p = 0.999), which tells us about the increased fidelity of the obtained results. The classification table highlighted a *sensitivity* of 96.4% (27 cases out of 28), the *specificity* being 63.6% (7 out of 11 cases), the average validation appreciated at the level of 87.2%.

The surface under the ROC curve, for the proposed model, was 0.912, with 95% confidence interval (0.819, 1.000) and with a significant difference from the value 0.5 (p <0.001) (fig. 1). Thus, the logistic regression classified the model as significantly better model than the random model.

The model includes the constant (B = 18.983) and the NISS values (B = - 369) (tab. 1). NISS is a predictor for survival of patients with severe trauma, OR (odds ratio) = .692 (95% CI, .538, .889). If the NISS value increases by one point, the probability of survival will decrease by approximately 30% (tab. 1). Age and biological gender showed no significance. The analysis of the classification graph (fig. 2) did not reveal possibilities for improving the specificity.

The model based on the estimation of physiological parameters and indicators during/immediately after hospital admission (MPMoIII)

The following hypotheses were formulated. *The null hypothesis* – the covariates included in the model cannot predict the probability of survival in transported severely traumatized patients better than a model that is based only on constant. *Alternative hypothesis* – at least a variable can predict the probability of survival in patients with severe trauma better than a model that is based only on constant.

The model presented the following features. After performing the *Omnibus Test of Model Coefficients* ($\chi2$ (df = 1) = 17.094 p <0.001) The null hypothesis was rejected. The coefficient of determination, *Nagelkerke R Square* = 0.51 (51%) was reduced from the model based on anatomical lesions. The fidelity of the results was confirmed by performing the *Hosmer-Lemeshow test*, ($\chi2$ (df = 7) = 3.338, p = 0.847). The classification table shows a *sensitivity* of 89.3% (25 cases out of 28), the *specificity* being 72% (8 out of 11 cases), the average validation appreciated at the level of 84.6%.

The surface under the ROC curve, for the proposed model, was 0.878, with 95% confidence interval (0.773, 0.983) and with a significant difference from the value 0.5 (p <0.001) (fig. 3). Thus, the logistic regression classified the model developed as significantly better model than the random model.

The model includes the constant (B = 14.385) and the values of MPMoIII (B= -.178) (tab. 2). MPMoIII is a predictor with OR = .837 (CI95% .735, .954), that means that if the value of MPMoIII increases by one point, the probability of survival decreases to almost 16% (tab. 2). Age and biological gender are the components of the score and were included in the model.

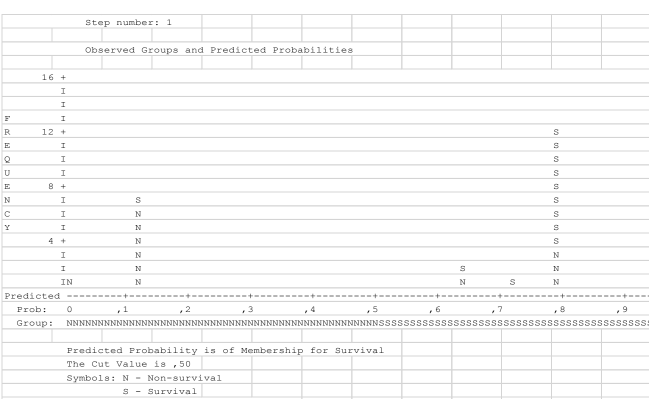

Fig. 2. The classification chart for the NISS model (N – non-survived, S – survived).

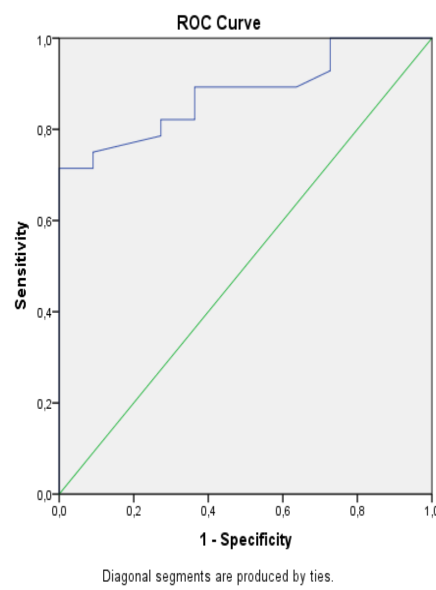

Fig. 3. The ROC curve of the predictive model for the probability of survival in transported patients with severe trauma. SPSS 22 Output.

