ORIGINAL ARTICLE

APACHE II or INCNS to predict mortality in traumatic brain injury: A retrospective cohort study

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ABSTRACT

BACKGROUND: Some scoring systems, such as Acute Physiology and Chronic Health Evaluation II (APACHE II), are used to predict mortality, but they are not specialized for traumatic brain injury. INCNS is a new scoring system for traumatic brain injury developed by Goa et al. INCNS score evaluates inflammation, nutrition, consciousness, neurological function and systemic condition. The present study aims to evaluate performances of Acute Physiology and Chronic Health Evaluation II (APACHE II) and INCNS to predict mortality in traumatic brain injuries.

METHODS: In this study, 78 patients who were treated in anaesthesiology intensive care unit with the diagnosis of traumatic brain injury were included. Patients under the age of 18, foreigners, patients with incomplete data were excluded from this study. Medical records were examined retrospectively. APACHE II and INCNS scores in the first 24 hours were counted up.

RESULTS: Of the 78 patients, 45 (57.7%) were males and 33 (42.3%) were females. The overall mortality was 34.6% (27/78). The mean APACHE II, INCNS score was 23.85±9.44 and 14.43±8.75, respectively. The area under the curve result of receiver operating characteristic curve analysis was 0.797 for the APACHE II and 0.847 for the INCNS.

CONCLUSION: The INCNS scoring system had higher discriminatory power than the APACHE II in predicting the mortality of TBI in the ICU. INCNS can be considered as a usable prognostic model for Turkish people.

Keywords: Acute Physiology and Chronic Health Evaluation II (APACHE II); INCNS scoring system; intensive care unit mortality; scoring system; traumatic brain injury.

INTRODUCTION

Traumatic brain injury (TBI) is the main reason of mortality and neurological disabilities all over the world.[1,2] TBI is common in both low income and high-income countries and affects all ages and genders.[2] Accurate and reliable prognostic scores in traumatic brain injury may allow the clinician to summarize clinical findings, to determine the severity of the situation, to categorize disease, thus leading to account for treatment targets, treatment expectancy and prognosis while providing information to patients and their families. Therefore, the search for an effective, reliable and easily applicable scoring system continues.

Acute Physiology and Chronic Health Evaluation II (APACHE II)[3] is a frequently used scoring system for predicting mortality in general intensive care units. However, APACHE II is not specific to the disease but includes only the Glasgow Coma Score (GCS) for TBI.[4]

Specifically for TBI, there are some scoring systems; GCS,[4] Full Outline of Unresponsiveness Score (FOUR),[5] Interna-

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tional Mission for Prognosis and Analysis of Clinical Trials in TBI model (IMPACT)[6] or Rotterdam Scoring System,[7] the data obtained by the evaluation of the computed tomography images at Helsinki Computerized Tomography scoring system.[1] However, although all these scoring systems are powerful in determining the severity of TBI, they may be insufficient to determine the prognosis due to deficiencies in systemic evaluation.

Gao et al.[8] developed Infection-Nutrition-Consciousness-Neurologic Function- Systemic Condition (INCNS) based on insufficient prognostic scores in neurocritical patients. INCNS score evaluates inflammation, nutrition, consciousness, neurological function and systemic condition (Table 1).[8]

In this study, our aim is to evaluate the performance of INCNS in predicting outcomes in patients with TBI and to examine its results in the Turkish population.

MATERIALS AND METHODS

After obtaining approval from the ethical committee for clinical research of Muğla Sıtkı Koçman University on 22/08/2019 (approval number: 10-VII), from 2017 to 2019, adults with TBI who were admitted to the Anesthesiology Intensive Care Unit of Muğla Sıtkı Koçman University Research and Training Hospital were enrolled in our study. Medical records of 97 isolated TBI patients were reviewed retrospectively. Patients under the age of 18, foreigners, patients with incomplete data were excluded from this study (Fig. 1).

Age, gender, presence of intracranial hemorrhage, type, and GCS in ICU were recorded in those 78 patients. The worst data in the first 24 hours and the APACHE II and INCNS scores were calculated. "Swallowing function" parameter in the INCNS score was not scored because of being not evaluated in any patient. Survival – death status of the patients from the intensive care unit was noted.

