THE OUTCOME PREDICTION USING NON-CONTRAST COMPUTED TOMOGRAPHY SCAN AND COMPUTED TOMOGRAPHY ANGIOGRAPHY SCAN IN ACUTE HEMORRHAGIC STROKE

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ABSTRACT

Background

Intracerebral haemorrhage (ICH) outcome depends on hematoma volume, location, and expansion.

Objectives

To assess the validity of neuroimaging signs for predicting the prognosis of patients with acute ICH in our population.

Patients and Methods

A prospective cohort study was performed on 90 patients with acute ICH admitted to Shar Hospital from March to October 2019. Inclusion criteria were ages of ≥18 years and spontaneous ICH, and exclusion criteria were trauma, brain tumour, and secondary ICH. Demographic features were recorded. Blackhole, swirl, island, Blend and spot signs, ICH location and volume, and ICH score were assessed by non-contrast computed tomography (CT) scan and CT angiography. Glasgow coma scale (GCS) and modified Rankin scale were used to assessing patients' outcomes

Results

Except for the ages of patients (p-values=0.01), other demographic characteristics had no significant associations with the expansion of hematoma and outcome. Modified Rankin Scale, GCS, and hematoma location and volume had statistically significant associations with hematoma expansion and outcome. Further, strong sensitivity of black hole (90.9%) and spot (92.8%) signs, strong specificity of Blend (92.6%) and spot signs (97.1%), substantial positive predictive value for spot sign (92.8%), substantial negative predictive value was for all signs. In addition, substantial accuracy of spot sign (95.8%), were found. Also, significant associations for all the signs, except Blend, with hematoma expansion were found.

Conclusion

It is better to use neuroimaging signs, at least the signs found on non-contrast CT scans, all together in clinical practice.

Keywords: *Blackhole sign; Blend sign; Intracerebral haemorrhage (ICH); Intracerebral haemorrhage (ICH) score; Island sign; Spot sign; Swirl sign.*

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INTRODUCTION

Intracerebral haemorrhage (ICH) is caused by ruptures of small arteries secondary to hypertension and other vascular abnormalities [1-3]. ICH incidence is variable across countries and ethnicities; it accounts for 8-24% of all strokes [4] .The prevalence of primary ICH in low/middle-income countries was twice its prevalence compared to high-income countries, 22 vs 10 per 100,000 person-year [4]. The incidence of ICH increases with ageing, and for all ages, the annual incidence rate is higher in men than women [5-6]. Also, the fatality rate of ICH is approximately 40% in the first month and 54% in the first year, and only 12-39% of patients achieve long-term functional independence [7].

The outcome of ICH depends on hematoma volume, location, and an extension to ventricles [8]. However, ICH leads to more severe disability and higher mortality than ischemic stroke [8].

Although some ICH will develop during sudden emotional stress or exertion, most occur during daily activities [9].The initial injury of ICH is by physical disruption of brain parenchyma due to compression[10-11]. However, the secondary injury is related to the clotting cascade, especially thrombin, after haemoglobin breakdown and endothelial damage [12]. Further, the risk factors that could be modified are hypertension, smoking, alcohol consumption, low triglycerides, decreased low-density lipoprotein, and drugs, including antithrombotic, anticoagulants, and sympathomimetics [13-15].

However, the non-modifiable risk factors include male gender and old age [13-15]. The clinical presentations vary by the location and size of ICH; besides, the main symptoms of ICH are headache, nausea, vomiting, decreased level of consciousness, sensorimotor deficits [16-19]. Usually, the neurological symptoms deteriorate in minutes to hours [9]. Further, the neurological deterioration, which occurs before and during hospital admission, indicates worsening of oedema or early hematoma enlargement [4] about 15–23% of patients have hematoma expansion and neurological deterioration in the first few hours [20].

The poor prognostic factors are as follows: old age, large hematoma volume, intraventricular extension, infratentorial location, hematoma expansion, contrast extravasation on computed tomography (CT), angiography (spot sign), and the use of anticoagulation [4, 21].

