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Evaluation of stroke mortality and related risk factors: A single-center cohort study from Gaziantep, Turkey

İnmede mortalite ve ilişkili risk faktörleri: Türkiye, Gaziantep'ten tek merkezli kohort çalışma

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Abstract

Aim: In most cases diabetes worsens the outcome of acute stroke. Acute hyperglycemia, higher C-reactive protein (CRP) and fibrinogen levels predict increased risk of in-hospital mortality. However, pneumonia is found to be major causes of death after stroke. In this study we aimed to define the risk factors of mortality of ischemic stroke.

Methods: This study was an analysis of retrospectively collected data of patients treated in intensive care unit (ICU) due to ischemic stroke.

Results: One hundred twenty-eight patients' files were evaluated. Mortality rate was 30.4% (n=39). The risk of stroke death was higher in presence of adverse events in ICU, presence of pneumonia findings, trans-tracheal intubation, long ICU stay, higher heart beats, lower SPO2 and pH levels, higher blood glucose and fibrinogen levels, higher CRP levels and the variation of CRP, higher APACHI-II, A^2DS^2 (risk of stroke) scores and lower GCS scores. Pneumonia was the most adverse event in ICU and the second most reason of the death.

Conclusions: APACHI-II, A^2DS^2 scores and GCS scores can predict the stroke death, and preventing the pneumonia may decrease acute mortality rate of ischemic stroke. CRP together with fibrinogen levels can be used as a prognostic factor in ischemic stroke.

Keywords: Stroke, Mortality, C-reactive protein, Fibrinogen

Öz

Amaç: Çoğu durumda diyabet akut inme sonucunu kötüleştirir. Akut hiperglisemi, yüksek CRP ve fibrinojen seviyeleri hastane içi mortalite riskinde artışın bir prediktörüdür. Ancak, pnömoni inme hastalarının en sık ölüm nedeni olarak görülmektedir. Bu çalışmada iskemik inmede mortalite için risk faktörlerini tanımlamayı amaçladık.

Yöntemler: Bu çalışma yoğun bakım ünitesinde (YBÜ) tedavi görmüş inme hastalarının retrospektif olarak toplanan verilerinin bir analizidir.

Bulgular: Yüz yirmi sekiz hastanın dosyası değerlendirildi. Mortalite oranı % 30,4 idi (n = 39). YBÜ'deki yan etkiler, pnömoni bulgularının varlığı, trans-trakeal entübasyon, uzun YBÜ'de kalma süresi mortalite ile ilişkiliydi. Yüksek nabız, düşük SPO2 ve pH seviyeleri de mortalite ile ilişkiliydi. Yüksek kan şekeri ve fibrinojen seviyeleri, yüksek CRP seviyeleri ve CRP varyasyonu mortalite ile ilişkili bulundu. Yüksek APACHI-II, A^2DS^2 skorları ve düşük GKS skorları mortalite ile ilişkili bulundu. Pnömoni YBÜ'deki en sık görülen advers olaydı ve ikinci en fazla ölüm nedeni oldu.

Sonuç: APACHI-II, A^2DS^2 skorları ve düşük GKS skorları mortaliteyi öngörebilir, pnömoniyi önlemek iskemik inmenin akut mortalite oranını azaltabilir. CRP, iskemik inme hastalarında fibrinojen düzeyleri ile birlikte prognostik faktörler içinde yer alması gerektiğini düşünmekteyiz.

Anahtar kelimeler: İnme, Mortalite, C-reaktif protein, Fibrinojen

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Introduction

Acute occlusion of an intracranial vessel causes reduction in blood flow. If this reduction lasts longer than several seconds cerebral ischemia occurs. Sudden death is very rarely because of cerebral infarction. Case fatality rate is about 20% at 1 month for stroke in general [1]. For all that, stroke remains the major cause of severe disability over the last two decades [2]. The most important factors that were found to affect the prognosis of a patient include severity of stroke, commonly measured by National Institute of Health Science scale (NIHSS), modified Rankin score (mRS), and Glasgow Coma Scale (GCS) scores [2,3].

Majority of acute stroke patients have disorders of glucose metabolism, and in most cases diabetes worsens the outcome of acute stroke. Acute hyperglycemia predicts increased risk of in-hospital mortality after ischemic stroke [4]. However, pneumonia is found to be major causes of death after stroke [5].

Several large prospective studies identified high fibrinogen plasma levels as an independent predictor of ischemic stroke and higher fibrinogen levels and CRP elevation increases risk of all-cause mortality in patients with acute ischemic stroke [6-9].

In this study, we aimed to define the risk factors of mortality of acute ischemic stroke.

Materials and methods

The present retrospective study was conducted at Sanko University, Faculty of Medicine. The approval for the study is obtained from the local Institutional Ethics Committee.