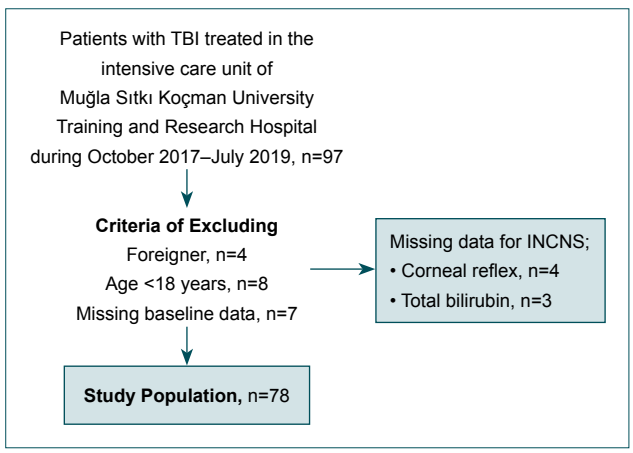

Figure 1. Flow chart displaying selective and exclusive process of patients with severe traumatic brain injury in the current study.

Statistical Analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software version 23.0. Continuous variables were expressed as mean±SD, median (interquartile range, IQR) and categorical variables were expressed as percentages. Continuous variables were analysed using Student's t-test for normally distributed variables, and Mann-Whitney U test for non-normally distributed variables. Categorical variables were analysed using Pearson's Chi-Square test analysis and Fisher's exact tests, when appropriate. In all tests, a P-value below 0.05 was considered statistically significant.

The receiver operating characteristics curve (ROC) analysis was used to determine the predictive power of APACHE II and INCNS. When a significant cut-off value was observed, the sensitivity, specificity, positive (PPV) and negative predictive values (NPV) were presented. While evaluating the area under the curve, a 5% type-I error level was used to accept a statistically significant predictive value of the test variables. Calibration of the prognostic models-defined as the accuracy of the estimated mortality rate-was assessed using the Hosmer-Lemeshow goodness-of-fit test, standardized mortality rate and calibration curves.

For the multivariate analysis, the possible factors identified with univariate analyses were further entered into the logistic regression analysis to determine independent predictors of mortality. Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. A 5% type-I error level was used to infer statistical significance.

PASS (2008) was used in power calculations. Post power levels for APACHE II and INCNS were calculated by referencing Table 4–5 statistical results. The AUC value of APACHE II is 0.797±0.049 and the AUC value of INCNS is 0.847±0.050 and the standard AUC value to be tested is 0.5 and the power level calculated for n=78 (27 Death, 51 Survival) is 99.44% for APACHE II and 99.99% for INCNS.

RESULTS

A total of 78 patients met the enrollment criteria of this study. The mean age of the patients was 47.11±17.07 years. Of these, 45 (57.7%) were males and 33 (42.3%) were females. The mean APACHE II and INCNS scores were 23.85± 9.44 and 14.43±8.75, respectively (Table 2). The APACHE II and INCNS scores were significantly higher in patients who died ($p<0.001$). Table 3 shows the distribution of APACHE II and INCNS scores between death and survival. The diagnosis of TBI included subarachnoid haemorrhage (n=21), subdural hematoma (n=14), concessional haemorrhage (n=20), epidural hematoma (n=17), brain edema (n=6). The overall mortality was 34.6% (27/78).

There was a statistically significant difference between APACHE II and INCNS scores according to mortality

Table 1. INCNS scoring system[8]

Variable	Points			
	0	1	2	3
Inflammation				
WBC (10^9/L)	4–10	2.9–3.9, 10.1–25.0	≤2.8, ≥25.1	–
Temperature (axillary, °C)	36–38.4	≤35.9, 38.5–40	≥40.1	–
Nutrition				
Albumin (g/L)	≥35	25–34.9	≤24.9	–
Consciousness				
Arousal	Spontaneous eye opening	Eye-opening to verbal command	Eye-opening to pain	None
Awareness	Correct response to question or commanda	Confused response to question or commanda	Non-reflex movements	None
Neurologic function				
Pupillary light reflex	Bilateral sensitive	–	Unilateral slow/ absent	Bilateral slow/absent
Corneal reflex	Bilateral sensitive	–	Unilateral slow/ absent	Bilateral slow/absent
Verbal response	Accurate speech	Confused/inappropriate speech	Incomprehensible speech/none	–
Motor response[c]	Unilateral/ bilateral muscle strength scores ≥4 Obeying to command	Unilateral/bilateral muscle strength scores of 2–3 Localizing to/with- drawal from pain	Unilateral muscle strength scores ≤1 Flexing/extending to pain	Bilateral muscle strength scores ≤1 None
Swallowing function	Water swallow test I–II	Water swallow test III–IV/unable to assess	–	–
Respiration	Not intubated, 12~24	Not intubated, ≤11/≥25	Breathes above ventilator rate	Breathes at ventilatorrate/ apnea
Systemic condition				
Age (y)	≤44	45~64	65~74	≥75
Heart rate	60–100	40–59, 101–149	≤39, ≥150	–
SBP (mmHg)	90–140	70–89, 141–199	≤69, ≥200	–
Blood glucose (mmol/L)	3.9–11.1	2.2–3.8, 11.2–19.3	≤2.1, ≥19.4	–
Serum sodium (mmol/L)	130–150	120–129, 151–159	≤119, ≥160	–
Serum potassium (mmol/L)	3.5–5.5	2.5–3.4, 5.6–6.9	≤2.4, ≥7.0	–
Serum creatinine (μmol/L)	44–132	≤43, 133–171	≥172	–
Total bilirubin (μmol/L)	≤34.1	34.2–102.5	≥102.6	–

