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Independent Predictors of One-Month Mortality in Patients with Intracranial Hemorrhage; a Cohort Study

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Abstract

Introduction: Predicting the outcome is one of the most frequent and important issues when approaching patients with intracranial hemorrhage (ICH).

Objective: This study aimed to evaluate the correlation of SUSPEKT score variables plus electrocardiogram (ECG) abnormalities with one-month mortality of patients with ICH presenting to emergency department (ED).

Methods: In this cohort study, adult patients presenting to the EDs of three educational hospitals, during one year, were followed and their one-month mortality rate as well as independent predictors of outcome among the variables of SUSPEKT score plus electrocardiography findings were evaluated.

Results: One hundred seventy-seven patients with the mean age of 63.07±14.89 years were studied (59.9%). The most common locations of intra-parenchymal hemorrhage were basal ganglia (53.7%) and cortex (36.2%). Ninety-two (52.0%) of cases had at least one ECG abnormality. The most frequent ECG abnormalities were ST segment depression (20.3%), T wave inversion (16.4%), and left ventricular hypertrophy (14.7%). Thirty (16.9%) cases died during the 30-day follow-up. Survived and non-survived cases were significantly different regarding the location of intra-parenchymal hemorrhage ($p < 0.0001$), presence of intraventricular hemorrhage (IVH) ($p = 0.007$), ST segment elevation ($p < 0.0001$), bradycardia ($p < 0.0001$), tachycardia ($p < 0.0001$), arterial fibrillation ($p < 0.0001$), blood sugar ($p = 0.044$), and serum level of potassium ($p = 0.022$).

Conclusions: The location of hemorrhage (basal ganglia), higher blood sugar, and presence of ECG abnormalities (ST segment elevation, tachycardia, bradycardia, atrial fibrillation) were among the independent predictors of one-month mortality of ICH patients in this study.

Key words: Cohort Studies; Electrocardiography; Intracranial Hemorrhages; Prognosis; Stroke

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INTRODUCTION

Cerebrovascular accident (CVA) is the first cause of debilitation and the second cause of death around the world (1). More than two-thirds of CVA cases occur in the developing countries and the mean age of the affected patients in these countries is 15 years lower than that of the developed countries (2). The general incidence of CVA in the developing countries was 20% higher than that in the developed countries between 2000 and 2008 (3).

The main risk factor of intracranial hemorrhage (ICH) is age, so that after the age of 50, the prevalence doubles (4). In addition, the risk factors of ischemic stroke and ICH in 22 countries showed that hypertension, smoking, waist to pelvis ratio, diet, and alcohol were the notable risk factors of ICH (5).

Numerous factors may cause ICH, the most common of which are trauma, hypertension, infarction, vascular malformations, neoplasms, coagulopathy, amyloid angiopathy, and vasculitis (6-8). In addition to describing the location, size, and pressure effect size, experts need to examine the risk of morbidity and mortality as well.

Predicting the outcomes of stroke has been the subject of several studies (9-11). Still, there is no valid and reliable scoring system available. A study in 2015 introduced SUSPEKT score to predict 30-day clinical outcome of ICH, which is an economical and reliable tool. According to the study, serum glucose, total hematoma volume, systolic blood pressure, intraventricular bleeding, serum potassium level, and age were independent and significant predictors of 30-day outcome in primary supratentorial ICH patients (12). On the

other hand, the frequency of electrocardiographic (ECG) changes such as ST segment elevation/depression and etc. in patients with ICH is considerably high (13). Baseline cardiovascular disease is common in these cases and evaluating the origin of ECG change and its correlation with outcomes in this setting is challenging (14). Based on the above-mentioned points, this study aimed to evaluate the correlation of SUSPEKT score variables plus ECG abnormalities with one-month mortality of patients with ICH presenting to emergency department (ED).

Methods

Study design and setting

This cohort study was carried out on patients presenting to EDs of three educational Hospitals (Imam Hossein, Loghman Hakim, and Shohadaye Tajrish), Tehran, Iran, between 2018 and 2019, following neurological chief complaint and final diagnosis of ICH. The variables of SUSPEKT score as well as ECG changes were recorded for all cases at the time of presentation to ED and the correlation of the mentioned variables with one-month outcome was studied. The protocol of the study was approved by Ethics Committee of Shahid Beheshti University of Medical Sciences. Researchers adhered to principles of Helsinki declaration regarding Ethical considerations in biomedical studies and confidentiality of patients' information.