This study was an analysis of retrospectively collected data of ischemic stroke patients treated in intensive care unit (ICU) in one hospital from January 2016 to June 2018. All patients' data were retrospectively recorded from hospitals' archives.

Age, gender, smoking history, anticoagulant drug history, former stroke history, immobilization, presence of pneumonia findings on the chest X-ray at the first day, intubation during the whole days in ICU, adverse events (pneumonia, hyperglycemia, acute renal failure etc.) in ICU, first day laboratory findings as glucose, potassium (K) sodium (Na), fibrinogen, troponin, creatine kinase (CK), Activated Partial Thromboplastin Clotting Time (APTT), international normalized ratio (INR), C-reactive protein (CRP), creatinine, arterial blood gas values as pH, PO_2, PCO_2, vital signs as pulse, systolic blood pressure, SPO_2, Glasgow Coma Scale (GCS) score, APACHI-II score and A^2DS^2(risk of stroke) (table 1) scores were recorded. If these items were not found in the hospital records, cases were excluded the study.

Statistical analysis

SPSS 25.0 (IBM Corporation, Armonk, New York, United States) and PAST 3 (Hammer, Ø., Harper, D.A.T., Ryan, P.D. 2001. Paleontological statistics) were used to analyze the variables. The conformity of the data to a normal distribution was assessed by the Shapiro-Wilk test and the variance homogeneity by the Levene test. For multivariate normal distribution Mardia (Dornik and Hansen omnibus) test and variance homogeneity were evaluated by Box omm test. Independent-Samples T test was used with Bootstrap results to compare normal distribution variables and Mann-Whitney U test was used with Monte Carlo results in comparison of variables that did not show normal distribution. The Wilcoxon Signed Ranks Test was used in conjunction with the Monte Carlo results in comparing two repetitive measurements of the CRP variable which did not show normal distribution. Pearson Chi-Square and Fisher Exact results were used to compare mortality with categorical variables, and odds ratio was calculated with 95% confidence intervals for meaningful results. Multiple Logistic regression test was used with the Backward (Wald) method in order to determine the cause - effect relationship with significant variables in univariate analyzes with mortality. The quantitative variables were shown as mean ± SD (Standard Deviation) and median (Maximum/Minimum), while the categorical variables were shown as n (%) in the tables. The variables were analyzed at 95% confidence level and the p-value was accepted as significant when it was lower than 0.05.

Table 1: Basic prognostic score (A^2DS^2 Score) (0-10 points)

Clinical Variables on Admission	Assigned Points
Age 75+	1
Atrial fibrillation	1
Dysphagia	2
Sex (male)	1
Stroke severity (NIHSS)*	
0-4	0
5-15	3
16+	5

*NIHSS: National Institute of Health Science scale

Results

Total 128 patients' files were evaluated in the study. Median age was 70 years (33-95) and female/male proportion was 62/66. All patients were charged to the ICU because of acute ischemic stroke. Mortality rate was determined as 30.4% (n=39).

In table 2 patient characteristics were evaluated. Age, gender, history of smoking, former stroke history, and taking any anticoagulant or anti-platelet drugs were not related to the risk of stroke. However the risk of stroke death was higher in presence of adverse events in ICU charge like pneumonia, hyperglycemia, hypertension etc., presence of pneumonia findings on chest X-ray at first day, trans-tracheal intubation in any day in ICU, long ICU stay duration. Also vital signs and arterial blood gas values of first day in ICU were evaluated (table 3). Higher heart beats, lower SPO_2 and pH levels were related to higher risk of stroke. On the other hand PO_2 and PCO_2 levels were not related to the risk of stroke.

Table 3 shows the laboratory findings. Higher blood glucose levels, higher fibrinogen and troponin levels, higher CK, creatinine values were related to the mortality. Higher CRP levels of the first day and the last day were related to the risk of stroke. In addition, the variation of CRP in days was related to the mortality. Na, K, APTT and INR levels were not related to the risk of stroke. APACHI-II, A^2DS^2 and GCS scores of first day are shown in table 3 too, and higher APACHI-II, A^2DS^2 scores and lower GCS scores were related to the mortality.

Infarct areas determined with the radiographic examination were evaluated, 43 of were left hemisphere, 42 right hemisphere and 39 of were pons.

Adverse events are shown in table 4 and pneumonia was the most adverse event noticed in ICU. The most common reason

of the stroke death was the severity of stroke, and pneumonia was the second common reason (table 5).