SBP: Systolic blood pressure; WBC: White blood cell. [a]The examiner may ask a question about the patient's name or command the patient to move eyeballs and/or hands, if appropriate. [b]Include evidence of visual pursuit or non-contingent behaviors. [c]Either the muscle strength test or motor response to a painful stimulus is performed in each patient.

(p<0.001). We, therefore, decided to calculate cut-off points for APACHE II and INCNS scores according to mortality by receiver operating characteristic analysis. Area under the curve was 0.797 with 0.049 standard error for APACHE II and 0.847 with 0.050 standard error for INCNS (Fig. 2). The INCNS score system showed significantly higher AUROCs compared to the APACHE II.

Results for APACHE II score were the cut-off point of 24.5, the sensitivity of 74.1%, the specificity of 72.5%, the positive predictive value of 74.1% and negative predictive value of 72.5%. Results for INCNS score were the cut-off point of 17.5, the sensitivity of 81.5%, the specificity of 82.4%, positive predictive value of 81.5% and a negative predictive value of 78.6% (Table 4 and Table 5).

Both scoring systems generated Hosmer-Lemeshow goodness-of-fit statistics test P-values >0.05, with INCNS (H-L statistics=6.72 p=0.956) having a better fit than APACHE II (H-L statistics=3.35, p=0.356).

According to logistic regression results, INCNS and APACHE II were found to be statistically significant in predicting mortality, while the INCNS score shows stronger performance (p<0.001 and p<0.05, respectively). When the INCNS score increases, mortality increases by 0.832 times, while APACHE II increases mortality by 0.873 times (Table 6).

Table 2. Patient demographic characteristics and results

Variables	Mean/Frequency
Gender, n (%)	
Female	33 (57.7)
Male	45 (42.3)
Age, mean (SD)	47.11 (17.07)
APACHE-II	
Mean (SD)	23.85 (9.44)
Median	16.25
Minimum	7
Maximum	47
INCNS	
Mean (SD)	14.43 (8.75)
Median	13.25
Minimum	1
Maximum	29
GCS	
Mean (SD)	8.02 (4.31)
Median	9
Minimum	3
Maximum	15

APACHE II: Acute Physiology and Chronic Health Evaluation II; INCNS: Infection Nutrition Consciousness Neurologic Function, Systemic Condition; GCS: Glasgow Coma Scale; SD: Standard deviation.

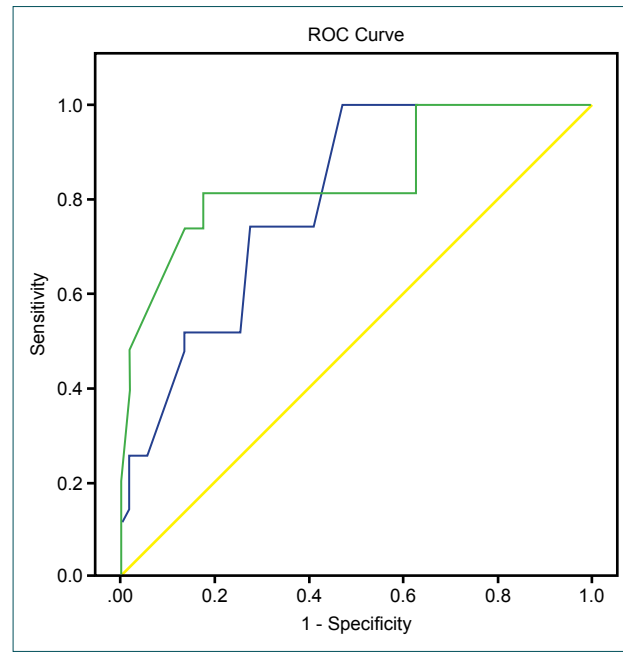

Figure 2. Receiver operating characteristic curves displaying predictive value of INCNS and APCHE II score for traumatic brain injury.