Table 2

Variables in the equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
MPMoIII	-.178	.067	7.144	1	.008	.837	.735	.954
Constant	14.385	5.272	7.445	1	.006			

Note: Constant – the value of the equation constant; B – the coefficients B; S.E. – standard errors, Wald – Wald statistic; df – degrees of freedom; Sig. – significance threshold; Exp (B) – values for odds ratio; 95% C.I. for EXP (B) – confidence interval for odds ratio.

The analysis of the classification graph (fig. 4) highlights the possibility of improving the specificity (increasing of the cut-off to .62 instead 0.5), but due to the fact that the results are not stable (standard error of MPMoIII coefficient had more than 30% of B), there is a chance of not highlighting the survivors (*overfitting*).

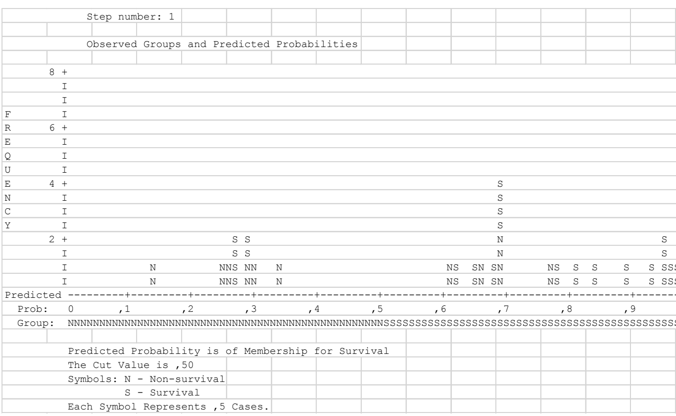

Fig. 4. The classification chart for the model MPMoIII (N – non-survived, S – survived).

The mixed model (NISS + MPMoIII)

For the mixed model, the following hypotheses were formulated. *The null hypothesis* – the covariates included in the model cannot predict the probability of survival in transported severely traumatized patients better than a model that is based only on a single constant. *Alternative hypothesis* – at least a variable can predict the probability of survival in patients with severe trauma better than a model that is based only on a single constant.

The Omnibus Test of Model Coefficients ($\chi 2$ (df = 1) = 32.023 p <0.001), being a significant one, allowed us to reject the null hypothesis and to analyze further, which of the studied covariates is relevant. The coefficient of determination, *Nagelkerke R Square* = 0.805 (80.5%), explaining 4/5 of the dispersion of the examined variable (probability of occurrence for an event), reached the optimal level for the prognostic models. The *Hosmer-Lemeshow test*, analyzing the model in terms of the ability to predict positive and negative results, presents the result as insignificant $\chi 2$ (df = 8) = 2.037, p = 0.980 and increased fidelity to the obtained results. The classification table shows a sensitivity of 96.4% (27 out of 28 cases), the specificity being 81.8% (9 out of 11 cases), the average validation appreciated at 94.5%. As with the coefficients of determination, the optimum values were reached.

The surface under the ROC curve, for the proposed model, constituted 0.977, with 95% confidence interval

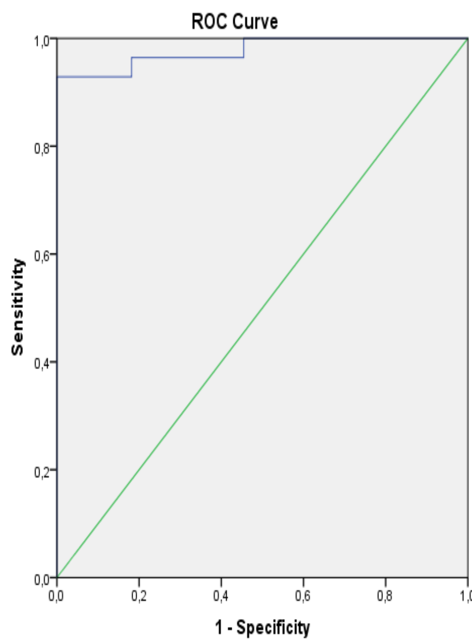

Fig. 5. The ROC curve of the predictive model for the probability of survival in transported patients with severe trauma. SPSS 22 Output.

