Hematoma Expansion Predictors: Laboratory and Radiological Risk Factors in Patients with Acute Intracerebral Hemorrhage: A Prospective Observational Study

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Background: Intracerebral hemorrhage (ICH) is considered a devastating neurologic emergency and carried a higher morbidity and mortality rates. Early hematoma expansion (HE) is considered one of the poor prognostic factors after ICH. Consequently, determination of the possible risk factors for HE could be effective in early detection of high-risk patients and hence directing management course aiming to improving ICH outcome. *Methods:* One-hundred and thirty-six spontaneous ICH patients were included and prospectively evaluated for the presence of HE. Demographic, laboratory, and certain radiological factors were studied and compared between those with HE and those without, the in-hospital mortality rates were assessed as well. *Results:* HE was observed in 30% of the studied cohort, those who developed HE had more neurologic impairment (Glasgow coma scale, median 9; National Institute of Health Stroke Scale, median 34), and higher in-hospital mortality rate (53.6%) than those without HE. HE was related to the presence of higher red blood cell distribution width (RDW), reduced total cholesterol, low-density lipoprotein-C (LDL-C), and Ca levels. Among the radiological factors, hematoma density (heterogeneous), and shape (irregular) are highly related to the occurrence of HE. The computed tomography angiography (CTA) spot sign among patients with ICH was associated with HE development. *Conclusions:* Abnormal RDW; low cholesterol, LDL, and Ca level; heterogeneous density, irregular shape hemorrhage, and presence of CTA spot sign were associated with the development of HE in the setting of spontaneous ICH.

Key Words: Intracerebral hemorrhage—hematoma expansion—predictors—spot sign—red cell distribution width—low-density lipoprotein

Introduction

Spontaneous intracerebral hemorrhage (ICH) accounts for 10%-20% of all strokes, with a high rate of mortality and morbidity among survivors in the acute phase.[1] Important etiologic factors in the elderly population in whom ICH is more common are hypertension, amyloid angiopathy, and anticoagulation.[2,3] Early hematoma growth occurs in ≈20%-40% of spontaneous ICH patients and is a major determinant of early deterioration and poor clinical outcome.[4]

Hematoma size on hospital admission has been shown to be one of the most important predictors of 30-day mortality.[5] Hematoma expansion (HE) is highly predictive of neurological deterioration[6–8] and is an independent predictor of mortality and functional outcomes.[9] Consequently, identifying reliable clinical and radiographic predictors of HE are needed. Owing to their importance

Abbreviations: ICH, intracerebral hemorrhage; HE, hematoma expansion; BP, blood pressure; GCS, Glasgow coma scale; NIHSS, National Institute of Health Stroke Scale; LDL, low-density lipoprotein; HDL, high-density lipoprotein; EHG, early hematoma growth; CTA, computed tomography angiography; RDW, red cell distribution width; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ESR, erythrocyte sedimentation rate

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as prognostic factors, ICH volume and expansion have been targeted by 2 different therapeutic interventions assessed in clinical trials: administration of activated recombinant factor VII[10,11] and aggressive blood pressure (BP) lowering.[12,13]

So, it will be particularly important to better predict which patients are most or least likely to benefit from such treatments.[10] Although the incidence of serious adverse events has been shown to be low at less than 1%, factor VIIa–related thrombotic complications can occur,[14] and it would be desirable to avoid treating patients in whom HE is unlikely. Also, attenuated hematoma growth has also been suggested in an acute BP reduction trial. Hence, hematoma growth is a key therapeutic target in ICH therapy.[12]

Patients and Methods

Patient Selection and Data Collection

From January 2017 to May 2018, we prospectively evaluated consecutive patients with acute primary ICH admitted to our emergency room within 12 hours from symptoms onset.

Patients aged more than or equal to 18 years with primary ICH were eligible for entry. The patients were diagnosed by baseline computed tomography (CT) within 6 hours after onset of symptoms. Patients with secondary causes of ICH, including underlying aneurysm, vascular malformation, dissection, or tumor, head trauma, venous infarction, or hemorrhagic transformation of ischemic infarction, and patients who underwent surgical evacuation or craniectomy before follow-up CT were excluded.

Clinical Assessment

We retrieved baseline clinical and demographic information, including age, sex, the time to baseline CT scan, comorbid conditions; including history of hypertension, atrial fibrillation, diabetes mellitus, dyslipidemia or prior ICHs; medications used on admission such as antiplatelet agents, anticoagulants, and statins.