Participants

The study population consisted of patients with ICH older than 18 years brought to emergency department within 24 hours from the initiation of neurological symptoms. The participants were selected using convenience sampling. The exclusion criteria were unstable hemodynamic, pregnancy/breastfeeding, old neurological disorder, sub arachnoid hemorrhage (SAH), history of cardiovascular disorders, brain tumor, history of neurosurgical procedures, failure to complete or understand the explanations, and failure to follow-up. Using convenience sampling, 177 patients were selected.

SUSPEK score

Based on this score, systolic blood pressure, serum potassium level, blood sugar, total hematoma size, age, and presence or absence of IVH were independent and significant predictors of 30-day outcome in ICH patients (16).

Data gathering

A researcher-designed checklist including demographics variables (age, gender), presenting vital signs (systolic blood pressure, diastolic blood pressure, and pulse rate), laboratory parameters (blood sugar, serum potassium level), characteristics of intra-parenchymal hemorrhage (location, size,), presence or absence of intraventricular hemorrhage (IVH) as well as ECG findings and one-month mortality was filled out for each patient. A senior emergency medicine resident under direct supervision of an emergency medicine specialist was responsible for data gathering. Brain CT scan was performed for all patients within 30 minutes after presentation to ED. Brain CT scans were interpreted by an emergency medicine physician and an expert radiologist (faculty board member). The exact hemorrhage Location, bleeding volume, and presence or absence of IVH were recorded for each patient. 30-day mortality was evaluated and recorded for all patients via telephone call or follow-up visits one month after discharge from ED.

Statistical analysis

The correlation of SUSPEKT score variables plus ECG changes with one-month mortality was evaluated using SPSS v.18. Findings were reported as mean ± standard deviation or number (%). Multivariate analysis was done to determine the independent predictors of one-month mortality among the evaluated variables. $P < 0.05$ was considered as the level of significance.

Results

One hundred seventy-seven patients with the mean age of 63.07±14.89 (23 - 98) years were studied (59.9%). The location of hemorrhage was supra-tentorial in 159 (89.8%) cases. The most common locations of intra-parenchymal hemorrhage were basal ganglia (53.7%) and cortex (36.2%). Ninety-two (52.0%) of cases had at least one ECG abnormality. The most frequent ECG abnormalities were ST segment depression (20.3%), T wave inversion (16.4%), and left ventricular hypertrophy (14.7%). Thirty (16.9%) cases died during the 30-day follow-up. Table 1 compares the baseline characteristics of cases between survived and non-survived cases. The two groups were significantly different regarding the location of intra-parenchymal hemorrhage ($p < 0.0001$), presence of IVH ($p = 0.007$), ST segment elevation ($p < 0.0001$), bradycardia ($p < 0.0001$), tachycardia ($p < 0.0001$), arterial fibrillation ($p < 0.0001$), blood sugar ($p = 0.044$), and serum level of potassium ($p = 0.022$).

Multivariate analysis

Based on multivariate analysis (Generalized linear models), independent predictors of one month mortality were blood sugar (RR = 1.0008; 95% CI:

Table 1: Comparing the baseline characteristics of patients with intracranial hemorrhage between survived and non-survived cases

