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Mortality and morbidity in patients with spontaneous intracerebral hemorrhage: A single-center experience

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Keywords
Cerebral Hemorrhage; Mortality; Morbidity

Abstract

Background: Intracerebral hemorrhage (ICH) is the most common cause of non-ischemic strokes. Considering high mortality and poor functional status following ICH, we investigated factors that can predict short-term outcome and affect recovery of these patients.

Methods: In this prospective descriptive study, 100 patients with non-traumatic ICH were included. Clinical and radiographic data were collected and extent of disability was measured by modified Rankin Scale (mRS) at discharge, 1 week, 1 month, and 3 months after discharge.

Results: 32 of 100 cases died at hospital and 6 more expired during 3-month follow-up. Risk factors of in-hospital mortality were warfarin use, surgical intervention, and high ICH score. Functional status of patients significantly improved 3 months after discharge. Factors associated with poor recovery were age older than 70, history of coronary artery disease (CAD), low Glasgow Coma Scale (GCS) at admission, elevated mean arterial pressure (MAP), longer hospitalization, and high ICH score.

Conclusion: ICH was associated with high rate of mortality (36%). Warfarin use, surgical intervention, and high ICH score were predictive of mortality during hospitalization and 3-month follow-up. Improvement of functional status began after 1 month and significantly improved 3 months after discharge.

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Introduction

Spontaneous intracerebral hemorrhage (ICH) is the most common cause of non-ischemic strokes[1] and accounts for 10%-20% of all strokes.[2] ICH annually occurs in 25 cases per 100000 of population[3] and the incidence, mortality, and morbidity is higher in Asian countries in comparison to the West.[4]

ICH is a devastating disease with mortality rate of up to 40%-50%[5] that usually happens in the first days.[6] Only 12%-39% of patients are functionally independent within 6 months and most of them will experience some degree of disability for the rest of their lives.[7,8]

Improvement of community health resulted in aging population, theoretically increasing the prevalence of ICH.[9] These patients need long-term care that costs a lot for the society.[10]

Various studies have identified old age, African-American and Asian ethnicities, male gender, vascular anomalies, neoplasms, hypertension (HTN), coagulopathy, heavy alcohol intake, and illicit drug use as risk factors of ICH.[11]

There are different treatment strategies for ICH, but since the exact pathophysiology of disease is unknown, few treatment modalities are actually beneficial. Thus, eliciting patient's prognosis can direct treating physicians as well as patients' families toward informed decision-making.[12]

There have been several studies on ICH prognostic factors, but most of them were performed in Western countries,[10] and little is known about outcome of ICH in Asia and particularly in developing countries. In addition, there is a relative lack of data about functional outcome of patients with ICH and factors that may affect the recovery process. To optimize treatment strategies, accurate knowledge about clinical and radiological ICH outcome predictors is crucial.

In this study, we aimed to investigate clinical and radiological predictors of in-hospital and 90-day mortality of spontaneous ICH. We also assess disability status and recovery process of survivors during 90 days of follow-up.

Materials and Methods

This prospective cohort study was performed in Shariati Hospital, affiliated to Tehran University of Medical Sciences, Tehran, Iran, from April 2015 to August 2019. All consecutive patients who were admitted to the hospital and had ICH, diagnosed by World Health Organization (WHO) criteria and confirmed by computed tomography (CT) scan, were included. Patients were excluded if they had traumatic ICH or an ICH followed by brain surgery, disagreed to participate in study, or could not be followed. Informed consents were taken from all patients or their relatives. The study was approved by the Ethics Committee of Tehran University of Medical Sciences.

We obtained detailed history of patients and recorded their information. We collected patient's characteristics (gender, age), vascular risk factors including diabetes mellitus (DM) (confirmed DM or usage of hypoglycemic drugs), HTN (confirmed HTN or antihypertensive drug use), dyslipidemia (confirmed dyslipidemia or lipid-lowering drug use), history of past stroke (confirmed by a medical record), cardiovascular diseases (CVDs), smoking, alcohol, and opium consumption, and drug history including aspirin, warfarin, and clopidogrel. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels and mean arterial pressure (MAP) at presentation, initial Glasgow Coma Scale (GCS), ICH score,[13] and pupillary response to light were also collected. All patients underwent a CT scan and we recorded details including size of hematoma (measured by formula ABC/2), site of hematoma (frontal, parietal, temporal, occipital, thalamus, basal ganglia, brain stem, cerebellum, multiple lobes), presence or absence of intraventricular hemorrhage (IVH), and midline shift (septum pellucidum deviation). In addition, we collected the length of hospital stay and any surgical intervention which was performed. Modified Rankin Scale (mRS) was used for assessing functional outcome and dependency in daily living activities. Follow-up interviews were conducted 4 times (at discharge, one week, one month, and three months after discharge) via phone calls and functional status was evaluated by mRS.