On admission, systolic and diastolic blood pressure, Glasgow coma scale (GCS) score, and National Institute of Health Stroke Scale (NIHSS) score were obtained for all patients. GCS score, NIHSS score, and ICH volume at baseline were used as markers of ICH severity.

Laboratory Parameters

The following laboratory tests were performed on admission: complete blood count, serum glucose, creatinine, serum calcium, prothrombin time, activated partial thromboplastin time. Serum albumin, total cholesterol, low-density lipoprotein (LDL-cholesterol), high-density lipoprotein (HDL-cholesterol), and triglyceride levels were determined in blood samples obtained on admission. The study protocol was approved by the local ethics committee.

Radiologic Data

All patients underwent 2 cranial CT scans: an initial CT scan on admission (<6 hours), and at 24 hours from symptoms onset (follow-up CT scan). All CT scans were performed according to the Radiology Department protocol, with an image matrix of 340_340, 1.5-mm-slice thickness. The initial CT scan was reviewed to identify ICH location (deep, lobar, pontine, cerebellar, or other), hematoma volume (ABC/2 method), midline shift (>10 mm displacement of septum pellucidum from the midline), and intraventricular extension. In this study, we measured the volumes of intraparenchymal hematomas excluding intraventricular hematomas whatever the increase its volume and growth due to difficulties in differentiation between growth and diffusion of a hematoma in the intraventricular space and difficulties in measuring the real volumes of hematomas in the cerebrospinal fluid.[15] The ICH volumes of the initial and follow-up CT scans were calculated using the formula ABC/2. Primary outcome was early hematoma growth, defined as an absolute growth greater than 12.5 cm^3 or relative growth greater than 33% from initial to follow-up CT.[16,17]

Hematomas were also classified by shape into the following two types; round "round and smooth margins" and irregular "irregular and multinodular margins". Also, hematomas were classified by the density of the clot into homogeneous and heterogeneously dense hematomas.[18] Unless contraindicated, imaging of the intracranial vasculature by CT angiography (CTA) was performed to exclude secondary causes of ICH. Also, to evaluate the presence or absence of the CTA spot sign (Fig. 1). This sign which was defined as 1 or more 1- to 2-mm foci of enhancement within the hematoma on CTA images that has been discontinuous from the adjacent normal or abnormal blood vessels.[19]

Statistical Analysis

Continuous variables were expressed as the mean ± SD and median (range) and the categorical variables were expressed as a number (percentage). Continuous variables were checked for normality by using Shapiro-Wilk test. Mann-Whitney U was used to compare 2 groups of none normally distributed data. Percent of categorical variables were compared using chi-square test or Fisher's exact test when was appropriate. All tests were 2 sided. *P* value less than 0.05 was considered statistically significant. All data were analyzed using Statistical Package for Social Science for windows version 20.0 (SPSS Inc., Chicago, IL) & MedCalc for windows version 13 (MedCalc Software bvba, Ostend, Belgium).

Results

One hundred and thirty-six patients with spontaneous ICH were included in this study (108 males and 28 females) with a mean age was 61.15 ± 10.13 years.