Rapid diagnosis is essential for the appropriate management and better functional results. In addition to the neurological history and examination, rapid neuroimaging with a non-contrast head CT scan is highly specific and sensitive for ICH and is essential to early diagnosis [22]. CT scan will reveal not only the location and size of the ICH but also the mass effects, intraventricular extension, hydrocephalus, and early signs of herniation [22-23].

MRI is sensitive as CT in determining the presence of haemorrhage but rarely offers additional information in the acute setting [24]. In addition, the time required for MRI can be detrimental due to a high risk of deterioration during the first few hours [24].

Computed tomography (CT) angiogram is very sensitive for identifying associated vascular abnormalities and contrast extravasation (spot sign) [25]. The spot sign in CT angiography indicates ongoing bleeding within an ICH and increased mortality [26]. Further, CT angiography is quick, inexpensive, and safe; the radiation exposure is similar to a chest or abdominal CT scan, while there is undoubtedly a financial cost to performing CT angiography, this will vary by system and is difficult to quantify universally [27].

However, performing a CT angiography is minimal compared to the costs of untreated stroke or the costs of inappropriate transportation for endovascular therapy [27].

Other neuroimaging signs indicating hematoma expansion are swirl, black hole, Blend, and island non-contrast CT scan [28-32]. Besides, a swirl sign indicates an active perioperative bleeding and unclotted blood, and a black hole sign is a swirl sign encapsulated within the haemorrhage with a clear border [28-30].

Further, a Blend sign in hematoma is a mixture of a hypoattenuating region with a nearby hyperattenuating region with a clear border [31]. Also, an island sign describes the extreme margin irregularities of the hematoma [32].

In the current study, we aimed to assess our population has predicted prognostic factors of patients with acute hemorrhagic stroke on plain non-contrast CT scan and CT angiography.

PATIENTS AND METHODS

A prospective cohort study was performed on 90 patients who had an acute ICH and were admitted to the Emergency Department of Shar Hospital, Sulaimani city, Kurdistan Region, Iraq. The study was performed from March to October 2019. Further, a formal acceptance letter was obtained from Shar Hospital before starting the study. Written informed consent was taken from the patients' families for their inclusion in this study.

The inclusion criteria were 18 years or older, and spontaneous ICH was confirmed on a non-contrast CT scan. Besides, the exclusion criteria were patients who had head trauma, brain tumour, or secondary ICH from a hemorrhagic transformation of ischemic infarction.

The demographic features of the patients, including age, gender, residency, occupation, marital status, body mass index (BMI), smoking and alcohol consumption habits, and past medical history of hypertension and diabetes mellitus (DM), were recorded. A non-contrast CT scan of the head was performed for all the patients. However, CT angiography was performed for only 48 (53.3%) patients due to their renal impairments. The neuroimaging signs of a black hole, swirl, island, Blend and spot signs, location of ICH, and ICH score were assessed by the non-contrast CT scan and CT angiography. Also, the ellipsoid technique (ABC/2, when A = length, B = width, and C = height) on a non-contrast CT scan was used to evaluate hematoma volume (33). Further, the Glasgow coma scale (GCS) and modified Rankin scale (scores of 0-6) (34) were used to assessing patients' outcomes.

The (IBM SPSS Statistics version 25) was used to analyze the data, and both descriptive and inferential statistics were used. In the descriptive statistics, means and standard deviations (SD) were used for continuous variables, and frequencies and percentages were used for categorical variables. Also, the Fisher Exact Test, Paired-Samples T-Test, Chi-Square test, and one-way ANOVA were used to determine the differences between groups. Further, a p-value of ≤0.05 was considered a statistically significant association.

RESULTS

The mean ± SD (standard deviation) of the ages of the patients were 64.3±16.1 years with a male: female ratio of 1.9:1. Further, the urban residencies of the patients were more common than rural residencies; (64, 71.1%) vs (26, 28.9%), and the occupations of the patients were as follows: public servant (36, 40%), housewife (27, 30%), Retired (20, 2.2%), and self-employed (7, 7.8%). Also, most of the patients (81, 90%) were married; however, few of them (6, 6.7%) were single and divorced (3, 3.3%).