Table 3. Distribution of the APACHE II and INCNS scores between death and survival

	Overall (n=78)	Survival (n=51)	Death (n=27)	p-value
APACHE				
Mean (SD)	23.85 (9.44)	20.49 (8.19)	30.22 (8.51)	<0.001
Minimum	7	7	21	
Maximum	47	41	47	
INCNS				
Mean (SD)	14.43 (8.75)	10.70 (6.96)	21.48 (7.40)	<0.001
Minimum	1	1	8	
Maximum	29	27	29	

APACHE II: Acute Physiology and Chronic Health Evaluation II; INCNS: Infection Nutrition Consciousness Neurologic Function, Systemic Condition; SD: Standard deviation.

Table 4. ROC curves for the APACHE II and INCNS compared to mortality

Significance of APACHE II ROC curve	
Area under the ROC curve (AUROC)	0.797
Standard deviation	0.049
95% confidence interval	0.701 to 0.893
p-value	<0.001
Significance of INCNS ROC curve	
Area under the ROC curve (AUROC)	0.847
Standard deviation	0.050
95% confidence interval	0.749 to 0.944
p-value	<0.001

APACHE II: Acute Physiology and Chronic Health Evaluation II; INCNS: Infection Nutrition Consciousness Neurologic Function, Systemic Condition; ROC: The receiver operating characteristics curve.

Table 5. Diagnostic scanning tests for the APACHE II and INCNS

Diagnostic scanning tests for APACHE II	
Cut-off	24.5
Sensitivity	74.1%
Specificity	72.5%
PPV	73.1%
NPV	72.8%
p-value	<0.001
Diagnostic scanning tests for INCNS	
Cut-off	17.5
Sensitivity	81.5%
Specificity	82.4%
PPV	81.5%
NPV	78.6%
p-value	<0.001

APACHE II: Acute Physiology and Chronic Health Evaluation II; INCNS: Infection Nutrition Consciousness Neurologic Function, Systemic Condition; ROC: The receiver operating characteristics curve.

Table 6. Regression analysis of the significant individuals associated with mortality

	OR (95% CI)	p-values
APACHE II	0.873 (0.785–0.971)	0.012
INCNS	0.832 (0.754–0.919)	<0.001

APACHE II: Acute Physiology and Chronic Health Evaluation II; INCNS: Infection Nutrition Consciousness Neurologic Function, Systemic Condition; OR: Odds ratio; CI: Confidence intervals.

DISCUSSION

In this retrospective cohort study, the performance of the APACHE II and INCNS score in predicting the outcome of TBI patients was compared.

The APACHE II scoring system was developed by Knaus in 1985 and is widely used worldwide to assess the status of critical patients in general intensive care units.[9] APACHE II scoring system consists of three parts: acute physiology score, age points and chronic health points.[3] The neurological status of the patients can only be evaluated using GCS; however, the verbal component of GCS cannot be tested in intubated patients. In addition, brain stem reflexes and respiratory pattern cannot be evaluated with GCS. Although this suggests that APACHE II may be insufficient in TBI, there are studies supporting the use of APACHE II in Neurological intensive care units.[5,9–12] Discrimination of the APACHE II for TBI was good in our study, as the AUROC that exceeded 0.80, which is the level considered to be satisfactory.[13]

The INCNS score system was developed considering APACHE II and Simplified Acute Physiology Score II (SAPS II) scoring systems used for critical illness and the characteristics of the neurocritical disease.[8] Assessment of neurological function includes pupillary light reflex, cornea reflex, verbal and motor response, swallowing function and respiration parameters. Arousal and awareness evaluations are considered together for consciousness. A thorough examination of neurological function and consciousness provides a clearer understanding of the severity of TBI. Systemic evaluation is similar to that of APACHE II and SAPS II. In addition to APACHE II, nutritional status is also examined in INCNS. Thus, the severity of the disease can be calculated in TBI. Gao et al.[8] found that AUROC for INCNS was 0.788 (95% CI, 0.759–0.817). In our study, AUROC was found to 0.847 (0.749 to 0.944). The discrimination of a prognostic model is considered slightly good because AUROC is >0.8.[13]

Pupil light reflex and corneal reflex are routine neurological assessments used in N-ICUs and are a convenient and simple approach to assess brainstem functions that play a role in maintaining basic functions, such as consciousness, breathing, heart rate and sleeping. INCNS differs from other scoring systems in that it contains parameters evaluating brainstem reflexes. Results from our study showed that the INCNS score had a significantly stronger predictive power in discriminative power, sensitivity and specificity than APACHE II. Therefore, the use of INCNS in N-ICUs may become common.