Variable	Survived		P-value
	Yes (n = 147)	No (n = 30)	
Gender			
Male	86 (81.1)	20 (18.9)	0.267
Female	61 (85.9)	10 (14.1)	
Age (Mean ± SD); year	62.58 ± 15.34	65.50 ± 12.41	0.329
Location of IPH			
Undifferentiated	0 (0.0)	2 (100.0)	
Cortical	62 (96.9)	2 (3.1)	< 0.0001
Basal ganglia	72 (75.8)	23 (24.2)	
Cerebellar	13 (81.3)	3 (18.8)	
Intraventricular hemorrhage			
Yes	41 (71.9)	16 (28.1)	0.007
No	106 (88.3)	14 (11.7)	
Volume of hemorrhage (Mean ± SD); cc	44.63 ± 24.60	50.93±27.99	0.213
Blood pressure (mmHg)			
Systolic	170.94 ± 30.08	169.17 ± 23.71	0.762
Diastolic	92.65 ± 14.83	95.83 ± 11.37	0.269
Electrocardiographic findings			
ST segment elevation	0 (0.0)	10 (100)	< 0.0001
ST segment depression	32 (88.9)	4 (11.1)	0.296
T wave inversion	21 (72.4)	8 (27.6)	0.095
QT prolongation	13 (100.0)	0 (0.0)	0.091
PR interval < 0.12 millisecond	13 (100.0)	0 (0.0)	0.091
Left ventricular hypertrophy	26 (100.0)	0 (0.0)	0.013
Bradycardia	0 (0.0)	4 (100.0)	< 0.0001
Tachycardia	0 (0.0)	8 (100.0)	< 0.0001
Arial fibrillation	0 (0.0)	7 (100.0)	< 0.0001
Laboratory parameters			
Blood sugar (mg/dl)	156.20 ± 67.25	184.00 ± 74.52	0.044
Serum potassium (mEq/L)	3.92 ± 0.48	3.69 ± 0.46	0.022

Data are presented as mean ± standard deviation (SD) or frequency (%). IPH: Intra-parenchymal hemorrhage.

1.0004 - 1.0013; p < 0.0001), ST segment elevation (RR = 2.24; 95% CI: 1.95 – 2.57; p < 0.0001), tachycardia (RR = 1.54; 95% CI: 1.26 - 1.87; p < 0.0001), atrial fibrillation (RR = 2.09; 95% CI: 1.71 – 2.54; p < 0.0001), hemorrhage in basal ganglia (RR = 1.08; 95% CI: 1.01 - 1.15; p = 0.014), and bradycardia (RR = 2.00; 95% CI: 1.62 – 2.46; p < 0.0001).

Discussion

The findings of the present study showed that location of hemorrhage (basal ganglia), higher blood sugar, and presence of ECG abnormalities (ST segment elevation, tachycardia, bradycardia, atrial fibrillation) are among the independent predictors of one-month mortality of ICH patients.

Szepesi et al. (2015) assessed the parameters predicting primary supra-tentorial cerebral hemorrhage and introduced a prognostic model to predict 30-day death. The results showed that parameters of serum glucose, total hematoma volume, systolic blood pressure, intraventricular hemorrhage, age, and serum potassium level were independent and significant predictors of 30-day death in primary supra-tentorial ICH patients.

Szepesi et al. reported that serum glucose level on admission notably correlated with death (12). This finding was supported by other studies (15, 16). Some studies have shown that the increase in blood pressure is not a predictor of outcome (17, 18). In addition, Lee et al. showed that the increase in blood sugar had a negative effect on the outcome of CVA patients (19). Moreover, definite and relative hematoma volume, hematoma index, and intraventricular hemorrhage were predictors of 30-day death after ICH. The study recommended that definite hematoma volume can be used as an economical method, which provides the same insight as relative hematoma volume. Hematoma volume is a renowned index to predict outcome in ICH patients (20, 21).

Based on the previous findings, high systolic blood pressure on admission correlates with the outcome (22). In addition, diastolic blood pressure is proportionate to ICH volume (23). Szepesi et al. reported that only systolic blood pressure was significantly related to 30-day outcome (12). Numerous studies have reported the significant relationship of intraventricular bleeding and the outcome of general and supra-tentorial ICH (16, 24). Expansion of hematoma is a determining factor for mortality and morbidity after ICH (25).

Brott et al. showed that the risk of four-week death was higher in patients with expanding hemorrhage (26). Szepesi et al. pointed out a notable relationship between serum potassium level and 30-day outcome, which was not reported by other studies. Mortality rate is higher among those with potassium levels outside the normal range (12). However, studies have shown that extra potassium in diet is related to lower rate of CVA (27).

Szepesi et al. reported that age had a predictive role in outcome (12). Some studies have shown that age is an independent predictor of death, while others have denied this or supported this only for individuals older than 80 years (21, 28). It is reported that low platelet count is a predictor of death, which is supported by other studies indicating that there is a significant relationship between low platelet count, absence of platelet function, and hematoma growth (29).

