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RESEARCH ARTICLE

CLINICAL INDICATORS AS PROGNOSTIC FACTORS OF MULTI-TRAUMA PATIENTS IN THE INTENSIVE CARE UNIT

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Abstract

Background: In recent years, there has been a growing interest in understanding the role of prognostic factors in patient outcome.
Aim: To investigate the role of clinical indicators, and severity-of-disease assessment scales, as prognostic factors in the outcome of multi-trauma patients in the ICU.
Material and Method: The sample consisted of 65 ICU multi-trauma patients treated in a hospital in Thessaloniki city, with an average stay of 16.5 days. Clinical indicators such as Glasgow Coma Scale, heart rate, mean arterial pressure, lactic acid, hemoglobin, urine output, as well as APACHE II and SAPS II scales, were recorded on the day of admission to the ICU.
Data analysis: Data were analyzed using multiple logistic regression and Mann-Whitney Test. Multiple logistic regression analysis was performed to examine the predictive capacity of specific indicators on patient outcome.
Results: The results of the analysis showed that in cases where all clinical indicators changed, then patient outcome may be affected by 79,4% (Relative Risk 3.846, $p<0.001$). Glasgow Coma Scale ($p=0.022$) and hemoglobin ($p=0.013$) were the strongest influencing factors related to patient outcome. Mann-Whitney analysis was used to evaluate the predictive value of Apache II and SAPS II and demonstrated that both systems could significantly predict patient outcome (APACHE II=0.019 and SAPS II=0.013).
Conclusion: Hemoglobin and Glasgow Coma Scale values upon multi-trauma patient admission to the ICU appear to be strong prognostic factors of patient outcome.

Keywords: Clinical indicators, evaluation scales, prognostic factors, outcome, trauma, ICU.

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INTRODUCTION

Patient severity-of-disease classification systems used in the Intensive Care Unit (ICU) are of great importance to the medical profession in order to objectively assess patient's severity status as well as to predict patient outcome. This is achieved by documenting physiological parameters and evaluating medical interventions aiming at the improvement of the care provided.[1]

Clinical indications

The Glasgow Coma Scale (GCS) developed in 1976, was the first attempt to assess a trauma patient's level of consciousness as well as the severity of a head injury based on a numeric expression.[2] Additionally, heart rate as well as mean arterial pressure (MAP) are dynamic parameters of vital importance for the ICU patient. Maintaining a MAP within certain limits is considered a key prerequisite, to ensuring tissue perfusion and the goal of hemodynamic monitoring and support is maintained with a MAP ≥ 65 mm Hg.[3-5]

Septic patients with normal blood pressure and elevated lactate levels (> 4mmol/L) are ten times more likely to be hospitalized.[1] Large amounts of lactate can be produced and released under aerobic conditions while the development of hyperlactatemia in septic conditions is complex.[6] Regardless of the mechanism involved, the increased concentration of lactate in the blood is a strong prognostic indicator however, lactate clearance is perhaps the strongest prognostic factor. Decreased lactate levels in the first 24-48 hours are associated with better patient outcome, while persistent hyperlactatemia and increasing levels are not.[7]

Coagulation disorders along with hypothermia and acidosis are referred to as the "trauma triad of death" in patients with very high mortality. Hemoglobin is an important indicator for making decisions regarding the care of patients in the ICU.[8] This is because the main purpose of treatment is to prevent acute anemia (Hb <9g/dl) and to ensure a satisfactory supply of oxygen to the tissues to prevent ischemia.[9] At the same time, hourly Urine Output monitoring of the ICU patient is necessary and a key part of nursing care. The term "acute renal failure" encompasses a range of disorders, from subclinical cases to renal replacement therapy.[10] The definition and staging of acute renal failure are based on changes in serum creatinine and urine output (<0.5 mL / kg / h), according to the RIFLE and AKIN criteria.[11]

Severity-of-disease classification systems of ICU patients

These are scales that give the user a numerical value, or severity-of-disease score, based on a number of clinical variables. This numerical value quantifies the severity-of-disease and is used in a mathematical equation, the solution of which is the probability of death during the patient's hospitalization.[12] The most widely used severity-of-disease classification systems in the ICU, are the APACHE and the SAPS system, which provide the means of calculating the probability of in-hospital death of ICU patients.