The mean ± SD of BMI was 27.7±3.4 Kg/m2. The history of patients was as follows: smoking (64, 71.1%), alcohol consumption (25, 27.8%), hypertension (62, 68.9%), and DM (54, 60%).

The mean ± SD of GCS, modified Rankin scale, hematoma volume detected on non-contrast CT scan, and ICH score at admission were 8.4 ± 2.8, 3.9±0.9, 38.3±12.4 ml, and 3.3±0.9, respectively. Besides, the ICH score distribution at presentation was as follows: score 1 (4, 4.4%), score 2 (15, 16.7%), score 3 (29, 32.2%), score 4 (38, 42.2%), and score 5 (4, 4.4%). Also, the ICH scores during the follow-up period, hematoma volume, modified Rankin scale at discharge, and the outcome of the patients are shown in Table 1.

There was a significant association of ages with the outcome of the patients (p-value = 0.01); however, this association was none significant for gender, residency, occupation, marital status, BMI, smoking, alcohol consumption, hypertension, and DM (p-values = 0.06, 0.7, 0.1, 0.5, 0.6, 0.8, 0.6, 0.3, and 0.5, respectively), as shown in Table 2. There were statistically significant associations of GCS, modified Rankin scale, and hematoma volume with the outcome of the patients (p-values = <0.001, 0.007, and 0.001, respectively), as shown in Table 3.

The validity results, extracted from Table 4, of black hole, swirl, Island, Blend, and CT angiography spot signs were as follows: sensitivity (90.9%, 54.5%, 40.9%, 27.3%, and 92.8%, respectively), specificity (32.4%, 70.6%, 72.1%, 92.6%, and 97.1%, respectively), positive predictive value (30.3%, 37.5%, 32.1%, 54.5%, and 92.8%, respectively), negative predictive value (91.7%, 82.8%, 79%, 79.7%, and 97.1%, respectively), and accuracy (46.6%, 66.7%, 64%, 76.7%, and 95.8%, respectively). There was a significant improvement in the modified Rankin scale and ICH score after discharge and three months, respectively, as compared to admission (Table 5). However, no significant difference was observed in hematoma volume in comparison to admission (Table 5). There was a significant association of age with the hematoma expansion (p-value = 0.01); however, no significant associations were found between gender, residency, occupation, marital status, BMI, smoking, alcohol consumption, hypertension, and DM (p-values = 0.1, 0.4, 0.3, 0.1, 0.3, 0.07, 0.3, 0.9, and 0.2, respectively), as shown in Table 6.

Further, our results showed statistically highly significant associations of GCS, modified Rankin scale, and site of the hematoma with the expansion of the hematoma (p-values = <0.001, <0.001, and <0.001, respectively), as shown in Table 7. In addition, there were significant associations between the black hole sign, swirl sign, and island sign with hematoma expansion. However, no significant differences were observed between the Blend sign and hematoma expansion (Table 8).

Table 1. Outcome of patients during follow-up.

Variable		No.	Percent
ICH score after one-month = mean ± SD (2.7 ± 0.9)	1	8	8.9
	2	32	35.6
	3	37	41.1
	4	13	14.4
	5	0	0.0
ICH score after three months = mean ± SD (2.1 ± 0.9)	1	21	23.3
	2	44	48.9
	3	20	22.2
	4	3	3.3
	5	2	2.2
Hematoma volume after 72 hours = mean ± SD (37.9 ± 12.5 ml)	≤30 ml	28	31.1
	>30 ml	62	68.9
Hematoma volume after 5-7 days = mean ± SD (36.8 ± 12.8 ml)	≤30 ml	28	31.1
	>30 ml	62	68.9
Modified Rankin scale at discharge = mean ± SD (3 ± 0.8)	2	29	32.2
	3	30	33.3
	4	31	34.5
	5	0	0.0
Outcome	Died	22	24.4
	Alive	68	75.6
Total		**90**	**100.0**

ICH = intracerebral haemorrhage.

Table 2. Distribution of demographic characteristics according to the outcome.

