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Evaluation of independent predictors of in-hospital mortality in patients with severe trauma

Евалуација независних предиктора интрахоспиталног морталитета код пацијената са тешком траумом

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SUMMARY

Introduction/Objective The aim of this study was to determine independent predictors and the best trauma scoring system (REMS, RTS, GSC, SOFA, APPACHE II) of in-hospital mortality in patients with severe trauma at the Department of Emergency, Emergency Center, Clinical Center of Serbia, Belgrade.

Methods Longitudinal study included 208 consecutive patients with severe trauma. In order to determine independent contributors to survival, univariate and multivariate Cox regression analyses were performed. The power of above mentioned scoring systems (measured at admission in the Emergency center) to predict mortality was compared using the area under the curve (AUC).

Results There were 208 patients (159 male, 49 female), with average age of 47.3±20.7 years. Majority of patients were initially intubated (86.1%), at admission to ED, and 59.6% patients were sedated before intubation. After finishing of diagnostic procedures, 17 patients were additionally intubated, and, at that time, 94.2% patients were on mechanic ventilation. The largest proportion of patients was traumatized in car crash (33.2%), followed by falls from the height (26.4%) and as pedestrians (22.6%) Patients had an average of 24.7±21.2 days spent in intensive care unit (ICU). The overall case-fatality ratio was 17/208 (8.2%). In Cox regression analysis only elevated heart rate (HR=1.03, p=0.012) and decreased arterial oxygen saturation (SpO2) (HR=0.91, p=0.033) singled out as independent contributors to in-hospital mortality of patients with severe trauma. REMS (AUC 0.72±0.64) and SOFA (AUC 0.716±0.067) scores were found fair and similar predictor of in-hospital mortality, while APACHE II (AUC 0.614±0.062) and RTS (0.396±0.068) were poor predictors.

Conclusion Results of this study showed important role of REMS, which appears to provide balance between the predictive ability and the practical application, and components of REMS in prediction of outcome in patients with severe trauma and that heart rate and SpO2 are independent predictors of in-hospital mortality.

Keywords: injury; Rapid Emergency Medicine Score; cohort study

САЖЕТАК

Увод/Циљ Циљ ове студије био је одређивање независних предиктора и најбољег траума скоринг система (*REMS*, *RTS*, *GSC*, *SOFA*, *APPACHE* II) интрахоспиталног морталитета код пацијената са тешком траумом, лечених у Ургентном центру Клиничког центра Србије у Београду.

Методе Лонгитудинална студија је укључила 208 консекутивних пацијената са тешком траумом, примљених у Ургентни центар Клиничког центра Србије у Београду. У циљу одређивања независних предиктора преживљавања, урађене су униваријантна и мултиваријантна Коксова регресиона анализа. Такође, утицај система скоровања раније поменутих скорова на пријему у Ургентни центар (УЦ) у предикцији морталитета поређен је коришћењем теста *Area under curve* (*AUC*).

Резултати Испитивани узорак чинило је 208 пацијената (159 мушкараца, 49 жена), просечног узраста 47,3±20,7 година. Већина пацијената била је иницијално интубирана (86,1%), на пријему у УЦ, а 59,6% пацијената било је седирано пре интубације. После завршетка дијагностичких процедура, 17 пацијената је додатно интубирано, тако да је на механичкој вентилацији било 94,2% пацијената. Пацијенти су најчешћи повређивани у саобраћајним несрећама (33,2%), приликом пада са висине (26,4%) и као пешаци (22,6%). Просечна дужина боравка у јединици интензивне неге износила је 24,7±21,2 дана. Леталитет је био 17/208 (8,2%). Коксовом регресионом анализом показано је да су повишена срчана фреквенца (*HR*=1,03, *p*=0,012) и снижена сатурација крви кисеоником (*XP*=0,91, *p*=0,033) независни предиктори смртног исхода пацијената са тешком траумом. *REMS* (*AUC* 0,72±0,64) и *SOFA* (*AUC* 0,716±0,067) показали су сличну предиктивну вредност, док су *APACHE* II (*AUC* 0,614±0,062) и *PTC* (0,396±0,068) били лоши предиктори интрахоспиталног морталитета код пацијената са тешком траумом.

Закључак Резултати студије показали су важну улогу компоненти *REMS* у предикцији исхода пацијената са тешком траумом као и да су срчана фреквенца и сатурација крви кисеоником независни предиктори интрахоспиталног морталитета.