Hemphill et al. (2001) assessed ICH score for predicting clinical outcome in patients with cerebral trauma, SAH, or ischemic stroke. The results showed that the parameters related to 30-day mortality were GCS, age>80 years, infra-tentorial origin of ICH, ICH volume, and intraventricular hemorrhage. All the 26 patients with ICH score =0 survived and the six patients with ICH score = 5 died. Thirty-day mortality significantly correlated with increase in ICH score. In addition, ICH score was a simple clinical tool to categorize patients. Using this tool, therapeutic protocols can be properly guided and efficient therapeutic plans can be adopted (30).

Takeuchi et al. (2015) examined changes in electrocardiogram of 118 patients with ICH and showed that 56% of them had abnormal electrocardiogram. The changes were 24% drop in ST section, 20% left ventricular hypertrophy, 19% longer QT section, and 19% reversed T-wave (31). Levis (2017) studied changes in electrocardiogram of patients with ICH and showed that abnormalities included reversed T wave, longer Q-T section, Osborn wave (j-wave), and U wave (32).

It seems that ECG changes after ICH could be introduced as one of the predictive factors of outcome, which are independent from variables that were previously reported in SUSPEKT score and other predictive tools. We need more studies in this regard without the limitations of the present study to be able to comment on the exact role of ECG findings in prediction of ICH outcome.

Limitations

Not considering a complete list of predictors confirmed in previous studies is one of the most important limitations of this study, which limits the generalizability of the findings of the present study.

Conclusions

The findings of the present study showed that location of hemorrhage (basal ganglia), higher blood sugar, and presence of ECG abnormalities (ST segment elevation, tachycardia, bradycardia, atrial fibrillation) are among the independent predictors of one-month mortality of ICH patients.

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Authors' contribution

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

Conflict of interest

None declared.

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References

1. Bonita R, Mendis S, Truelsen T, Bogousslavsky J, Toole J, Yatsu F. The global stroke initiative. The Lancet Neurology. 2004;3(7):391-3.
2. Truelsen T, Bonita R, Jamrozik K. Surveillance of stroke: a global perspective. International Journal of Epidemiology. 2001;30(suppl_1):S11.
3. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. The Lancet Neurology. 2009;8(4):355-69.
4. Adeoye O, Broderick JP. Advances in the management of intracerebral hemorrhage. Nature Reviews Neurology. 2010;6(11):593.