Demographic characteristics		Outcome		p-values
		Died (%)	Alive (%)	
Age (year)	<40	1 (4.5)	4 (5.9)	0.01*
	40-49	0 (0)	11 (16.2)	
	50-59	0 (0)	14 (20.6)	
	60-69	7 (31.8)	18 (26.5)	
	≥70	14 (63.6)	21 (30.9)	
Gender	Male	18 (81.8)	41 (60.3)	0.06**
	Female	4 (18.2)	27 (39.7)	
Residency	Urban	15 (68.2)	49 (72.1)	0.7*
	Rural	7 (31.8)	19 (27.9)	
Occupation	Housewife	4 (18.2)	23 (33.8)	0.1**
	Self-employed	0 (0)	7 (10.3)	
	Public servant	12 (54.5)	24 (35.3)	
	Retired	6 (27.3)	14 (20.6)	
Marital status	Married	21 (95.5)	60 (88.2)	0.5**
	Single	1 (4.5)	5 (7.4)	
	Divorced	0 (0)	3 (4.4)	
BMI	Normal (18.5-24.99)	5 (22.7)	12 (17.6)	0.6*
	Overweight (25-29.99)	12 (54.5)	44 (64.7)	
	Obese (≥30)	5 (22.7)	12 (17.6)	
Smoking	Yes	16 (72.7)	48 (70.6)	0.8**
	No	6 (27.3)	20 (29.4)	
Alcohol consumption	Yes	7 (31.8)	18 (26.5)	0.6**
	No	15 (68.2)	50 (73.5)	
Hypertension	Yes	17 (77.3)	45 (66.2)	0.3**
	No	5 (22.7)	23 (33.8)	
DM	Yes	12 (54.5)	42 (61.8)	0.5**
	No	10 (45.5)	26 (38.2)	

*** Fisher's exact test; **Chi-square test.**

Table 3. Distribution of clinical scales and hematoma volume according to the outcome.

Variables		Outcome		p-values
		Died (%)	Alive (%)	
GCS	Minor brain injury (13-15)	0 (0)	9 (13.2)	**<0.001***
	Moderate brain injury (9-12)	2 (9.1)	33 (48.5)	
	Severe brain injury (3-8)	20 (90.9)	26 (38.2)	
Modified Rankin scale	2	1 (4.5)	8 (11.8)	**0.007****
	3	0 (0)	19 (27.9)	
	4	12 (54.5)	30 (44.1)	
	5	9 (40.9)	11 (16.2)	
Hematoma volume	≤30 ml	0 (0)	26 (38.2)	**0.001***
	>30 ml	22 (100.0)	42 (61.8)	

***Chi-square test; ** Fisher's exact test. CT = computed tomography.**

Table 4. Validity test results in comparison to the outcome.

Validity tests		Outcome		
		Died (%)	**Alive (%)**	**Total (%)**
Blackhole sign	Yes	20 (30.3)	46 (69.7)	66 (100.0)
	No	2 (8.3)	22 (91.7)	24 (100.0)
Swirl sign	Yes	12 (37.5)	20 (62.5)	32 (100.0)
	No	10 (17.2)	48 (82.8)	58 (100.0)
Island sign	Yes	9 (32.1)	19 (67.9)	28 (100.0)
	No	13 (21.0)	49 (79.0)	62 (100.0)
Blend sign	Yes	6 (54.5)	5 (45.5)	11 (100.0)
	No	16 (20.3)	63 (79.7)	79 (100.0)
Total		22 (24.4)	68 (75.6)	90 (100.0)
CT angiography spot sign	Yes	13 (92.8)	1 (7.2)	14 (100.0)
	No	1 (2.9)	33 (97.1)	34 (100.0)
Total		**14 (29.2)**	**34 (70.8)**	**48 (100.0)**

Table 5. Distribution of Modified Rankin scale according to admission and discharge.

Variables	(Mean ± SD)			p-values
Modified Rankin scale	**Admission**	**Discharge**		<0.001*
	3.9 ± 0.9	3 ± 0.8		
ICH score	Admission	After one month	After three month	<0.001**
	3.2 ± 0.9	2.6 ± 0.8	2.1 ± 0.8	
Hematoma volume	Admission	After 72 hours	After 5-7 days	0.7**
	38.4 ± 12.7	38.1 ± 12.9	37.1 ± 13	

*Paired t-test; **One way ANOVA analysis; SD = standard deviation.