Кључне речи: повреде; *Rapid Emergency Medicine Score* (*REMS*); кохортна студија

INTRODUCTION

Trauma remains an increasingly common entity and one of the leading causes of death among young adults, killing million people worldwide. Therefore trauma is significant factor of morbidity, disability, mortality and has important financial and social impact [1]. Keeping in mind frequency and consequences of trauma, it is very important to define predictors of outcome with certain level of accuracy. However, this issue is related to measuring quality of trauma system, including feasibility, ethical considerations, risk assessment and other type of evaluation. All these activities have the same goal, to support the concept of preventable death resulting from poor medical care [2].

In order to assess injury severity and predict prognosis, many different trauma scoring systems are used. These measures vary widely in terms of design, complexity and accuracy in predicting mortality after severe trauma [3, 4]. Besides that, the robustness of certain trauma scoring system depends on population under study. For example, the presence of very healthy patients who will probably survive as well as elder patients or patients with severe comorbidity who probably won't survive might significantly affect the ability of the scoring system to correctly predict the outcome [5]. Furthermore, the use of trauma scoring systems helps clinicians in management of trauma patients. Besides that, prediction of severe trauma is associated with presence of comorbidity, time interval between trauma and its care, treatment settlements [6].

Over the last decades many scoring system have been developed and used for trauma. The Revised Trauma Score (RTS) is most used physiological score. It is widely used in hospital and pre-hospital patients (pre-hospital triage). It consists of the Glasgow Coma Scale (GSC), systolic blood pressure and respiratory rate [7]. The Rapid Emergency Medicine Score (REMS) was developed for predicting in-hospital mortality in nonsurgical emergency department (ED) patients [8]. REMS incorporates GSC, age, mean arterial pressure (MAP), respiratory rate, hart rate and arterial oxygen saturation (SpO2). The most spread used scoring system is The Acute Physiology and Chronic Health Evaluation (APACHE II). This is the scoring system that evaluates the severity of surgical, non surgical and intensive care unit (ICU) patients. APACHE II consists of the body temperature, respiratory rate (RR), heart rate, MAP, oxygenation of arterial blood, arterial pH, serum sodium and potassium levels, serum creatinine, haematocrit, white cell count and GCS [9]. The Sequential Organ Failure Assessment (SOFA) was designed in 1994 for assesses the severity of illness in patients in the ICU [10]. The score incorporates PaO2/FiO2 mmHg, MAP, vasopresors, serum creatinine, serum bilirubine, platelets and GSC.

Bearing in mind all mentioned above, the aim of this study was to determine independent predictors and the best trauma scoring system (REMS, RTS, GSC, SOFA, APPACHE II) of in-hospital mortality in patients with severe trauma at the Department of Emergency, Emergency Center, Clinical Center of Serbia, Belgrade.

METHODS

Study design

Prospective cohort study included 208 consecutive patients with severe trauma admitted to the Emergency Center, Clinical Center of Serbia in Belgrade, from June 1, 2015 to June 1, 2016. Patients were followed until discharge or death. The study was approved by the Ethics Committee of the Faculty of Medicine, University of Belgrade (decision no. 29/IV-19; 25-APR-2016).

Inclusion and exclusion criteria

All patients with severe trauma, aged over 18 years, were included in the study. Mechanism of injury was established, as Injury Severity Score (ISS) over 15 [10]. Exclusion criteria were unknown identity of person, absence of accompanying person, patients transferred from other emergency centers, patients intubated and reanimated at the place of injury, sedated patients.

Data collection

Data on demographic characteristics, personal history, concomitant therapy, and mechanism of injury were collected by questionnaire. Additionally, for all patients ISS, RTS, and REMS were determined at admission in the Emergency center (EC) [7, 8, 10]. Furthermore, SOFA score and APACHE II score were determined at the admission in ICU [9, 10]. Information on clinical characteristics (body temperature, systolic and diastolic blood pleasure-DBP, HR, RR, SpO2), blood sample analyses (serum sodium and potassium levels, serum creatinine, serum bilirubine, haematocrit, leucocytes count, platelets) and other analyses (PaO2/FiO2 mmHg, vasopresors, oxygenation of arterial blood, arterial pH) were obtained from medical records. Inital vital signs (HR, RR, SBP, DBP and SpO2) and GCS recorded imeadetly upon arrival at ED. The assessments of neinvasive blood pressure, HR, SpO2 (determinated by peripheral puls oxymetar) done by Infinity Vista Xl Drager monitor. Normal ranges of hemodynamic and respiratory parameters are defined by ATLS classification of shock [11]. For example, arterial hypotension is defined as systolic blood pressure lower than 90 mmHg, tachycardia is defined as heart rate faster than 100 beats per minute (BPM).