Data were analyzed using SPSS software (version 19, SPSS Inc., Chicago, IL, USA). Results were presented as mean ± standard deviation (SD) and percentages for numerical and nominal variables, respectively. The prognostic significance of patients' characteristics and clinical and radiologic factors was initially evaluated by univariate analysis (Mann-Whitney U test for continuous variables and Fisher's exact test for nominal ones). The variables found to be significantly related to the outcome were subjected to multiple logistic regression analysis. Cox regression model was applied for survival analysis. All P-values were considered statistically significant when they were less than 0.05.

Results

Among 111 patients who were admitted and had inclusion criteria, 100 patients could be followed till 3 months and enrolled in the study. 59 (59%) of them were men and 41 (41%) were women. Mean age of patients was 59.8 ± 18.1 years. Major risk factors found in the past history of patients were as follows: HTN (65%), history of CVD (27%), and history of cerebral stroke (25%) (Table 1). Prevalence of aspirin, clopidogrel, and warfarin use was 36%, 9%, and 15%, respectively. On admission to the hospital, mean GCS score was 12.3 ± 3.6 and pupils were responsive to light in 80% of patients. According to brain CT scan, location of hematoma was in frontal lobe (13%), parietal lobe (9%), temporal lobe (6%), occipital lobe (1%), thalamus (18%), basal ganglia (16%), cerebellum (8%), and brain stem (1%), and 28% of patients had hematoma in more than one of locations above. Mean volume of hematoma was 47.00 ± 7.37 cc and 43% of patients had midline shift. Hospitalization time was 15.8 ± 27.2 days (range: 1 day to 158 days) and 22% of patients underwent surgical interventions. Mortality rate in 90 days of follow-up was 38% including 32 patients who died in the hospital and 6 who passed away after discharge (2 in first week, 2 in one month, and 2 in 3 months after discharge).

In univariate analysis, GCS, SBP, DBP, MAP, pupillary light response, hematoma volume, midline shift, surgical intervention, and ICH score were significantly related to in-hospital death. (Table 1).

After multivariate analysis, warfarin use, surgical intervention, and ICH score were related to in-hospital mortality and clopidogrel had protective effect ($P < 0.05$). Applying Cox regression model to analyze determinant factors of mortality within 90 days revealed ICH score as the only significant factor ($P < 0.001$).

Sixty-two patients survived more than 3 months and were evaluated by mRS at discharge, in 1 week, 1 month, and 3 months after discharge (Figure 1). There were no significant changes in mRS after 7 days and 1-month post-discharge, but significant improvement occurred 3 months post-discharge ($P < 0.001$). Factors that had negative impact on improvement were age more than 70 ($P = 0.004$), history of CVD ($P = 0.021$), GCS less than 13 ($P = 0.001$), SBP more than 150 mmHg ($P = 0.003$), MAP more than 100 mmHg ($P = 0.004$), hospitalization more than 1 month ($P = 0.004$), and higher ICH score ($P = 0.028$).

Table 1. Demographic, clinical, and radiologic characteristics of patients in relation to their final status at discharge (in-hospital mortality versus survivors)

Variable	In-hospital mortality (n = 32)	Survivors (n = 68)	P
Age (year) (mean ± SD)	62.60 ± 18.90	58.50 ± 17.80	0.286
Men (%)	56.3	60.3	0.701
CVD (%)	18.8	30.9	0.202
Diabetes (%)	31.3	17.6	0.126
HTN (%)	62.5	66.2	0.719
Hyperlipidemia (%)	12.5	13.2	> 0.999
History of past stroke (%)	28.1	23.5	0.621
Smoking (%)	15.6	11.8	0.751
Alcohol use (%)	9.4	1.5	0.095
Opioid use (%)	9.4	4.4	0.381
Aspirin use (%)	28.1	39.7	0.260
Warfarin use (%)	21.9	11.8	0.232
Clopidogrel use (%)	6.3	10.3	0.715
tPA administration (%)	3.1	1.5	0.540
GCS score (mean ± SD)	9.60 ± 4.20	13.60 ± 2.50	< 0.001
SBP (mmHg) (mean ± SD)	143.10 ± 31.40	159.70 ± 35.70	0.030
DBP (mmHg) (mean ± SD)	85.00 ± 18.20	95.20 ± 20.20	0.019
MAP (mmHg) (mean ± SD)	104.40 ± 21.60	116.70 ± 23.80	0.016
Pupillary response to light (%)	53.3	92.6	< 0.001
Days of hospitalization (mean ± SD)	17.60 ± 33.50	15.00 ± 24.00	0.655
Hematoma volume (cc) (mean ± SD)	91.30 ± 109.70	27.10 ± 36.20	0.004
Midline shift (%)	59.4	35.3	0.023
Surgical intervention (%)	40.6	13.4	0.002
ICH score (mean ± SD)	2.62 ± 0.78	0.85 ± 0.72	< 0.001