Table 6.Distribution of demographic characteristics according to the hematoma volume.

Variables		No expansion (%)	Expansion (%)	P-values
Age (year)	<40	2 (7.7)	3 (4.7)	0.01*
	40-49	7 (26.9)	4 (6.3)	
	50-59	6 (23.1)	8 (12.5)	
	60-69	7 (26.9)	18 (28.1)	
	≥70	4 (15.4)	31 (48.4)	
Gender	Male	20 (76.9)	39 (60.9)	0.1**
	Female	6 (23.1)	25 (39.1)	
Residency	Urban	17 (65.4)	47 (73.4)	0.4*
	Rural	9 (34.6)	17 (26.6)	
Occupation	Housewife	5 (19.2)	22 (34.4)	0.3**
	Self-employed	3 (11.5)	4 (6.3)	
	Public servant	13 (50.0)	23 (35.9)	
	Retired	5 (19.2)	15 (23.4)	
Marital status	Married	21 (80.8)	60 (93.8)	0.1**
	Single	4 (15.4)	2 (3.1)	
	Divorced	1 (3.8)	2 (3.1)	
BMI	Normal (18.5-24.99)	7 (26.9)	10 (15.6)	0.3*
	Overweight (25-29.99)	16 (61.5)	40 (62.5)	
	Obese (≥30)	3 (11.5)	14 (21.9)	
Smoking	Yes	19 (73.1)	45 (70.3)	0.7**
	No	7 (26.9)	19 (29.7)	
Alcohol consumption	Yes	9 (34.6)	16 (25.0)	0.3**
	No	17 (65.4)	48 (75.0)	
Hypertension	Yes	18 (69.2)	44 (68.8)	0.9**
	No	8 (30.8)	20 (31.3)	
DM	Yes	13 (50.0)	41 (64.1)	0.2**
	No	13 (50.0)	23 (35.9)	

***Fisher's exact test; **Chi-square test; BMI = body mass index; DM = Diabetes mellitus.**

Table 7. Distribution of clinical scales and site of hematoma according to hematoma volume expansion.

Variable		No expansion (%)	Expansion (%)	p-values
GCS	Minor brain injury (13-15)	5 (19.2)	4 (6.3)	
	Moderate brain injury (9-12)	21 (80.8)	14 (21.9)	**<0.001***
	Severe brain injury (3-8)	0 (0)	46 (71.9)	
Modified Rankin scale	2	6 (23.1)	3 (4.7)	
	3	14 (53.8)	5 (7.8)	**<0.001***
	4	6 (23.1)	36 (56.3)	
	5	0 (0)	20 (31.3)	
Site	Lobar	8 (30.8)	45 (70.3)	
	Subarachnoid	4 (15.4)	0 (0)	
	Intraventricular	0 (0)	1 (1.6)	
	Temporal	0 (0)	3 (4.7)	
	Parietal	0 (0)	1 (1.6)	
	Putman	6 (23.1)	0 (0)	
	Thalamus	4 (15.4)	0 (0)	**<0.001****
	Cerebellar	1 (3.8)	4 (6.3)	
	Basal ganglia	0 (0)	1 (1.6)	
	Putman and thalamus	1 (3.8)	0 (0)	
	Lobar and parietal	1 (3.8)	6 (9.4)	
	Lobar and temporal	0 (0)	3 (4.7)	
	Lobar and thalamus	1 (3.8)	0 (0)	

*Chi-square test; **Fisher's exact test; GCS = Glasgow coma scale.

Table 8. Distribution of CT signs according to hematoma volume.

Variable		No expansion (%)	Expansion (%)	p-values
Blackhole sign	Yes	13 (50.0)	53 (82.8)	**0.001***
	No	13 (50.0)	11 (17.2)	
Swirl sign	Yes	1 (3.8)	31 (48.4)	**<0.001***
	No	25 (96.2)	33 (51.6)	
Island sign	Yes	3 (11.5)	25 (39.1)	**0.01****
	No	23 (88.5)	39 (60.9)	
Blend sign	Yes	1 (3.8)	10 (15.6)	**0.1****
	No	25 (96.2)	54 (84.4)	

*Chi-square test; **Fishers exact test.