Statistical analysis

Baseline characteristics of the study sample (mean, standard deviation, percentages) are presented. Nonparametric test was used for the comparisons between groups (Mann – Whitney test for continuous variables). Moreover, the predictive factors were tested in univariate and multivariate models using Cox proportional hazard regression models for reaching clinical outcome (death). In these analyses death was considered as dependent variable. All variables that were associated ($p < 0.100$) with the outcome in the univariate analysis were analyzed together in multivariate Cox proportionate hazard regression model in order to determine independent predictors of in-hospital mortality in patients with severe trauma. The power of scoring systems to predict mortality was compared using the area under the curve (AUC). All analyses were performed using the SPSS (Statistical Package for Social Sciences), version 17.0. Probability level of <0.05 was considered statistically significant.

RESULTS

The characteristics of 208 patients with severe trauma are shown in Table 1. There were 159 (76.4%) male and 49 (23.6%) female patients, with average age of 47.3±20.7 years. Almost all patients (99.5%) came to Emergency Department (ED) by ambulance. Average time spent in Emergency ambulance prior to hospitalization was 1.3 hours. The largest proportion of patients was traumatized in car crash (33.2%), followed by falls from the height (26.4%) and as pedestrians (22.6%) (Figure 1). The overall case-fatality ratio was 17/208 (8.2%).

Regarding clinical characteristics, values of systolic and diastolic blood pressure and number of respirations were in normal range, while average heart rate was elevated (110±25 bits per minute) and SpO2 was decreased (85.4±4.5 %) (Table 1).

Majority of patients were initially intubated (86.1%), at admission to ED, and 59.6% patients were sedated before intubation. After finishing of diagnostic procedures, 17 patients were additionally intubated, and, at that time, 94.2% patients were on mechanic ventilation (Table 1).

Different values of scale scores at admission to ED and ICU are shown in Table 2. Based on their values, it is obvious that included patients suffered from severe trauma which requires hospitalization in ICU. There is a statistically significant difference between REMS and SOFA score values between dead and alive patients (Table 3), p value for the REMS score is 0.002 and for the SOFA score p value is 0.003 (according to the Mann – Whitney test).

Patients had an average of 24.7±21.2 days spent in ICU.

According to the results of univariate Cox proportional regression analysis, following variables entered in multivariate model (p<0.100): HR (p=0.008), SpO2 (p=0.019), REMS (p=0.058), SOFA on admission (p=0.077) (Table 4). These variables were statistically significant in univariate analyses. After multivariate Cox regression model using above mentioned variables significant in univariate analysis, only elevated heart rate (HR=1.03, p=0.012) and decreased of SpO2 (HR=0.91, p=0.033) at admission remained significant, i.e. singled out as independent contributors to in – hospital mortality of patients with severe trauma. On the other words, an increase of heart rate for one unit is associated with increase of risk of death for 3%. Additionally, a decrease of SpO2 for one unit is associated with increase of risk of death for 9%.

We compared RTS, REMS, APACHE II and SOFA in predicting in – hospital mortality by using Receiving Operating Curve (ROC) analysis (Figure 2). REMS (AUC 0.72 ± 0.64) and SOFA (AUC 0.716 ± 0.067) were found fair and similar predictors of in- hospital mortality. On the other hand APACHE II (AUC 0.614 ± 0.062) and RTS (0.396 ± 0.068) were found poor predictors of in-hospital mortality.

DISCUSSION

The assessment of outcome in severe trauma patients is a demanding task due to the diversity and variation in severity of trauma, and consequently, heterogeneity of patient population. Additional factors which may influence the assessment of outcome in these patients are related to the issue of appropriate assignment of severity of symptoms and presence of different comorbidities [11].

Our mortality rate is 8.2% which is higher than in other study where were mortality rate found to be around 5% [1]. This difference may be because in these studies all traumatized patients were included, and one of our inclusion criteria was ISS over 15. Considering this inclusion criterion our patients had greater mortality risk.

In our study the largest proportion of patients was traumatized in car crash (33.2%), followed by falls from the height (26.4%) and as pedestrians (22.6%). Our findings were similar like in previous studies [12].

Our finding of predictive role of age in in-hospital mortality in univariate analysis was not significant, which is opposite than in the other studies [13, 14]. Myamato et al. and Jawa et al. found that older age was an indicator of in-hospital mortality [13, 14]. The possible reason for different findings might be a larger sample size and different statistical approach in these studies.