Table 2: Patient characteristics

	Total (n=128) Median (Min/Max)	Alive (n=89) Median (Min/Max)	Dead (n=39) Median (Min/Max)	p
Age	70 (33 / 95)	70 (33 / 90)	73 (40 / 95)	0.060 [1]
	n (%)	n (%)	n (%)	
Gender				
Female	62 (48.4)	43 (48.3)	19 (48.7)	0.999 [2]
Male	66 (51.6)	46 (51.7)	20 (51.3)	
Anticoagulants or antiplatelet medication history				
No	40 (31.3)	27 (30.3)	13 (33.3)	0.445 [2]
Yes	88 (68.8)	62 (69.7)	26 (66.7)	
Adverse events in ICU				
No	73 (57.0)	58 (65.2)	15 (38.5)	0.007 [2]
Yes	55 (43.0)	31 (34.8)	24 (61.5)	
Smoking				
No	97 (75.8)	67 (75.3)	30 (76.9)	0.999 [2]
Yes	31 (24.2)	22 (24.7)	9 (23.1)	
Former Stroke history				
No	97 (75.8)	63 (70.8)	34 (87.2)	0.071 [2]
Yes	31 (24.2)	26 (29.2)	5 (12.8)	
Pneumonia findings on admission at chest X-ray				
No	68 (53.1)	58 (65.2)	10 (25.6)	<0.001 [2]
Yes	60 (46.9)	31 (34.8)	29 (74.4)	
Days of under intubation	7 (1 / 120)	3 (2 / 95)	7 (1 / 120)	0.445 [2]
Days of staying in ICU	8 (1 / 120)	7 (2 / 95)	12 (1 / 120)	0.006 [2]
Intubation				
No	83 (64.8)	82 (92.1)	1 (2.6)	<0.001 [2]
Yes	45 (35.2)	7 (7.9)	38 (97.4)	

[1] Mann Whitney U Test (Monte Carlo), [2] Independent samples t-Test (Bootstrap)

Table 3: Laboratory findings, clinical scores and other clinical descriptive values

	Total (n=128) Mean±SD	Alive (n=89) Mean±SD	Dead (n=39) Mean±SD	p
Systolic blood pressure (mmHg)	137.66±33.12	138.81±28.58	135.05±42.01	0.625 [1]
	Median (Min/Max)	Median (Min/Max)	Median (Min/Max)	
Pulse/min	88.5 (52 / 125)	88 (52 / 122)	101 (60 / 125)	0.028 [2]
SPO_2 %	94 (50 / 100)	94 (85 / 100)	93 (50 / 100)	0.045 [2]
PO_2 (mmHg)	80 (16 / 364)	83 (29 / 257)	74 (16 / 364)	0.404 [2]
PCO_2 (mmHg)	39 (18 / 80)	39 (24 / 48)	39 (18 / 80)	0.122 [2]
pH	7.4 (7.16 / 7.52)	7.41 (7.19 / 7.52)	7.37 (7.16 / 7.52)	0.008 [2]
Glucose level (mg/dl)	153.5 (51 / 490)	136 (71 / 440)	226 (51 / 490)	0.001 [2]
Potassium (mmol/L	4.2 (2.9 / 6.6)	4.2 (2.9 / 6.1)	4.2 (3.2 / 6.6)	0.874 [2]
Sodium (mmol/L)	140 (124 / 159)	140 (129 / 159)	140 (124 / 155)	0.454 [2]
APACHI-II score	16 (8 / 36)	14 (8 / 32)	19 (8 / 36)	<0.001 [2]
A^2DS^2 score	6 (0 / 10)	5 (0 / 9)	8 (4 / 10)	<0.001 [2]
Fibrinogen (µmol/L)	407 (190 / 964)	396 (190 / 754)	428 (229 / 964)	0.020 [2]
Troponin (mg/dl)	0.02 (0 / 23.3)	0.018 (0 / 16.3)	0.05 (0 / 23.3)	<0.001 [2]
Creatine Kinase (mmol/L)	86 (8 / 34295)	76 (8 / 1713)	119 (22 / 34295)	0.003 [2]
Creatinine (mg/dl)	0.97 (0.01 / 9.9)	0.9 (0.01 / 5.17)	1.2 (0.61 / 9.9)	0.002 [2]
APTT (sec)	33.45 (20.7 / 226.6)	33.5 (20.7 / 226.6)	33.4 (20.8 / 72.1)	0.403 [2]
INR	1.19 (0.94 / 4.59)	1.16 (0.94 / 4.59)	1.25 (1.02 / 4.36)	0.055 [2]
Days of under intubation	7 (1 / 120)	3 (2 / 95)	7 (1 / 120)	0.445 [2]
Days of staying in ICU	8 (1 / 120)	7 (2 / 95)	12 (1 / 120)	0.006 [2]
GCS	10 (3 / 15)	11 (3 / 15)	5 (3 / 12)	<0.001 [2]
CRP on admission (mg/L)	20 (3 / 285)	16.7 (3 / 269)	44.2 (3 / 285)	0.021 [2]
CRP on the last day (mg/L)	49.7 (3 / 325)	26 (3 / 271)	154 (21 / 325)	<0.001 [2]
Variation of CRP (first day-last day)	9.45 (-235.4 / 312.6)	5 (-235.4 / 254.3)	73.4 (-113.6 / 312.6)	<0.001 [2]