DISCUSSION

We collected our patients in Shar Hospital in Sulaimani city during eight months period. We aimed to assess neuroimaging signs as predictable prognostic factors for patients with acute ICH on plain non-contrast CT scans and CT angiography in our population. We then chose black hole, swirl, Island, and Blend signs on non-contrast CT scans and spot signs on CT angiography as compared to the outcome of the patients.

Except for the ages of the patients in the current study, other demographic characteristics of the patients did not have significant associations with the expansion of hematoma volume and the outcome. Further, the mean age of the patients was 64.3 years, which was less than the median age (68 years) found by the study of Sporns et al.[35]. Although the study of Sporns et al.[35]did not find a significant association of ages with the outcome (p-value = 0.292), our result showed a significant association of patients' ages with the outcome (p-value = 0.01).

Also, other demographic characteristics in the study of Sporns et al.[35] such as gender, history of hypertension, and DM, same as our findings, were statistically none significant. Further, by considering that an advance in age is a risk factor for developing stroke [36] and due to the continuous conflicts in our region and the Middle East, the age in our population is younger than the age in other populations of the world [37]. Therefore, we consider patients' age as confounding to the neuroimaging signs in our study.

The clinical scales of GCS modified Rankin scale and hematoma location and volume measured by ellipsoid technique on non-contrast CT scan [33] had statistically significant associations with the expansion of hematoma volume and the outcome. Our findings were parallel with the findings found in the study of Sporns et al.[35], and Huynh et al.[38]. It is the fact that the skull is a fixed container, and any addition in its contents will increase pressure on brain tissue; thence, increased hematoma volume of the ICH in the current study had a significant association with the outcome of the patients.

Furthermore, our results showed strong sensitivity of black hole sign and spot sign and strong specificity of Blend and spot signs.

Besides, the positive predictive value was substantial only for spot signs; however, the negative predictive value was substantial for all the signs but with slight differences; Island and Blend signs were less strong than other signs. Also, the accuracy of the spot sign was extreme; however, the accuracy of other signs was weaker. Moreover, there were significant associations of black hole sign, swirl sign, and island sign with hematoma expansion. However, this association was none significant for the Blend sign. Thus, our results were partly agreed with the study of Sporns et al.[35]. They found that black holes and Blend signs had significant associations with the outcome of their patients. Further, they also found hypodensities, which overlapped with the black hole sign due to both hypodensities, on non-contrast CT scan as a least specific sign; however, they found that spot sign on CT angiography as the most sensitivity sign [35].

Although the CT angiography is quick and not costly as compared to the costs of untreated stroke [26-27], there are times that it cannot be performed, e.g., when the patient is contraindicated for its contrast media due to allergy or renal impairment [35]. Likewise, we could perform CT angiography only for 48 (53.3%) of our patients. Thus, other neuroimaging signs on non-contrast CT scans for acute ICH are valuable alternatives when used collectively for predicting hematoma expansion and outcome of the patient [35].

In conclusion, the black hole and spot signs had strong sensitivity, and Blend and spot signs had strong specificity. However, a strong positive predictive value was found only for spot signs. Besides, the negative predictive value was strong for all the signs. Further, strong accuracy was only found for spot signs. Also, significant associations for all the signs with hematoma expansion were found, except the Blend sign. Therefore, it is reasonable to use all the signs altogether, especially when there are contraindications for CT angiography or lack of availability.

Conflict of Interests

The authors had nothing to declare.

REFERENCES

1. Hong KS, Bang OY, Kang DW, Yu KH, Bae HJ, Lee JS, et al. Stroke statistics in Korea: part I. Epidemiology and risk factors: a report from the Korean stroke society and clinical research centre for stroke. J Stroke. 2013; 15(1):2–20.

2. Charidimou A, Gang Q, Werring DJ. Sporadic cerebral amyloid angiopathy revisited: recent insights into pathophysiology and clinical spectrum.J Neurol Neurosurg Psychiatry. 2012; 83(2):124–37.