In our study, regarding the trauma scoring system, REMS is similar to or better than the other system. REMS has similar results as the SOFA, the advantages of REMS is more rapid and less invasive then SOFA. APACHE II and RTS were found poor predictors of in-hospital mortality [15]. Imhoff et al. [16] and Lee et al. [17] found that the REMS scoring system, performed in the ED, was a strong predictor of in-hospital mortality. Slight differences between REMS and RTS as predictors of in-hospital mortality can be observed in both studies. REMS scoring system is easier and simpler than RTS because it is consisting of six variables (GSC, age, MAP, respiratory rate, hart rate, SpO2) which are easy to obtain. Taking all this into account, REMS scoring system can be highly applicable at the ED and in the prehospital treatment of patients. Our findings support the growing body of literature examining the use of REMS in judgment after major injury [18, 19].

In the present prospective cohort study, we demonstrated that heart rate and SpO2 at admission are independent predictors of in-hospital mortality in patients with severe trauma. Using the Cox proportional hazard regression models we demonstrated that an increase of heart rate for one unit is associated with increase of risk of death for 3%, while a decrease of SpO2 for one unit is associated with increase of risk of death for 9%. Both these variables are components of the REMS, which has been developed for predicting in-hospital mortality in nonsurgical emergency department (ED) patients [20]. Our work confirms that in the most severely injured patients, initial measurement of REMS components, especially HR and SpO2, are reliable indicators of those who are at the greatest risk of in-hospital death. These findings are opposite then in the literature, Imhof and collaborators found that heart rate do not have statistically significant contribution in mortality prediction, on the other hand age and GSC have high statistically significant contribution in mortality prediction [16]. These opposite findings can be explained by autonomic compensation to severe trauma [21]. In our study we had only severe traumatized patients which is different between Imhof et al. regarding to the SpO2 we have same finding like in the other studies [16, 22].

It is well known that determination of vital signs such as SpO2 and heart rate upon arrival at the ED are frequently used as prognostic indicators for adverse outcome in patients with severe trauma. On the other hand, analysis of heart rate variability provides insight into adequacy of autonomic compensation to severe trauma in pre-hospital settings [21]. In the same study, authors stated that their findings support the fact that autonomic balance and pulse pressure are associated with mortality, and may give important diagnostic and prognostic findings in management of patients with severe trauma. Physiological response to injury with consequent reductions of central blood volume includes increased heart rate and peripheral vascular resistance. These autonomic compensations are mediated by decrease of parasympathetic and activation of sympathetic efferent neural way to the heart and vasculature [23, 24]. Additionally, alterations of tissue perfusion and oxygenation due to an impaired microcirculation have been shown to contribute to the subsequent development of organ dysfunction and unfavorable outcome [25, 26]. In line with these results, low oxygen saturation values at baseline have been associated with the development of multiorgan dysfunction and death [27, 28, 29].

Some limitations of our study have to be mentioned. First, a total of 208 patients with severe trauma were enrolled in this study, and the larger sample size would be beneficial for generalizability of the results. Second, traumatized patients who died in pre-hospital settings were not included in the analysis, which represents a type of selection bias. Third, the patient's vital parameters varied over time, so the values presented might not be representative. Fourth, the lack of available data regarding the presence of comorbidities and their management was not included and may have resulted in a bias in the outcome.

CONCLUSION

In conclusion, results of this study showed important role of REMS, which appears to provide balance between the predictive ability and the practical application, and components of REMS in prediction of outcome in patients with severe trauma and that HR and SpO2 are independent predictors of in-hospital mortality.

Conflict of interest: None declared.

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Table 1. Patients' characteristics

Variable	Values
Age (years) *	47.3±20.7
Gender** Male Female	 159 (76.4%) 49 (23.6%)
Arrival at ED by:** Emergency Private car	 207 (99.5%) 1 (0.5%)
Time spent in Ambulance on admission (hours)*	1.3±0.5
Systolic blood pressure (mmHg)*	118.8±36.1
Diastolic blood pressure (mmHg)*	71.2±22.4
Heart rate (bpm)*	110±25
Number of respirations*	14±10
Saturation (%)*	85.4±4.5
Intubation** Yes No	 179 (86.1%) 29 (13.9%)
Mechanic ventilation** Yes No	 196 (94.2%) 12 (5.8%)
Sedation** Yes No	 124 (59.6%) 84 (40.4%)
Hemodynamics** Stable Unstable	 138 (66.3%) 70 (33.7%)
Inotrop support** Yes No	 70 (33.7%) 138 (66.3%)