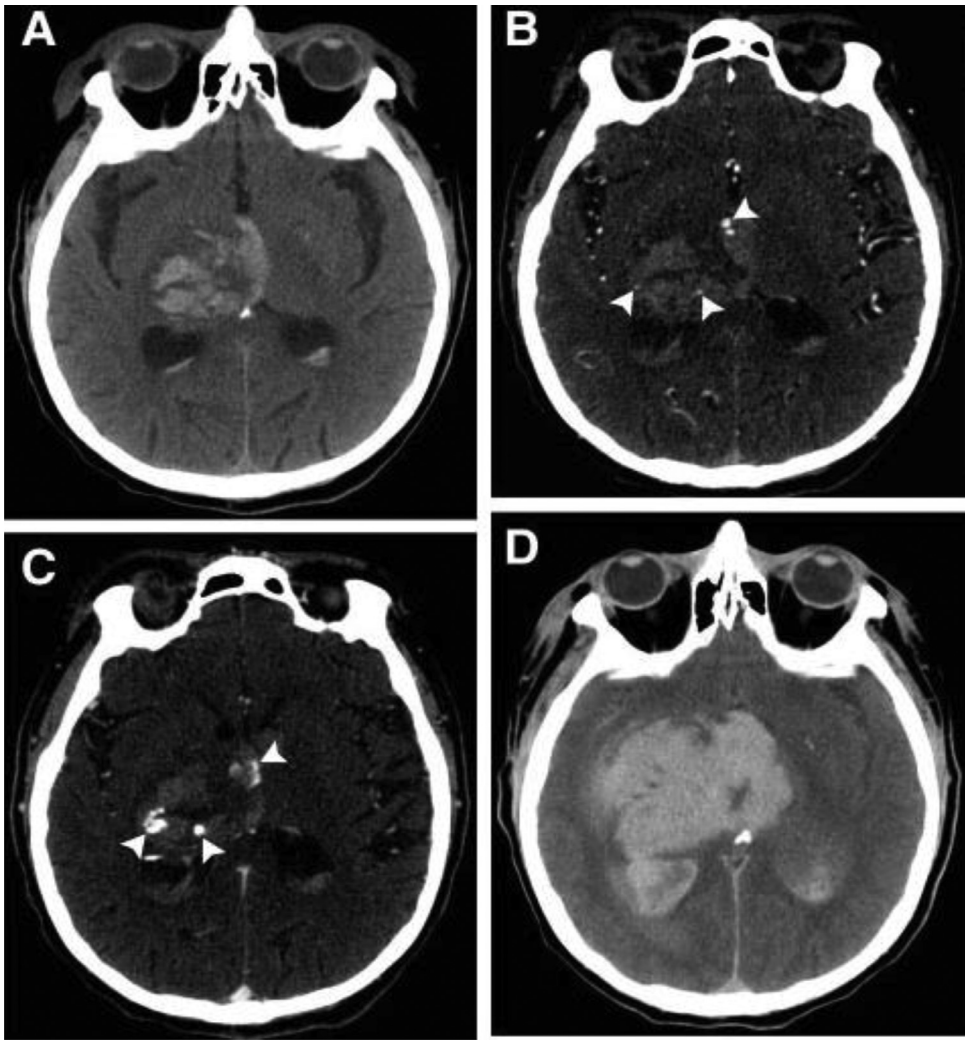

Figure 1. *A 67-year-old man on warfarin therapy for atrial fibrillation, also he was on daily aspirin intake presented with sudden syncope followed by prolonged coma (INR on admission was 2.7). (A) Non-enhanced CT demonstrates a right thalamic intracranial hematoma "ICH" (24 mL) with mild contralateral midline shift, and associated intraventricular hemorrhage "IVH". (B) Axial CTA source image in spot windows demonstrates 3 foci of contrast pooling within the ICH (arrowheads), consistent with spot signs. The largest spot sign measures 10 mm in maximum axial dimension. (C) Delayed CTA acquisition 48 seconds after the first-pass CTA shows that the spot signs increased in volume and changed in morphology (arrowheads). (D) NCCT 8 hours after the baseline CTA demonstrates marked interval expansion of both the ICH (94 mL) and IVH. The patient died shortly after the follow-up NCCT.*

Baseline hematoma volume was 27.84 ± 22.21 cm. Fifty-eight (43%) patients demonstrated an irregular-shaped hemorrhage and 55 patients (41%) had ICH with heterogeneous density while CTA spot sign was demonstrated in 24 patients (17.6%). HE was observed in 41 patients (30.1%; Table 1). No significant difference was observed between patients who developed HE and those without regarding the demographic, premorbid drug history, or vascular risk factors (Table 2). Patients with HE had a median GCS of 9 (range, 4-14) and showed more neurologic deficits according to NIHSS scale (median, 34) than those in the nonexpander group (median, 9). Patients who developed HE showed a higher rate of in-hospital mortality than those without expansion (22 patients (53.6%) versus 6 (6.3%), respectively (Table 3).

Among the evaluated laboratory parameters (Table 4) in the present study, patients in the HE group showed a significantly higher red cell distribution width (RDW, 15.6 ± 1.62), low total cholesterol (160.9 ± 24.89 mg/dL), low LDL-C (122.67 ± 27.59 mg/dL), and low serum Ca (8.8 ± 2.3 mg/dL) than those without HE (RDW, 14.26 ± 1.05; total cholesterol, 194 ± 57 mg/dL; LDL, 142 ± 58 mg/dL, and Ca, 10.9 ± 1.7 mg/dL).