3. Rost NS, Greenberg SM, Rosand J. The genetic architecture of intracerebral haemorrhage. Stroke. 2008(7); 39:2166–73.

4. An SJ, Kim TJ, Yoon BW. Epidemiology, Risk Factors, and Clinical Features of Intracerebral Hemorrhage: An Update. J Stroke. 2017; 19(1):3-10.

5. Jolink WM, Klijn CJ, Brouwers PJ, Kappelle LJ, Vaartjes I. Time trends in incidence, case fatality, and mortality of intracerebral hemorrhage. Neurology. 2015; 85(15):1318–24.

6. Stein M, Misselwitz B, Hamann GF, Scharbrodt W, Schummer DI, Oertel MF. Intracerebral haemorrhage in the very old: future demographic trends of an ageing population. Stroke. 2012; 43(4):1126–8.

7. Liotta EM, Prabhakaran S. Warfarin-associated intracerebral haemorrhage is increasing in prevalence in the United States. J Stroke Cerebrovasc Dis. 2013; 22(7):1151–5.

8. Keep RF, Hua Y, Xi G. Intracerebral haemorrhage: mechanisms of injury and therapeutic targets. Lancet Neurol. 2012; 11(8):720–31.

9. Manno EM, Atkinson JL, Fulgham JR, Wijdicks EF. Emerging medical and surgical management strategies in the evaluation and treatment of intracerebral haemorrhage. Mayo Clin Proc. 2005; 80(3):420–33.

10. Qureshi AI, Suri MF, Ostrow PT, Kim SH, Ali Z, Shatla AA, et al. Apoptosis as a form of cell death in intracerebral haemorrhage. Neurosurgery. 2003; 52(5):1041–7.

11. Graham DI, McIntosh TK, Maxwell WL, Nicoll JA. Recent advances in neurotrauma. J Neuropathol Exp Neurol. 2000; 59(8):641–51.

12. Xi G, Reiser G, Keep RF. The role of thrombin and thrombin receptors in ischemic, hemorrhagic and traumatic brain injury: deleterious or protective? J Neurochem. 2003; 84(1):3–9.

13. Sturgeon JD, Folsom AR, Longstreth WT Jr, Shahar E, Rosamond WD, Cushman M. Risk factors for intracerebral haemorrhage in a pooled prospective study. Stroke. 2007; 38(10):2718–25.

14. 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. Lancet. 2010; 376(9735):112–23.

15. Chan S, Hemphill JC. Critical care management of intracerebral haemorrhage. Crit Care Clin. 2014; 30(4):699–717.

16. European Stroke Initiative Writing C, Writing Committee for the EEC, Steiner T, Kaste M, Forsting M, Mendelow D, et al. Recommendations for managing intracranial haemorrhage - part I: spontaneous intracerebral haemorrhage. The European Stroke Initiative Writing Committee and the Writing Committee for the EUSI Executive Committee. Cerebrovasc Dis. 2006; 22(4):294-316.

17. Vespa PM, O'Phelan K, Shah M, Mirabelli J, Starkman S, Kidwell C, et al. Acute seizures after intracerebral haemorrhage: a factor in progressive midline shift and outcome. Neurology. 2003; 60(9):1441–6.

18. Fang MC, Go AS, Chang Y, Hylek EM, Henault LE, Jensvold NG, et al. Death and disability from warfarin-associated intracranial and extracranial haemorrhages. Am J Med. 2007; 120(8):700–5.

19. Divani AA, Majidi S, Luo X. The ABCs of accurate volumetric measurement of cerebral hematoma. Stroke. 2011; 42(6):1569–74.

20. Hemphill JC III, Greenberg SM, Anderson CS. Guidelines for the management of spontaneous intracerebral haemorrhage. A guideline for healthcare professionals from the American Heart Association/ American Stroke Association. Stroke. 2015; 46(7):2032–60.

21. Miyagi T, Koga M, Yamagami H, Okuda S, Okada Y, Kimura K, et al. Reduced estimated glomerular filtration rate affects outcomes three months after intracerebral haemorrhage: the stroke acute management with urgent risk-factor assessment and improvement-intracerebral haemorrhage study. J Stroke Cerebrovasc Dis. 2015; 24(1):176–82.