*Mean ± SD;
**Values are presented as frequencies (%)

Table 2. Scores at admission

Scale	Mean±SD
GCS	8.5±4.1
ISS	33.1±10.2
RTS	5.5±1.5
REMS	10.0±4.1
APACHE II	18.5±8.6
SOFA	7.5±3.1

GCS – Glasgow Coma Scale; ISS – Injury Severity Score; RTS – Revised Trauma Score; REMS – Rapid Emergency Medicine Score; APACHE II – Acute Physiology and Chronic Health Evaluation; SOFA – Sequential Organ Failure Assessment

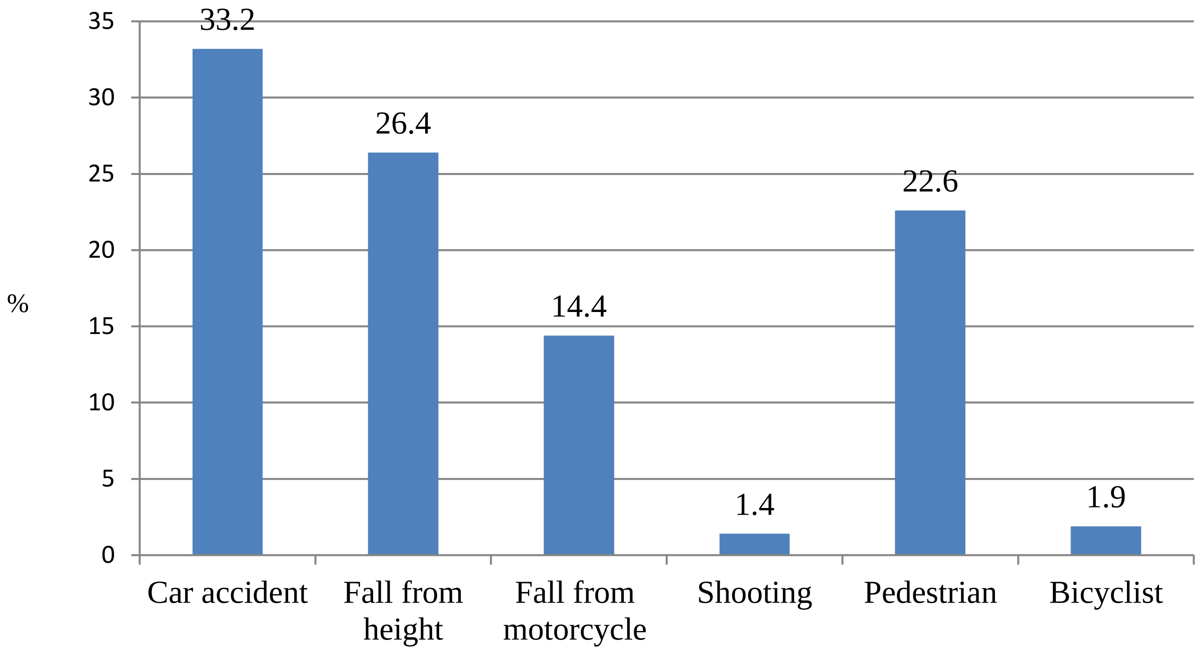

Figure 1. Mechanisms of injury

Table 3. Injury scores

Scores	Dead (mean ± SD)	Alive (mean ± SD)	p value
REMS	13.17 ± 4.36	9.73 ± 3.94	0.002
RTS	5.01 ± 1.39	5.54 ± 1.45	0.162
GSC	7.18 ± 3.14	8.58 ± 4.20	0.330
SOFA	9.59 ±3.04	7.39 ± 2.96	0.003
APACHE	21.41 ± 6.65	18.28 ± 8.61	0.126

GCS – Glasgow Coma Scale; RTS – Revised Trauma Score; REMS –Rapid Emergency Medicine Score; APACHE II – Acute Physiology and Chronic Health Evaluation; SOFA – Sequential Organ Failure Assessment