5. O'donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. The Lancet. 2010;376(9735):112-23.
6. Koivunen RJ, Satopää J, Meretoja A, Strbian D, Haapaniemi E, Niemelä M, et al. Incidence, risk factors, etiology, severity and short-term outcome of non-traumatic intracerebral hemorrhage in young adults. European journal of neurology. 2015;22(1):123-32.
7. Kasmaei VM, Asadi P, Zohrevandi B, Raouf MT. An epidemiologic study of traumatic brain injuries in emergency department. Emergency. 2015;3(4):141.
8. Biffi A, Anderson CD, Battey TW, Ayres AM, Greenberg SM, Viswanathan A, et al. Association between blood pressure control and risk of recurrent intracerebral hemorrhage. Jama. 2015;314(9):904-12.
9. Khambu B, Paudel P, Bista P, Sharma R, Deo K, Rajiv J, et al. Utility of Intracerebral Hemorrhage Score for Predicting Prognostic Value in Hypertensive Bleed. Post-Graduate Medical Journal of NAMS. 2018;18(1).
10. Wayan N, Anne S, Tjokorda M. Combination Intracerebral Hemorrhage-graeb Score Improves Prediction of Outcome in Spontaneous Intracerebral Hemorrhage. Biomedical and Pharmacology Journal. 2019;12(1):463-7.
11. Rordorf G, Mcdonald C, Edlow JA. Spontaneous intracerebral hemorrhage: Treatment and prognosis. interventions. 2017;1:2.
12. Szepesi R, Széll IK, Hortobágyi T, Kardos L, Nagy K, Lánczi LI, et al. New prognostic score for the prediction of 30-day outcome in spontaneous supratentorial cerebral haemorrhage. BioMed research international. 2015;2015.
13. Sakr YL, Lim N, Amaral AC, Ghosn I, Carvalho FB, Renard M, et al. Relation of ECG changes to neurological outcome in patients with aneurysmal subarachnoid hemorrhage. International journal of cardiology. 2004;96(3):369-73.
14. Togha M, Sharifpour A, Ashraf H, Moghadam M, Sahraian MA. Electrocardiographic abnormalities in acute cerebrovascular events in patients with/without cardiovascular disease. Annals of Indian Academy of Neurology. 2013;16(1):66.
15. Fogelholm R, Murros K, Rissanen A, Avikainen S. Admission blood glucose and short term survival in primary intracerebral haemorrhage: a population based study. Journal of Neurology, Neurosurgery & Psychiatry. 2005;76(3):349-53.
16. Stead LG, Jain A, Bellolio MF, Odufuye A, Gilmore RM, Rabinstein A, et al. Emergency Department hyperglycemia as a predictor of early mortality and worse functional outcome after intracerebral hemorrhage. Neurocritical care. 2010;13(1):67-74.
17. Tuhrim S, Horowitz DR, Sacher M, Godbold JH. Volume of ventricular blood is an important determinant of outcome in supratentorial intracerebral hemorrhage. Critical care medicine. 1999;27(3):617-21.
18. Tetri S, Juvela S, Saloheimo P, Pyhtinen J, Hillbom M. Hypertension and diabetes as predictors of early death after spontaneous intracerebral hemorrhage. Journal of neurosurgery. 2009;110(3):411-7.
19. Lee S-H, Kim BJ, Bae H-J, Lee J, Lee J, Park B-J, et al. Effects of glucose level on early and long-term mortality after intracerebral haemorrhage: the Acute Brain Bleeding Analysis Study. Diabetologia. 2010;53(3):429-34.
20. Nilsson OG, Lindgren A, Brandt L, Säveland H. Prediction of death in patients with primary intracerebral hemorrhage: a prospective study of a defined population. Journal of neurosurgery. 2002;97(3):531-6.
21. Gomis M, Ois A, Rodriguez-Campello A, Cuadrado-Godia E, Jiménez-Conde J, Subirana I, et al. Outcome of intracerebral haemorrhage patients pre-treated with statins. European journal of neurology. 2010;17(3):443-8.

22. Reinhard M, Neunhoeffer F, Gerds TA, Niesen W-D, Buttler K-J, Timmer J, et al. Secondary decline of cerebral autoregulation is associated with worse outcome after intracerebral hemorrhage. Intensive care medicine. 2010;36(2):264-71.
23. Kumar MA, Rost NS, Snider RW, Chanderraj R, Greenberg SM, Smith EE, et al. Anemia and hematoma volume in acute intracerebral hemorrhage. Critical care medicine. 2009;37(4):1442-7.
24. Ruiz-Sandoval JL, Chiquete E, Romero-Vargas S, Padilla-Martínez JJ, González-Cornejo S. Grading scale for prediction of outcome in primary intracerebral hemorrhages. Stroke. 2007;38(5):1641-4.
25. Davis S, Broderick J, Hennerici M, Brun N, Diringer M, Mayer S, et al. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. Neurology. 2006;66(8):1175-81.
26. Brott T, Broderick J, Kothari R, Barsan W, Tomsick T, Sauerbeck L, et al. Early hemorrhage growth in patients with intracerebral hemorrhage. Stroke. 1997;28(1):1-5.
27. D'Elia L, Barba G, Cappuccio FP, Strazzullo P. Potassium intake, stroke, and cardiovascular disease: a meta-analysis of prospective studies. Journal of the American College of Cardiology. 2011;57(10):1210-9.
28. Juvela S. Risk factors for impaired outcome after spontaneous intracerebral hemorrhage. Archives of Neurology. 1995;52(12):1193-200.
29. Ziai WC, Torbey MT, Kickler TS, Oh S, Bhardwaj A, Wityk RJ. Platelet count and function in spontaneous intracerebral hemorrhage. Journal of Stroke and Cerebrovascular Diseases. 2003;12(4):201-6.
30. Hemphill JC, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score. Stroke. 2001;32(4):891-7.
31. Takeuchi S, Nagatani K, Otani N, Wada K, Mori K. Electrocardiograph abnormalities in intracerebral hemorrhage. Journal of Clinical Neuroscience. 2015;22(12):1959-62.
32. Levis JT. Ecg diagnosis: deep T wave inversions associated with intracranial hemorrhage. The Permanente journal. 2017;21.