Relation of HE to radiological parameters is showed in Table 5. The frequency of HE was significantly higher in those with ICH of heterogeneous density (32 cases), irregular-shaped hematoma (33 cases) than those with *homogeneous* density (9 cases) and regular-shaped hematoma (8 cases). Patient who developed HE had higher frequency of CTA spot sign (21 cases, 87%) than those nonexpanders (3 cases, 12.5%).

Table 1. *Baseline characteristics and potential baseline factors of the studied group*

Baseline characteristics	All patients ($N = 136$)	
Age, y, mean ± SD	61.15 ± 10.13	
Male sex, *n* (%)	108	(79.4%)
Antiplatelet pretreatment, *n* (%)	25	(18.4%)
Statin pretreatment, *n* (%)	32	(23.5%)
GCS, median (range)	12 (4-15)	
NIHSS, median (range)	12 (2-42)	
mRS, median (range)	3 (1-6)	
SBP, mm Hg, mean ± SD	178.38 ± 25.74	
DBP, mm Hg, mean ± SD	104.41 ± 15.85	
Glucose, mg/dL, mean ± SD	157.34 ± 35.71	
Creatinine, mg/dL, mean ± SD	1.12 ± 0.64	
Hemoglobin, g/dL, mean ± SD	14.55 ± 1.76	
Leukocyte count, 10^3 u/L, mean ± SD	12.32 ± 4.51	
Platelet count, 10^3 u/L, mean ± SD	194.92 ± 47.72	
RDW, mean ± SD	14.66 ± 1.38	
PT, s, mean ± SD	12.68 ± 2.01	
INR, mean ± SD	1.06 ± 0.16	
Albumin g/dL, mean ± SD	3.93 ± 0.62	
Calcium, mg/dL mean ± SD	10.1±2.5	
Total cholesterol, mg/dL, mean ± SD	184.42 ± 49.54	
LDL-C, mg/dL, mean ± SD	136.58 ± 43.79	
HDL-C, mg/dL, mean ± SD	42.87 ± 12.33	
Triglycerides, mg/dL, mean ± SD	119.58 ± 52.68	
ESR, mm/h, mean ± SD	22.76 ± 20.58	
ICH volume, mL, mean ± SD	27.84 ± 22.21	
Intraventricular extension, *n* (%)	61	(44.9%)
ICH location, lobar, *n* (%)	37	(27.2%)
ICH shape, regular, *n* (%)	78	(57.4%)
ICH density, homogenous, *n* (%)	81	(59.6%)
CTA spot sign, *n* (%)	24	(17.6%)
Hematoma expansion, *n* (%)	41	(30.1%)

Abbreviations: CTA, CT angiography; DBP, diastolic blood pressure; ESR, Erythrocyte sedimentation rate; GCS, Glasgow coma scale; HDL, high-density lipoprotein; LDL, low-density lipoprotein; mRS, modified rankin scale; NIHSS, National Institute of Health Stroke Scale; RDW; red cell distribution width; SBP, systolic blood pressure.

Table 2. *Comparison between patients with and without hematoma expansion regarding demographic and vascular risk factors*

Variables	All patients ($N = 136$)	Hematoma expansion				*P* value
		No ($N = 95$)		Yes ($N = 41$)		
		No.	%	No.	%	
Age, y, mean ± SD		60.60 ± 8.07		62.43 ± 13.82		.239*
Gender						
Male	108	79	73.1	29	26.9	.100§
Female	28	16	57.1	12	42.9	
Hypertension						
Absent	38	25	65.8	13	34.2	.520§
Present	98	70	71.4	28	28.6	
Antiplatelet drugs						
Not used	111	77	69.4	34	30.6	.796§
Used	25	18	72	7	28	
Anticoagulant						
Not used	132	91	68.9	41	31.1	.315§
Used	4	4	100	0	0	

Qualitative data were expressed as a number (percentage).
*Mann Whitney U test.
§Chi-square test; $p < 0.05$ is significant.