The severity-of-disease based on APACHE II and SAPS II scores is calculated by adding the individual scores and dividing by the number of factors. In addition, by summing each patient's individual risk of death, based on the two equations as they emerge and dividing by the number of patients, an average predicted mortality rate can be calculated.[13]

APACHE II (Acute Physiology and Chronic Health Evaluation)

The APACHE II severity-of-disease system is the most frequently used system today[1]. It contains only 17 physiological variables, compared to the 34 of the original system, and the maximum score is 71.[12] This severity-of-disease scoring system is based on three distinct modules and specifically on the acute physiology during patient admission to the ICU (with parameters such as temperature, mean arterial pressure, heart rate, respiratory rate, PaO2 or A-aDO_2, pH, Sodium (Na) and Potassium (K), creatinine, hematocrit, white blood cell count and Glasgow Coma Scale, age and severe organ failure - liver, renal or heart failure, or if the patient is immunocompromised).[12]

The APACHE II severity-of-disease scale is based on the worst values during the first 24 hours of care in the ICU[11] regarding common physiological measurements and the Glasgow Coma Scale[14]. Highest scores correspond to severe conditions and a higher risk of death. The assessment is not repeated, during hospitalization, it is, by definition, conducted upon admission to the ICU. Only when the patient leaves the unit and is re-admitted can a new Apache II score be calculated.[1,13]

SAPS II (Simplified Acute Physiologic Score II)

Similar to the APACHE scale, SAPS is calculated from the worst values obtained during the first 24 hours of admission to the ICU. In 1993 Le Gall et al used logistic regression analysis to develop the SAPS II scale, which includes 17 variables (12 physiological variables, age, type of admission, and 3 disease-related variables). Higher SAPS values indicative severe conditions and all scores are used in a mathematical equation which predict in-hospital mortality.[14-15] It has excellent prediction accuracy for a wide range of predicted mortality rates.[12]

The purpose of this study was to investigate a) the role of severity-of-disease classification systems upon admission of multi-trauma patients to the ICU as predictors of mortality and b) the association between the severity-of-disease systems and patient outcome.

METHODOLOGY

Sample and procedure

The sample consisted of 65 patients who were treated in the ICU of a large hospital in Thessaloniki from 8/7/2012 to 7/2/2014. Patient inclusion criteria were multiple injuries, and specifically severe injuries to two or more organ systems due to violent external factors.

Instrument

Data were collected from the patients' medical notes on the day of admission. Patients' Glasgow Coma Scale, heart rate, blood pressure, levels of lactic acid, hemoglobin, 24-hour urine output, patient outcome as well as APACHE II and SAPS II severity-of-disease scales were recorded.

Additional clinical data of trauma patients were recorded. These included the patients' gender, age, cause of injury (mechanism of trauma), pupil reaction, need for intubation or tracheostomy, catheter placement to measure intracranial pressure, if the patient had undergone surgery or had suffered blood loss and received a mass blood transfusion. The above data were not included as clinical indicators in the statistical analysis; however they were taken into account indirectly regarding the severity-of-disease scales and commenting on the samples clinical data.

Statistical analysis

Data analysis was conducted using multiple logistic regression and Mann-Whitney Test. Multiple linear logarithmic regression was performed to test the predictive power of selected patient outcome indicators and Mann-Whitney analysis was used to assess the predictive value of APACHE II and SAPS II scores in ICU patients.