Table 4. Results of univariate Cox regression analysis

Variable	Hazard ratio	95% Confidence Interval	p-value
Age	0.99	0.97-1.01	0.330
Gender	0.59	0.17-2.07	0.414
Admission to EC	0.05	0.00-0.75	0.856
Time spent in ambulance on admission	1.53	0.52-4.56	0.443
Systolic blood pressure	0.99	0.98-1.00	0.173
Diastolic blood pressure	0.98	0.96-1.00	0.109
Heart rate	1.03	1.01-1.05	**0.008**
Number of respirations	1.01	0.96-1.07	0.593
Saturation	0.90	0.82-0.98	**0.019**
Comorbid hypertension	1.11	0.37-3.31	0.857
Mechanism of injury	1.01	0.75-1.37	0.939
GCS	1.00	0.87-1.14	0.964
Breathing	20.35	0.00-26.05	0.856
Intubation	1.04	0.13-8.31	0.973
Mechanic ventilation	0.05	0.00-5.83	0.711
Sedation	1.70	0.65-4.43	0.282
Hemodynamic	1.19	0.46-3.06	0.723
Inotrop support	0.81	0.31-2.15	0.676
RTS	0.90	0.61-1.33	0.606
REMS	1.10	1.00-1.22	**0.058**
APACHE II on admission in ICU	0.99	0.94-1.06	0.870
SOFA on admission in ICU	1.17	0.98-1.38	**0.077**
Mechanic ventilation in ICU	0.05	0.01-5.83	0.914
Hemorrhage	1.48	0.56-3.94	0.427
Surgical intervention	0.80	0.29-2.20	0.660

Bold values denote statistical significance (p<0.100)

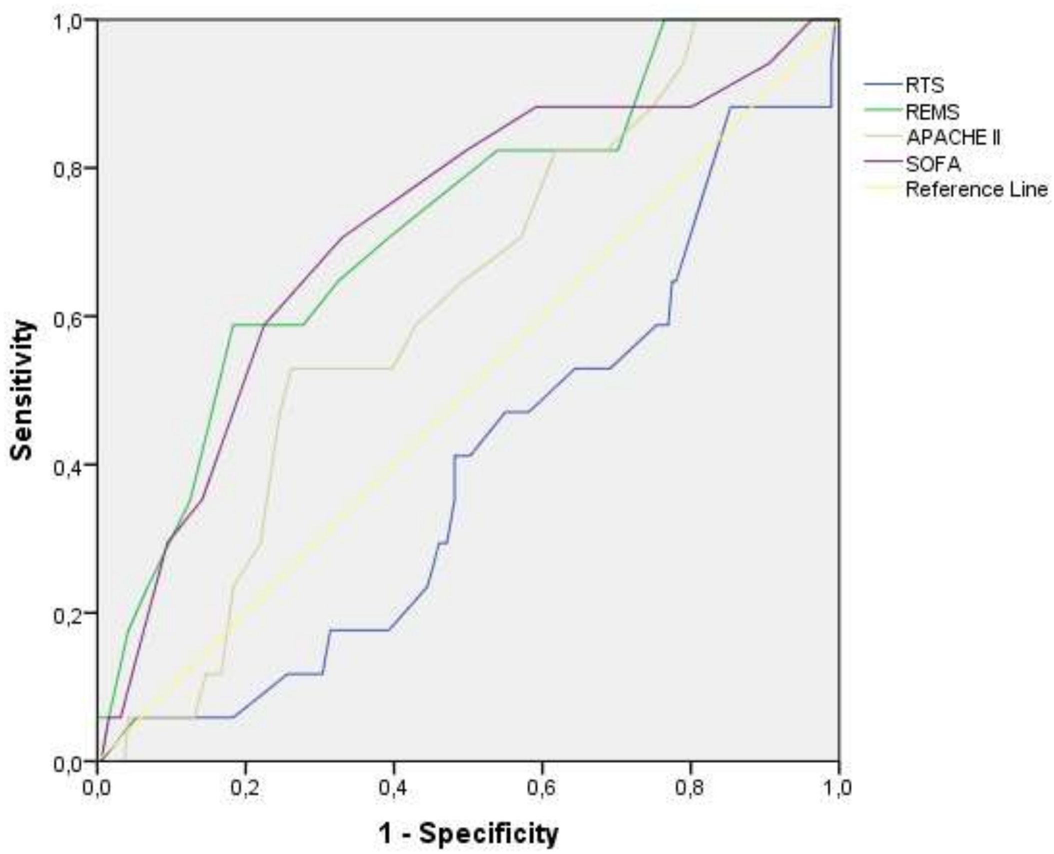

Figure 2. Area under curve for the injury scores;

RTS – Revised Trauma Score; REMS –Rapid Emergency Medicine Score; APACHE II – Acute Physiology and Chronic Health Evaluation; SOFA – Sequential Organ Failure Assessment