Table 3. *Comparison of clinical data and in-hospital mortality rate between patients with and without hematoma expansion*

Variables	Hematoma expansion				*P* value
	No (*N* = 95)		Yes (*N* = 41)		
	No.	%	No.	%	
SBP, mm Hg, mean ± SD	178 ± 22.13		179.26 ± 32.03		.990*
DBP, mm Hg, mean ± SD	104.31 ± 16.67		104.63 ± 13.98		.770*
Glucose, mg/dL, mean ± SD	160.77 ± 36.34		149.39 ± 33.25		.098*
GCS, median (range)	13 (8-15)		9 (4-14)		<.001*
NIHSS, median (range)	9 (2-39)		34 (2-42)		<.001*
In-hospital mortality	6	(6.3%)	22	(53.6%)	−<.001§

Abbreviations: DBP, diastolic blood pressure; GCS; Glasgow coma scale; NIHSS, National Institute of Health Stroke Scale; SBP, systolic blood pressure.

Qualitative data were expressed as a number (percentage).

*Mann Whitney U test.

§Chi-square test; p< 0.05 is significant.

Discussion

Spontaneous ICH is considered the deadliest stroke subtype, accounts for approximately 15% of all acute strokes with a higher mortality and disability rates.[20,21] Predictors of poor outcome in patients with ICH include location and baseline hematoma volume but not all are modifiable. HE is a further predictor of poor outcome that could be a potentially modifiable marker.[22] The frequency of HE differs strongly across different studies. In the present study, HE was recorded in 41 (30.1%) patients of the studied cohort. A nearly similar frequency of 31.9%,[23] 31.7%,[24] and 25.8%[25] were recorded while lower rates of 14%[15] and 19.1%[26] were recorded by others. However, higher prevalence of 40%, 50% and 73% were recorded by Dowlatshahi et al,[27] Flibotte et al,[28] and Davis et al,[29] respectively. These differences in prevalence could be attributed to variations in definition of HE, time from symptom onset to initial CT and assessment techniques. According to Fisher,[30] HE not only attributed to the originally ruptured vessel, but also caused by secondary mechanical shearing of the neighboring vessels (Avalanche model).

In this study, several risk factors for HE had been studied including clinical, laboratory, and radiological factors. No relation was observed between the occurrence of HE and any of demographic or vascular risk factors.

Laboratory Parameters and HE

In the current study, no significant difference was observed between hematoma expanders and nonexpanders regarding platelet count but compromised platelet function could play a role in HE in this study as a low serum calcium level was demonstrated in those with HE

Table 4. *Comparison of laboratory data between patients with and without hematoma expansion*

Variables	Hematoma expansion		*P* value*
	No (*N* = 95)	Yes (*N* = 41)	
RDW, mean ± SD	14.26 ± 1.05	15.60 ± 1.62	<.001
Platelet count, 10^3 u/L, mean ± SD	188.84 ± 45.49	185.85 ± 51.98	.137
Leukocyte count, 10^3 u/L, mean ± SD	12.51 ± 4.80	11.87 ± 3.78	.419
Total cholesterol, mg/dL, mean ± SD	194.57 ± 53.99	160.9 ± 24.89	<.0001
Triglycerides, mg/dL, mean ± SD	123.86 ± 54.91	109.67 ± 46.22	.339
LDL-C, mg/dL, mean ± SD	142.58 ± 48.06	122.67 ± 27.59	.003
HDL-C, mg/dL, mean ± SD	42.52 ± 12.82	43.65 ± 11.23	.607
PT, Sec. mean ± SD	12.76 ± 2.21	12.51 ± 1.47	.862
INR, mean ± SD	1.06 ± 0.18	1.04 ± 0.11	.486
Creatinine, mg/dL, mean ± SD	1.15 ± 0.68	1.07 ± 0.55	.427
AST, u/L, mean ± SD	25.6 ± 12.9	24.04 ± 16.49	.592
ALT, u/L, mean ± SD	20.83 ± 8.46	20.06 ± 9.85	.665
Albumin g/dL, mean ± SD	3.89 ± 0.67	4.01 ± 0.47	.233
ESR, mm/h, mean ± SD	23.58 ± 23.67	21.85 ± 10.35	.166
Calcium, mg/dL, mean ± SD	10.9 ± 1.7	8.8 ± 2.3	.000

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ESR, erythrocyte sedimentation rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RDW, red cell distribution width.

Qualitative data were expressed as a number (percentage).

*Mann Whitney U test.