CVD: Cardiovascular disease; HTN: Hypertension; tPA: Tissue plasminogen activator; GCS: Glasgow Coma Scale; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; ICH: Intracerebral hemorrhage; SD: Standard deviation

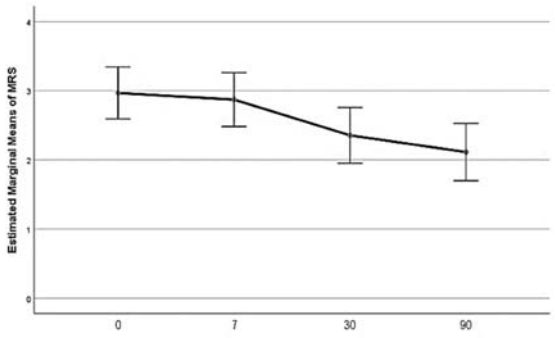

Figure 1. Modified Rankin Score (mRS) at discharge, 7, 30, and 90 days post-discharge

Discussion

Non-traumatic ICH is a catastrophic disease with high mortality and long-term morbidity that in contrast to ischemic stroke, not much progress has been made in recent years to improve the outcome of patients.[14,15] It usually occurs in adults. Like most reported series, men were more commonly affected.[16] Depending on patient characteristics, 1-month mortality has been reported from 13.1% to 61.0% (median: 40.4%). In our study, it was 36% which is concordant with other series.[17]

In line with previous studies, this study revealed that warfarin use was a predictor for mortality. It may be due to tendency of hematoma to expand rapidly and concomitant underlying disease.[18] Interestingly, clopidogrel had mild protective effect. There was not any significant difference in volume of hematoma, site of hemorrhage, and age among patients taking clopidogrel. Anti-inflammatory properties of clopidogrel can be an explanation for its protective effect.[19] However, further studies with more patients are needed to prove its efficacy.

Conflicting results have been reported for impact of hematoma evacuation. Some studies have found surgical intervention to be associated with increased mortality, while others failed to show an association.[20] It is difficult to compare results across studies due to various indications and different outcome measures. In this study, surgery was a predictive factor of in-hospital fatality. Usually patients with larger hematomas or clinical deterioration undergo surgical intervention and this can explain the association of surgical evacuation and poor prognosis.

Site of hemorrhage is a factor that correlates with mortality in most studies; specifically, infratentorial hemorrhage is associated with poor prognosis,[21] but in our study, location of hematoma was not significantly related to mortality which is probably due to low number of patients in some groups such as brain stem.

ICH score is a prognostic tool used to determine survival outcome after non-traumatic ICH.[13] It is based on GCS, ICH volume, the presence of IVH, ICH origin, and age of the patient (≥ 80 years). In this study, mortality increased with higher grades of ICH score. Mortality rate in score 0, 1, and 2 was 0%, 13.5%, and 60.0%, respectively, while all patients with ICH score of 3 and 4 passed away which was more prevalent compared to other studies.[13]

There was no statistically significant association between the 3-month outcome and the presence of comorbidities. Concomitant diseases such as atherosclerosis may have a role in pathogenesis of ICH but not in outcome.

The mRS was used for assessment of functional outcome and was performed at discharge, 7 days, 1 month, and 3 months after discharge. Significant improvement in mRS began 1 month after discharge, and after 3 months from discharge, mRS was significantly lower than 1 month. Thus, usually the physician and patient's relatives must wait at least 1 month to see significant clinical improvement.

Factors that worsened improvement were age (more than 70 years), GCS (less than 13), SBP (more than 150 mmHg), MAP (more than 100 mmHg), duration of hospitalization (more than 1 month), and high ICH score.

One of the limitations of this study was that we did not consider socioeconomic status of patients, whereas it can affect the recovery process. Some patients died at hospital before examinations being completed that led to missing data. In addition, number of patients was relatively low and a multicenter study with high number of patients is required to determine the risk factors.

Conclusion

ICH was associated with high rate of mortality (36%). Warfarin use, surgical intervention, and high ICH score were predictive of mortality during hospitalization and 3-month follow-up. Improvement of functional status began after 1 month and significantly got better after 3 months from discharge.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

None.