APTT: Activated Partial Thromboplastin Clotting Time, INR: International normalized ratio, CRP: C-reactive protein, GCS: Glasgow Coma Scale, [1] Mann Whitney U Test (Monte Carlo), [2] Independent samples t-Test (Bootstrap), [3] Wilcoxon sing ranks Test (Monte Carlo), Min: Minimum, Max: Maximum, SD: Standard deviation

Table 4: Number of adverse events in ICU

Adverse events	n (%)
Pneumonia	22 (17.18)
Pneumonia + renal problems	6 (4.6)
Pneumonia + seizure	3 (2.3)
High blood pressure	8 (6.25)
Hyperglycemia	3 (2.34)
Seizure	3 (2.34)
High blood pressure + Hyperglycemia	1 (0.78)
Acute renal failure	2 (1.56)
Myocardial infarction	2 (1.56)
Lung edema due to congestive heart failure	1 (0.78)
Gastrointestinal system hemorrhage	1 (0.78)
None	76 (59.3)

Table 5: The causes of death

Causes	n (%)
Severity of stroke	26 (66.6)
Pneumonia	8 (20.5)
Cardiac problems	3 (7.6)
Gastrointestinal system hemorrhage	1 (2.5)
Acute renal failure	1 (2.5)

Discussion

We determined that mortality of ischemic stroke rate was high in this study. Thirty-nine of these patients died. Fatality rate of 30.4% which is quite high but slightly lower than previous studies [10,11]. We should underline that 13 (33.3%) patients died within the first week. The first two weeks after the stroke enclose the acute phase. That's why the acute period is the critical period for patients with stroke. Treatments at the acute phase to decrease mortality would be best targeted. Morbidity and mortality after stroke usually ascend from complications. These include both medical and neurological complications. The neurological complications include brain edema, hemorrhagic transformation, seizures, delirium and recurrent stroke. Medical complications are said to be less frequent than the medical complication [12]. Pneumonia is the most seen complication after stroke. The incidence of pneumonia among the majority of neurology ICU (NICU) studies ranged between 9.5 and 56.6% [13-18]. Among mixt type ICU studies, this incidence has ranged between 17 and 50% [19-22] and appeared to be similar to NICU studies. Similar to these studies pneumonia rate in our study was 24%. Also presence of pneumonia findings at chest X-ray on admission was related to mortality.

In-hospital mortality is related to stroke severity and related complications [12,23]. NIHSS, mRS, and GCS are directly related to early mortality in ischemic stroke. NIHSS more than 15, mRS more than 3, A^2DS^2 score between 5 and 10 and GCS <8 were significantly associated with high mortality similar to previous studies [24,25].

Atrial fibrillation, ischemic heart disease, and diabetes, history of stroke, ex-smoker status, older age, and more severe stroke are accepted as predictive factors of mortality in most of the previous studies. More than half of acute mortality was scribed to the secondary complications, especially pneumonia [25,26]. However in our study, smoke status and taking anticoagulants or antiplatelet medications due to cardiac problems were not related to mortality.

Higher blood glucose level at the time of admission was related to high mortality. It is known that hyperglycemia increases growth of the infarct core in patients with surrounding hypoperfusion, suggesting that hyperglycemic blood is toxic to ischemic brain [27].

Several large prospective studied identified high fibrinogen plasma levels as an independent predictor of myocardial infarction and ischemic stroke [6-8]. Similarly to these studies fibrinogen levels were higher in ischemic stroke patients in our study (407µmol/L), also higher fibrinogen levels were related to mortality (396/428 µmol/L).

This study also demonstrated that CRP elevation was associated with an increased risk of all-cause mortality in patients with acute ischemic stroke [9]. In our study median CRP levels of death patients were more than 2 folds of survived patients. Furthermore, differently from other studies we found that CRP levels on admission, on the last day and the variation of CRP were all related to the mortality rate.

Conclusion

APACHI-II, A^2DS^2 score and GCS score can predict the mortality, pneumonia was the most adverse event noticed in

ICU, and pneumonia was the second most common cause of the mortality after severity of stroke. Therefore preventing the pneumonia may decrease the acute mortality rate of ischemic stroke. CRP together with fibrinogen levels should be used as prognostic factor for severity in ischemic stroke patients.

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