RESULTS

Based on the sample demographic characteristics, of the 65 patients included in the study, 56 were men (86%) and 9 were women (14%), with a mean age of 49.95 (± 22.93) years. The average length of stay in the ICU was 16.49 (± 19.65) days, while 14 participants died (21.5%) in the ICU during the study. The clinical characteristics of the study population are listed in Table 1. Variable mean values evaluated as predictors of patient outcome are presented in Table 2. Correlations between the variables evaluated as factors predicting patient outcome are presented in Table 3. Based on the analysis: a) a moderate positive statistically significant relationship was observed between heart rate and lactic acid ($p < .01$), b) a moderate positive relationship between blood pressure and urine output ($p < .01$), and c) a moderate negative relationship between lactic acid and hemoglobin ($p < .01$) were observer. In addition, the Glasgow Coma Scale presented low to moderate ratios with blood pressure and urine output, which were not statistically significant. The results of the analysis showed that in cases where all clinical indicators change then patient's outcome can be affected by 79.4% (Relative Risk 3,846, $p < 0.001$). The most prevalent factors affecting patient outcome were Glasgow Coma Scale ($p = 0.022$) and hemoglobin ($p = 0.013$). The findings of the multiple linear logarithm regression analysis are presented in Table 4.

Mann-Whitney analysis was used to assess the prognostic value of the APACHE II and SAPS II scores in ICU patients, showed that both indicators could significantly influence patient outcome. The results of the analysis are presented in Table 5.

DISCUSSION

In this study, the results of the statistical analysis demonstrated that in cases where all clinical indicators change, then patient outcome can be greatly affected. In particular, Glasgow Coma Scale, and even more so hemoglobin, were indicators that mostly influenced patient outcome of multi-trauma patients. The analysis also showed that the APACHE II and SAPS II severity-of-disease assessment systems could predict patient outcome equally well.

The Glasgow Coma Scale (GCS) is the most widely used predictor scale since it is well known, easy to use, and can be repeated.[16-17] It is considered superior to other indicators and prognostic scales with undeniable results in relation to patient outcome.[18] However, the relationship between the initial score of the GCS (pre-resuscitation) and mortality are non-linear, which calls into question its use as a continuous measure embedded in outcome predicting systems.[19-22] If patients demonstrate an increase of GCS during the first 24 hours after admission by 2 points, then they are seven times more likely to survive.[16,20,21,22] Based on the findings of this study, Glasgow Coma Scale assessment of a multi-trauma patient admitted to the ICU is a very strong independent prognostic factor, since the lower the score the greater the chances of a negative outcome. These findings are in line with many studies that suggest that the Glasgow Coma Scale significantly affects patient outcome.[23-30]

The literature suggests that there is a difference of opinion in regards to hemoglobin being a predictive factor for the need of a mass blood transfusion [8,9,31] thus future search is needed to identify this factor as an independent variable related to patient outcome in multi-trauma patients. Care management of patients with Traumatic Brain Injury (TBI) focuses on preventing secondary ischemic injury. Studies reporting the prevalence of anemia, especially in trauma patients, vary in inclusion criteria, in defining "significant" anemia (hemoglobin 8-10g/dL) and in the timing of hemoglobin assessment. Anemia is usually defined when hemoglobin concentration is less than 12-13g/dL. Multicenter clinical studies have shown that anemia is one of the most common medical complications in severely ill patients and that hemoglobin concentrations tend to decrease at a rate of approximately 0.5g/dL per day.[32] Hemoglobin concentrations are generally maintained above 9 g/dL during the first days after injury.[33]

In our study, hemoglobin was the most important prognostic factor that influenced multi-trauma patient outcome in the ICU, since lower values caused a negative outcome. Of the 65 patients in the sample, 14 who died had hemoglobin Hb <11g/dL. Therefore, based on the above, all 14 had anemia, 6 of them had "significant" anemia (Hb 8-10g/dL), 3 had marginally "significant" anemia (Hb 10.1-10.6g/dL), and the other 5 had a hemoglobin value of Hb <8g/dL. All 51 multi-trauma survivors had a hemoglobin value of Hb> 8g / dL.