Surgical interventions are frequently used in TBI.[14] Although there was no statistically significant difference, the mortality of patients undergoing surgical procedures increases compared to the patients treated conservatively.[12] Surgically treated patients are scored with the APACHE II scoring system while the presence of surgery is not evaluated with INCNS. This may be a limitation for INCNS.

Considering the effects of genetic differences on systemic diseases and cultural differences on nutrition, prognostic models may have different consequences for societies. We aimed to investigate the prognostic performance of INCNS on the Turkish population by determining the exclusion criteria for foreign

patients in this study. INCNS can be considered as a usable prognostic model for Turkish people based on the results.

Our study has potential limitations. One limitation is the retrospective design of this study and the other limitation is the use of a single ICU data. These two situations limit the generalization of the use of our INCNS results in other ICUs.

According to the results, the prognostic performance of INCNS and APACHE II scoring systems in the evaluation of TBI patients in our intensive care unit was shown to be good. The INCNS had higher discriminatory power than the APACHE II in predicting the mortality of TBI in the ICU. To verify INCNS's prognostic performance, it is recommended to conduct prospective studies in N-ICUs and further elaborate the limitations of INCNS.

Ethics Committee Approval: Approved by the local ethics committee.

Peer-review: Internally peer-reviewed.

Authorship Contributions: Concept: G.G., C.G.; Design: G.G., C.G., S.G.D.; Supervision: G.G., S.G.D.; Resource: G.G., C.G.; Materials: C.G., Y.K.; Data: C.G., Y.K.; Analysis: C.G.; Literature search: G.G., C.G.; Writing: G.G., C.G., S.G.D.; Critical revision: G.G., S.G.D.

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Travmatik beyin hasarında mortaliteyi tahmin etmede APACHE II mi INCNS mi?: Geriye dönük kohort çalışma

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AMAÇ: Mortaliteyi belirlemede akut fizyoloji ve kronik sağlık değerlendirme II (APACHE II) skorlama sistemi gibi birçok skorlama sistemi kullanılmasına rağmen travmatik beyin hasarına özgü değildir. INCNS travmatik beyin hasarı için Gao ve ark. tarafından geliştirilmiş yeni bir skorlama sistemidir. INCNS skorlama sistemi, enflamasyon, nutrisyon, bilinç, nörolojik fonksiyonlar ve sistemik durumu değerlendirmektedir. Çalışmamızın amacı travmatik beyin hasarında mortaliteyi tahmin etmede APACHE II ve INCNS'nin performansını değerlendirmektir.
GEREÇ VE YÖNTEM: Travmatik beyin hasarı nedeniyle anestezi yoğun bakım ünitesinde tedavi edilen 78 hasta çalışmaya alındı. Hastaların tıbbi kayıtları geriye dönük olarak incelendi. On sekiz yaşından küçük olanlar, yabancılar, eksik verileri olan hastalar çalışma dışı bırakıldı. Hastaların ilk 24 saat içindeki verileri ile APACHE II ve INCNS skorları hesaplandı ve kayıt edildi.
BULGULAR: Yetmiş sekiz hastanın 45'i (%57.7) erkek, 33'ü (%42.3) kadındır. Mortalite oranı %34.6 (27/78) olarak hesaplanmıştır. APACHE II ve INCNS skorlarının ortalaması sırasıyla 23.85±9.44 ve 14.43±8.75'dir. ROC eğrisi altında kalan alan APACHE II için 0.797, INCNS için 0.84'dür.
TARTIŞMA: INCNS skorlama sistemi; yoğun bakım ünitesinde travmatik beyin hasarı mortalitesini belirlemede APACHE II skorlama sistemine göre daha güçlüdür ve Türk hasta popülasyonuna uygun olduğu söylenebilir.
Anahtar sözcükler: Akut fizyoloji ve kronik sağlık değerlendirme II (APACHE II); INCNS skorlama sistemi; skorlama sistemi; travmatik beyin hasarı; yoğun bakım ünitesi mortalitesi.

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