Table 5. *Comparison between patients with and without hematoma expansion regarding radiological data*

Variables	All patients ($N = 136$)	Hematoma expansion				P value
		No ($N = 95$)		Yes ($N = 41$)		
		No.	%	No.	%	
Time to initial CT, hours, mean ± SD		5.87 ± 2.06		2.39 ± 1.33		<.001*
initial hematoma volume, mean ± SD		27.19 ± 23.58		29.34 ± 18.84		.144*
ICH location						
Lobar	37	25	67.56	12	32.43	.580
Deep	81	59	72.8	22	27.16	
Brainstem	18	11	61.11	7	38.89	
ICH shape						
Regular	78	70	89.7	8	10.3	<.001§
Irregular	58	25	43.1	33	56.9	
ICH density						
Homogeneous	81	72	88.9	9	11.1	<.001§
Heterogeneous	55	23	41.8	32	58.2	
Ventricular extension						
Absent	75	57	76	18	24	.83
Present	61	38	62.3	23	37.7	
CTA spot sign						
Absent	89	82	92.1	7	7.9	<.001§
Present	24	3	12.5	21	87.5	
Not available	23	10	43.5	13	56.5	

Qualitative data were expressed as a number (percentage).
*Mann Whitney U test.
§Chi-square test; $p < 0.05$ is significant.

than those without HE. In concordant with ours, Morotti et al in 2016[31] and Inoue et al in 2013[32] had demonstrated a strong association between low serum Ca level and HE in the setting of spontaneous ICH. Platelets have an essential role in the hemostatic process, through a complex series of responses.[33]

Ca^{++} is a common second messenger for most signaling pathways in platelets and plays an important role in platelet activation and aggregation and the thrombus formation.[34] In addition, serum Ca^{++} levels are directly involved in clotting cascade.[35,36] Therefore, patients with low Ca^{++} levels may have impaired hemostatic mechanisms.[37,38] Serum Ca^{++} also seems to play a role in inducing arterial relaxation and secondary BP reduction through activation of perivascular receptors.[39] Therefore, lower levels of Ca^{++} may lead to HE through elevated BP.

In our study, RDW is significantly higher in those with HE than those without. This is agreed with Altintas et al in 2015[40] who demonstrated that a greater admission RDW value was independently associated with hypertensive hematoma growth in the first 12 hours. Patel et al[41] argued the association between elevated RDW and bleeding to the presence of multiple comorbidities such as hypertension, diabetes, and previous stroke in those patients, impaired serum antioxidant level as well as higher level of inflammatory biomarkers[42].

Abnormal lipid profile has been previously demonstrated in both ischemic and hemorrhagic strokes. In the setting of ICH, it was reported that low levels of LDL-C[43] and total cholesterol[44] were associated with increased risk of ICH and hematoma growth[23,45] as well as higher mortality after ICH.[46,47] Similarly, our present study demonstrated lower levels of LDL-C and total cholesterol in hematoma expander patients than in those non expanders.

This relationship between LDL-C and HE could be attributed to the role of serum cholesterol levels for maintaining vessel wall integrity. Development of smooth muscle cell necrosis within the media of vessel wall was observed in association with lower cholesterol levels, thus lessening the resistance to vessel wall rupture.[48] In addition, platelet agreeability was modified by cholesterol levels by their action on the platelet activating factor, so that lower cholesterol levels may decrease platelet aggregation consequently, increasing the risk of ICH growth.[49,50]

Radiological Parameters and HE

The timing of imaging is essential when assessing HE as expansion represents an intermediate phase between initial hematoma volume and the final (stabilized) volume.[22] In the current study, hematoma expanders had shorter time elapsed between the symptom onset and the initial CT in comparison to nonexpanders. This was in agreement with many previous studies.[51-53] In another prospective study,[54] it was reported that HE could be seen within the first 8 hours after symptom onset in the group of

patients, who were presented a final clinically relevant HE (>12.5 mL) on 24 hours follow-up CT scan. Even despite the fact that the vast majority of the HE is observed in the first hours after stroke onset, others reported or the possibility for HE to take place later on and up to 24 hours.[7,55] HE is a dynamic process, not only bleeding from the originally ruptured vessel, but there is a following repeated bleeding episodes from multiple secondary ruptured vessels in the perihematoma zone exposed to pressure and ischemia by the hematoma mass effect.[54]

Patients with ICH frequently presented with hematomas in various shapes either regular or irregular and with heterogeneous attenuation on noncontract CT. It was proposed that this could potentially predict the risk of HE due to the fact that this may signify on-going bleeding.[54]

In the current study, the incidence of HE was significantly higher in patients with irregular shaped than in those with regular hematomas. This finding was consistent with two earlier Japanese studies conducted by Fujii et al in 1994[56] and 1998[15] who reported that irregular-shaped hematoma was an independent predictor of hematoma growth and they mentioned that this irregularity indicate multiple leaking vessels feeding the hematoma. Different from our results, others [18,57,58] did not confirm this association between irregular-shaped hematoma and HE.