Mean blood pressure (MAP), heart rate (HR), lactic acid (Lac) and 24-hour Urinary Output, are study indicators that did not significantly affect patient outcome, and in turn, their role in the trauma patient outcome is not often explored. Patients' heart rate who were finally admitted to the hospital did not differ significantly from those who were discharged from the ICU. Thus, pulse rate cannot be used to predict patient outcome, regardless of the type of injury in their study of more than 10,000 injured people, including patients with blunt force and penetrating trauma, found that tachycardia (HR> 100bpm) was not a significant predictor of their outcome, even though they were in critical condition. In trauma patients low systolic blood pressure is closely related to poor patient outcome and the immediate need for intervention compared to tachycardia.[34-35] There is an ongoing discussion regarding the target value related to hypotension in trauma patients. Systolic Blood Pressure (SBP) of <90mmHg has been used to diagnose patients with potentially life-threatening hemorrhagic shock. Nevertheless, even with the increase in the value of hypotension, Systolic Arterial Pressure (SAP) upon admission alone remains a poor prognostic factor of hospital mortality.[36-38]

Hemodynamic instability is common in patients with TBI and thus mean arterial pressure (MAP) is mentioned in many studies as an independent prognostic indicator of outcome. However, there are many severity-of-disease scales that use systolic blood pressure (SBP) as a variable for scoring and predicting patient outcome.[37] The statistical analysis of factors during this study, demonstrated that blood pressure was not statistically related to patient survival and increased mortality. Murray et al. support the limited effect of mean arterial pressure.[5] There are, however, previous studies that have highlighted the association between mean arterial pressure (MAP) and increased mortality.[26,39]

Although monitoring critically ill patients' lactic acid is common and perhaps offers an assessment of the patient's condition, however its prognostic value and influence in improving patient outcome remains unknown, is the only study in the literature used, in which lactates are referred to as "modifiable" prognostic factors.[35]

In addition to the clinical indicators investigated regarding their role in predicting trauma patient outcome, the present study found that both severity-of-disease systems recorded, APACHE II (Acute Physiology and Chronic Health Evaluation II) and SAPS II (Simplified Acute Physiology Score II) had significant prognostic value. Regarding the comparison of the two systems, the results of this study do not support a clear superiority of the one system over the other.

There are many reports that examine the differences between APACHE II and SAPS II, based on their popularity and perceived accuracy depending on the group of patients they are used for. Numerous studies have shown that there is no significant difference in accuracy between the two models and there is not a specific model that can be applied to a single patient with good accuracy. Some studies have shown that SAPS II performs better than APACHE II for specific diseases.[40] Other reports have the opposite conclusion for other diseases.[41, 42] Gortzis et al argue that the APACHE II scale is the most important variable among seven rating scores with increased probability of survival.[43]

One of the major differences between APACHE II and SAPS II is that APACHE II is disease specific and thus has a better prognosis of mortality in different patient groups. This is reported by Ting et al in their study, although they found that SAPS II and APACHE II ultimately had the same predictive outcome in clinical use.[27]

A research study tthat took place in a Greek ICU including 342 patients found that both the APACHE II and the SAPS II system underestimated the mortality of the sample. This finding is consistent with other studies in which the mortality rates predicted by both systems were lower than those observed.[44] Neither of the two systems demonstrated a statistically significantly difference at predicting mortality when comparing the difference in percentages between the two systems in the subgroups of survivors and non-survivors.