22. Orito K, Hirohata M, Nakamura Y, Takeshige N, Aoki T, Hattori G, et al. Leakage sign for primary intracerebral haemorrhage: a novel predictor of hematoma growth. Stroke. 2016; 47(4):958–63.

23. Moon JS, Janjua N, Ahmed S, Kirmani JF, Harris-Lane P, Jacob M, et al. Prehospital neurologic deterioration in patients with intracerebral haemorrhage. Crit Care Med. 2008; 36(1):172–5.

24. Smith EE, Rosand J, Greenberg SM. Hemorrhagic stroke. Neuroimaging Clin N Am. 2005; 15(2):259–72.

25. Dastur CK, Yu W. Current management of spontaneous intracerebral haemorrhage. Stroke Vasc Neurol. 2017; 2(1):21-9.

26. Delgado Almandoz JE, Yoo AJ, Stone MJ. Systematic characterization of the computed tomography angiography spot sign in primary intracerebral haemorrhage identifies patients at highest risk for hematoma expansion: the spot sign score. Stroke. 2009; 40(9):2994–3000.

27. Douglas V, Shamy M, Bhattacharya P. Should CT Angiography be a Routine Component of Acute Stroke Imaging? Neurohospitalist. 2015; 5(3):97-8.

28. Kim J, Smith A, Hemphill JC, Smith WS, Lu Y, Dillon WP, et al. Contrast extravasation on CT predicts mortality in primary intracerebral haemorrhage. AJNR Am J Neuroradiol. 2008; 29(3):520–5.

29. Al-Nakshabandi NA. The swirl sign. Radiology. 2001; 218(2):433.

30. Li Q, Zhang G, Xiong X, Wang X-C, Yang W-S, Li K-W, et al. Black Hole Sign: Novel Imaging Marker That Predicts Hematoma Growth in Patients With Intracerebral Hemorrhage. Stroke J Cereb Circ. 2016; 47(7):1777–81.

31. Li Q, Zhang G, Huang Y-J, Dong M-X, Lv F-J, Wei X, et al. Blend Sign on Computed Tomography: Novel and Reliable Predictor for Early Hematoma Growth in Patients With Intracerebral Hemorrhage. Stroke. 2015; 46(8):2119–23.

32. Li Q, Liu QJ, Yang WS, Wang XC, Zhao LB, Xiong X, et al. Island Sign: An Imaging Predictor for Early Hematoma Expansion and Poor Outcome in Patients With Intracerebral Hemorrhage. Stroke. 2017; 48(11):3019-25.

33. Shulman JG, Jara H, Qureshi MM, Lau H, Finn B, Abbas S, et al. Perihematomal oedema surrounding spontaneous intracerebral haemorrhage by CT: Ellipsoidal versus morphometric volumetry. Medicine (Baltimore). 2020; 99(28):e20951.

34. Krishnamurthi RV, Moran AE, Forouzanfar MH, Bennett DA, Mensah GA, Lawes CM, et al. The global burden of hemorrhagic stroke: a summary of findings from the GBD 2010 study. Glob Heart. 2014; 9(1):101–6.

35. Sporns PB, Kremmling A, Schwake M, Minnerup J, Nawabi J, Broocks G, et al. Triage of 5 Noncontrast Computed Tomography Markers and Spot Sign for Outcome Prediction After Intracerebral Hemorrhage. Stroke. 2018; 49(10):2317-22.

36. Boehme AK, Esenwa C, Elkind MS. Stroke Risk Factors, Genetics, and Prevention. Circ Res. 2017; 120(3):472-495.

37. World Health Organization. Global Health Estimates: Life expectancy and leading causes of death and disability [Internet]. Life expectancy; 2019 [cited 2020 August 28]. Available from: https://www.who.int/gho/mortality_burden_disease/life_tables/situation_trends_text/en/.

38. Huynh TJ, Symons SP, Aviv RI. Advances in CT for prediction of hematoma expansion in acute intracerebral haemorrhage. Imaging Med. 2013; 5(6):539–51.