References

1. Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. Lancet 2009; 373(9675): 1632-44.
2. Gonzalez-Perez A, Gaist D, Wallander MA, McFeat G, Garcia-Rodriguez LA. Mortality after hemorrhagic stroke: Data from general practice (The Health Improvement Network). Neurology 2013; 81(6): 559-65.
3. Koivunen RJ, Satopaa J, Meretoja A, Strbian D, Haapaniemi E, Niemela M, et al. Incidence, risk factors, etiology, severity and short-term outcome of non-traumatic intracerebral hemorrhage in young adults. Eur J Neurol 2015; 22(1): 123-32.
4. Bhatia R, Singh H, Singh S, Padma MV, Prasad K, Tripathi M, et al. A prospective study of in-hospital mortality and discharge outcome in spontaneous intracerebral hemorrhage. Neurol India 2013; 61(3): 244-8.
5. Yan F, Yi Z, Hua Y, Shen Y, Li M, Ding Y, et al. Predictors of mortality and recurrent stroke within five years of intracerebral hemorrhage. Neurol Res 2018; 40(6): 466-72.
6. McDowell MM, Kellner CP, Sussman ES, Bruce SS, Bruce RA, Heuts SG, et al. The role of admission timing in the outcome of intracerebral hemorrhage patients at a specialized stroke center. Neurol Res 2014; 36(2): 95-101.
7. Gebel JM Jr, Jauch EC, Brott TG, Khoury J, Sauerbeck L, Salisbury S, et al. Relative edema volume is a predictor of outcome in patients with hyperacute spontaneous intracerebral hemorrhage. Stroke 2002; 33(11): 2636-41.
8. Flemming KD, Wijdicks EF, Li H. Can we predict poor outcome at presentation in patients with lobar hemorrhage? Cerebrovasc Dis 2001; 11(3): 183-9.
9. Sennfalt S, Norrving B, Petersson J, Ullberg T. Long-term survival and function after stroke. Stroke 2018; STROKEAHA118022913.
10. Liu J, Wang D, Yuan R, Xiong Y, Liu M. Prognosis of 908 patients with intracerebral hemorrhage in Chengdu, Southwest of China. Int J Neurosci 2017; 127(7): 586-91.
11. Al-Mufti F, Thabet AM, Singh T, El-Ghanem M, Amuluru K, Gandhi CD. Clinical and Radiographic Predictors of Intracerebral Hemorrhage Outcome. Interv Neurol 2018; 7(1-2): 118-36.
12. Mustanoja S, Putaala J, Koivunen RJ, Surakka I, Tatlisumak T. Blood pressure levels in the acute phase after intracerebral hemorrhage are associated with mortality in young adults. Eur J Neurol 2018; 25(8): 1034-40.
13. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: A simple, reliable grading scale for intracerebral hemorrhage. Stroke 2001; 32(4): 891-7.
14. Wartenberg KE, Mayer SA. The STICH trial: The end of surgical intervention for supratentorial intracerebral hemorrhage? Curr Neurol Neurosci Rep 2005; 5(6): 473-5.
15. Gregson BA, Broderick JP, Auer LM, Batjer H, Chen XC, Juvela S, et al. Individual patient data subgroup meta-analysis of surgery for spontaneous supratentorial intracerebral hemorrhage. Stroke 2012; 43(6): 1496-504.
16. An SJ, Kim TJ, Yoon BW. Epidemiology, risk factors, and clinical features of intracerebral hemorrhage: An Update. J Stroke 2017; 19(1): 3-10.
17. van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: A systematic review and meta-analysis. Lancet Neurol 2010; 9(2): 167-76.
18. Ferrete-Araujo AM, Egea-Guerrero JJ, Vilches-Arenas A, Godoy DA, Murillo-Cabezas F. Predictors of mortality and poor functional outcome in severe spontaneous intracerebral hemorrhage: A prospective observational study. Med Intensiva 2015; 39(7): 422-32.
19. Bao XC, Chen H, Fang YQ, Yuan HR, You P, Ma J, et al. Clopidogrel reduces the inflammatory Response of lung in a rat model of decompression sickness. Respir Physiol Neurobiol 2015; 211: 9-16.
20. Koivunen RJ, Satopaa J, Haapaniemi E, Strbian D, Meretoja A, Mustanoja S, et al. Predictors of early mortality in young adults after intracerebral hemorrhage. Stroke 2014; 45(8): 2454-6.
21. Poon MT, Fonville AF, Al-Shahi SR. Long-term prognosis after intracerebral haemorrhage: Systematic review and meta-analysis. J Neurol Neurosurg Psychiatry 2014; 85(6): 660-7.