In conclusion, both systems failed to adequately predict mortality and their customization is considered necessary before their use in this specific ICU population. This conclusion agrees with the findings of a similar Greek study that evaluated these two systems in a Greek ICU.[13]

Lastly, it is noted that conclusions regarding the quality of health care provided in Greek ICUs in relation to that offered in ICUs where APACHE II or SAPS II were developed cannot be safely drawn. This is perhaps due to the statistically significant differences regarding ICU mean mortality values and other factors, such as different ICU patient sample composition or systematic overtime error associated with the time interval between diagnosis and admission to the ICU (lead-time bias).[13]

A possible limitation of the APACHE II and SAPS II models is that they are based solely on data obtained during the first 24 hours after admission to the ICU, and that they do not take into account complications that may occur during treatment. It has been shown that the accuracy of prognostic models based on data from the first 24 hours after admission to the ICU is maintained at an acceptable level only for patients who remain in the ICU for a short period of time.[45] After this initial period, the strength of the system decreases potentially due to the excessive risk of death associated with acquired infections or other iatrogenic complications for patients that remain in the ICU for an extensive period.

Intracranial hypertension often develops in acute trauma-related brain injury, which is why patients with severe head injury (GCS≤8) are more at risk for developing intracranial hypertension and therefore require admission to the ICU for closer monitoring and observation.[46] Elevated intracranial pressure (ICP) is an important predictor of mortality in patients with severe head injury and evidence has revealed that aggressive treatment of elevated ICP reduces mortality and improves patient outcome. [47,48] Guidelines for managing severe head trauma recommend starting treatment with an ICP threshold above 20mmHg[38]. Therefore, all patients diagnosed with a head injury with a GCS score of 8 or less should have ICP monitoring. [49]

There are various studies that argue that increased ICP is a strong independent predictor of mortality in the ICU and that monitoring and early detection of increased pressure requires treatment based on international guidelines. However, the results of ICP monitoring remain controversial.

In a study conducted in 2014 of approximately 11,000 patientsfound that ICP monitoring did not significantly reduce mortality and that injured patients did not benefit from intracranial pressure catheter placement.[50, 51] Given the substantial difference among clinical settings, future studies with larger samples are need to confirm these findings. In our study, although the placement of an ICP monitoring catheter was recorded, it was not used as an indicator in the statistical analysis of patient outcome. This could therefore be considered as a significant limitation of the study.

Abnormal pupil reaction was recorded in our study, but was not included in the statistical analysis as a variable in terms of outcome. This may also be considered as a limitation, as the literature suggests that there are many published studies that confirm this association.[17,28] Patients with severe head trauma who exhibit strong pupil reaction are five times more likely to survive, compared to those with a poor reaction.[16] A study of 1636 patients, conducted by Fulkerson et al. concluded that pupil reaction was the strongest predictor for both patients who survived and those with a negative outcome.[51] Thus, pupil anisocoria and lack of ocular response are indicators, associated with higher mortality. However, traumatic mydriasis and ocular damage to ocular neurons should be distinguished from this condition.[23]

In our study gender (56 men and 9 women) was not used as a variable regarding patient outcome. The existing literature is controversial regarding the impact of gender on patient outcome. Although few studies suggest that gender may influence patient outcome, however, the majority conclude that gender does not affect mortality.[52-55] According to researchers Reinikainen et al hormonal and immune responses caused by severe trauma or critical illness are different according to the patient's gende and men seem to be more prone to septic complications than women.[7] In young trauma patients, women had a higher survival rate compared to men. However, according to other studies, female trauma patients do not have favorable results. In this study, gender did not demonstrate a statistically significant effect on patient outcome.[56, 57]

In this study, patients age was recorded, but was not included in the analysis. Studies have shown a strong correlation between age and poor outcome in trauma patient.[57] Therefore, this is another limitation and it is clear that age is indeed one of the main prognostic factors and has a significant effect on mortality.[58-63] However, while almost all studies indicate age as a risk factor, there are differences among age groups. For example, there are studies that show that people over the age of 75 are at higher risk, while others have found a lower age limit, ie over the age of 60. A possible explanation for this is the fact that patients admitted to the ICU exhibit different medical conditions as well as the increase in life expectancy overall observed in recent years.