Table 3

Variables in the equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
MPMoIII	-.331	.202	2.686	1	.101	.718	.484	1.067
NISS	-.400	.175	5.247	1	.022	.670	.476	.944
Constant	46.233	22.835	4.099	1	.043			

Note: Constant – the value of the equation constant; B – the coefficients B; S.E. – standard errors, Wald – Wald statistic; df – degrees of freedom; Sig. – significance threshold; Exp (B) – values for odds ratio; 95% C.I. for EXP (B) – confidence interval for odds ratio.

```
             Step number: 1

             Observed Groups and Predicted Probabilities

       20 +
          I
          I
F         I
R      15 +
E         I
Q         I
U         I
E      10 +
N         I
C         I
Y         I
        5 +N
          IN
          IN            S
          IN            N N         N N                               S           N  N  SSS    S SS
Predicted ---------+---------+---------+---------+---------+---------+---------+---------+---------+------
  Prob:   0        ,1        ,2        ,3        ,4        ,5        ,6        ,7        ,8        ,9
  Group:  NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS

          Predicted Probability is of Membership for Survival
          The Cut Value is ,50
          Symbols: N - Non-survival
                   S - Survival
          Each Symbol Represents 1,25 Cases.
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Fig. 6. Chart of classification for the model MMMIII and NISS (N – non-survived, S – survived).

(0.938, 1.000) and with a significant difference from the value 0.5 (p <0.001) (fig. 5). Thus, the logistic regression classified the model as significantly better model than the random model.

The model includes the constant (B = 46.233), the values of MPMoIII (B = -.331) and NISS (B = -.400). The adjustment of NISS to MPMoIII improved the characteristics of the model (the coefficient of determination, sensitivity and specificity). At the same time, NISS represents an efficient covariate, OR = 0.670 (CI95% .476, .944), MPMoIII being insignificant. OR = .718 (CI95% .484, 1.067) (tab. 3). The resampling by bootstrapping showed the significance of parameter MPMoIII (tab. 4). The analysis of the classification graph (fig. 6) does not reveal possibilities of improving the specificity/sensitivity.

Thus, this model is one of perspective, combining an anatomical score with a physiological one, in order to predict the survival in patients with severe trauma transported to the specialized institution.

Table 4

Resampling by bootstrap (997 samples)

	B	Bias	Std. Error	Sig.	95% C.I. for B	
					Lower	Upper
MPMoIII	-.331	.202	2.686	.004	-40.230	-.166
NISS	-.400	.175	5.247	.005	-47.976	-.202
Constant	46.233	22.835	4.099	.002	29.144	5836.065

Note: Constant – the value of the equation constant; B – the coefficients B; Std. Error – standard errors;
Sig. – significance threshold; 95% C.I. B – confidence interval for the coefficients.

Discussion and conclusions

In our research, three predictive models have been developed for the survival rate of severely traumatized patients transferred from district hospitals to the EMI. The model that includes NISS, an anatomical score, has been proven as relevant, the effect of anatomical lesions for this category of patients being estimated quantitatively by the coefficient of determination, the OR and the coefficient for the logistic regression equation. The coefficient of determination constituted .641 (64.1%), compared to .41 (41%) estimated for traumatized hospitalized directly in the EMI. Thus, it can confirm that interhospital transfer of patients increases the effect of the anatomical lesions on the treatment results (outcomes).

The MPMoIII model also predicted the survival rate of a patient with severe trauma. The coefficient of determination constituted .51 (51%), being close to the NISS effect and confirms the idea that the physiological parameters, as well as some indicators of the patient's condition at the admission to the hospital have a prospective predictive potential. The combination of NISS and MPMoIII in the mixed model increased the coefficient of determination over .80 (80%), a practically ideal value, the sensitivity and specificity also being over 80%. But, the significance for MPMoIII was obtained only by resampling.

Thus, all these models are perspective models (especially the combined model) for predicting survival in severely traumatized patients transported to the EMI from district hospitals.

On the one hand, the proposed models can't be recommended for use in daily practice due to limitations related to the particularities of the pilot study. The most important of them – a small number of respondents was analyzed, which cannot ensure a high level of accuracy of the coefficients in the logistic regression equation (for example in the NISS covariate mixed model it had a coefficient B = -0.400 and a standard error = .175). On the other hand, the models have a potential to be improved by supplementing with efficient variables.

The implementation procedure can't be initiated without obtaining an accuracy of the coefficients (narrow confidence intervals) and validation of the elaborated models, both obtained in studies with higher level of evidence.

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