Regarding hematoma density, it is either *homogeneous* or *heterogeneous*. Heterogenicity refers to a mixture of hypoattenuation and hyper attenuation within the hematoma on noncontrast CT and represents on-going bleeding, it originally descends from observations of patients with epidural hematomas.[59] It was observed that the finding of a zone of hypoattenuation within the hyperattenuated hematoma correlated to active bleeding.[60] In the current study, presence of heterogeneous hematoma on the initial noncontrast CT was associated with a higher frequency of HE than in those with homogenous hematoma. This was in line with the study conducted by Barras et al in 2009[18] who reported that hypoattenuated foci on the initial CT scan predicted HE that was confirmed later by others.[57]

Another determinant for HE is the spot sign which is tiny enhancing foci within the hematoma seen at computed tomography angiography.[61] The CT angiography (CTA) spot sign has emerged recently as an independent predictor of HE, and could be a possible tool in guiding therapies in both research and clinical care.

In the present study, spot sign was recorded in 17% of our cohort. Spot sign is considered as a marker of active bleeding and was reported to be a strong risk factor for HE and unfavorable outcome in many previous studies.[61–64] In line with these previous data, the present study showed that the frequency of CTA spot sign was significantly higher in hematoma expanders than in those without HE. Consequently, the presence of spot sign in the present study was associated with HE and it is considered a risk factor for HE occurrence among our cohort.

Hematoma Expansion and In-hospital Mortality

ICH carried a poor prognosis than ischemic stroke. It is considered a major cause of morbidity with a mortality rate of 54% at 1 year with half of the events related to case fatality occurring in the first few days after admission.[20] Previously, it was demonstrated that HE strongly influence mortality with hazard ratio of mortality reaches 5% with every 10% increase in ICH volume.[65]

In the present study, estimation of in-hospital mortality showed a higher mortality rate in the HE group (53.6%) than in those without HE (6.3%). Keeping with this observation, many previous studies had demonstrated a strong relationship between HE and bad outcome as well as mortality after ICH on the other hand.[27,52,66]

HE restriction might be an important future strategy for limiting final hematoma volume, saving brain tissue – and improving survival and functional outcome after ICH. Thus, prediction and effective observation of postadmission HE is of essential clinical importance.

Several prediction scores have been created and validated to identify those at risk of HE. They depend on many parameters either clinical or radiological aiming to early prediction of HE and hence help in early intervention to improve patient outcome. A 9-point clinical prediction score assess four clinical predictors including warfarin use, time to initial CT, baseline ICH volume, and CT angiography spot sign.[26] The high score (4-9) has significant positive correlation with greater risk of HE, In-hospital, and 3-month mortality.[30] Similarly, a 24-point clinical prediction algorithm (BRAIN)[67] was derived and validated, with the score items similar to the prediction score with addition of recurrent ICH and IVH. PREDICT A and B[68] scores include GCS or NIHSS, respectively.

In conclusion, we observed an association between the occurrence of HE and many laboratory and radiological parameters. Moreover, HE strongly influences the in-hospital mortality rates.

Recommendation

It is advisable to early identify those patients at risk of HE and should be carefully monitored during their hospital stay to improve their functional outcome and minimizing mortality. Further studies are needed to study the effect of modification of these risk factors ahead of presentation or after with follow up these patients.

Authors' Contributions

T.H.M.E., N.S., A.A.B. carried out the work. T.H.M.E., N.S. developed the research plan, selected and collected the patients, performed the clinical examination of the

patients and their diagnosis, gathered clinical data, and prepare and write the manuscript, designed the study. A. A.B. had done the Radiological work of the study and was involved in the interpretation of the imaging study. All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors read and approved the final version to be published.

Ethics Approval and Consent to Participate

The study was approved from the Institutional Ethics Committee of the Faculty of Medicine, Zagazig University. Written informed consent was obtained from all study participants after explaining the details and benefits as well as risks to them. Surrogate consent from the patient's legal guardian or designated health proxy was permitted in cases where the patient did not have decision-making capacity.

Competing Interests

The authors declare that they have no competing interests.

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