Age is the most important factor influencing GCS scores as well as long-term outcomes.[64] Recent evidence suggests that GCS in elderly patients may be higher than in younger patients with similar trauma. This study showed that elderly patients with moderate TBI had a higher GCS than younger patients.[65] However, it is difficult to predict which patients should be offered aggressive medical treatment. After all, trauma is no longer a condition involving only young people.[66] Despite increased mortality in elderly patients, significant survival rates have been achieved. Therefore, active treatment should not be withdrawn solely on the basis of age.[59]

LIMITATIONS

A limitation of this study was that the sample included were ICU patients from one hospital. The severity of patients computed tomography (CT) scan upon admission (Marshall classification of traumatic brain injury - Marshall scale) was not recorded and included in the study as a prognostic factors to investigate its role on patient outcome.

CONCLUSIONS

In conclusion, the present study revealed:

The Glasgow Come Scale and hemoglobin appeared to significantly affect multi-trauma patient outcome. The severity-of-disease systems APACHE II and SAPS II, demonstrate significant predictive capacity. Perhaps, simple clinical indicators could be replaced by complex evaluation systems as prognostic models since they combine outcome prediction data and are often more accurate than simple clinical variables. The plethora of trauma severity-of-disease systems available demonstrate that there is a need for an internationally applicable system that can predict different outcomes in different patient populations. This goal can be achieved by using a single scoring system, taking into account all the necessary variables and converting the severity-of-disease into a numerical value. This offers clinicians the ability to speak a common language, safely determine initial prognosis and enable time sensitive decisions involving treatment while prioritizing the provision of limited resources and resolving ethical dilemmas in order to offer the best possible outcome to multi-trauma patients in the ICU.

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ANNEX

Table 1. Clinical characteristics of sample

	Yes	No
Transfusion during the first 24 hours	29 (44.6%)	36 (55.4%)
Blood loss during the first 24 hours	40 (61.5%)	25 (38.5%)
Surgery in the first 24 hours	20 (30.8%)	45 (69.2%)
Intubation	62 (95.4%)	3 (4.6%)
Tracheotomy	19 (29.2%)	46 (70.8%)
Intracranial pressure catheter placement and monitoring	17 (26.2%)	48 (73.8%)
Normal pupil reaction	46 (70.8%)	19 (29.2%)

Table 2. Factors predicting mortality

	Mean value	Standard Deviation
Glasgow Coma Scale	9,38	1,05
Heart Rate	85,46	0,98
Mean Arterial Pressure	88,00	15,80
Lactic Acid	2,95	0,44
Hemoglobin	12,20	1,31
24-hour Urine Output	2946,09	10,22

Table 3. Correlations between mortality predictors

	1	2	3	4	5
1. Glasgow Coma Scale	-				
2. Heart Rate	.19	-			
3. Mean Arterial Pressure	.28	.12	-		
4. Lactic Acid	.01	.44**	.04	-	
5. Hemoglobin	.02	-.16	-.15	-.56**	-
6. 24-hour URINE OUTPUT	.25	.11	.40**	.19	-.18

Table 4. Clinical indicators in relation to patient outcome based on multiple linear logarithmic regression analysis

Clinical indicators	Ratio of Risk Factors Complementary Probabilities (Relative Risk)	95% confidence interval		p-value
Glasgow Coma Scale	1,363	1,046	1,776	0,022
Heart Rate	1,021	0,980	1,064	0,329
Mean Arterial Pressure	1,028	0,966	1,093	0,389
Lactic Acid	0,839	0,441	1,594	0,591
Hemoglobin	3,533	1,307	9,548	0,013
24-hour Urine Output	1,000	0,999	1,001	0,951

Table 5. Evaluation of APACHE II and SAPS II indicators in terms of patient outcome

Prediction Scale	Patient Outcome	N (n)	Mean	p-value
APACHE II	**Death**	11	28,95	0,019
	Survival	31	18,85	
SAPS II	**Death**	11	28,64	0,013
	Survival	30	18,20	