



ROLE OF MULTIPHASIC CT ANGIOGRAPHY IN PREDICTION OF INTRACEREBRAL HEMORRHAGE EXPANSION

Radiodiagnosis

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ABSTRACT

Intracerebral hemorrhage is a devastating form of stroke. The overall incidence of spontaneous ICH worldwide is 24.6 per 100,000 person-years (1). Up to one third of patients with ICH experience hematoma growth in the first few hours after stroke onset. Accurate stratification of ICH expansion risk is crucial to identify those patients at highest risk of clinical deterioration because of active bleeding and therefore most likely to benefit from anti-expansion therapies.(2,3)The success of future interventions aimed at preventing hematoma expansion and subsequent poor outcome will likely depend on the accurate selection of patients at risk for hematoma expansion (4,5) The sensitivity of the spot sign in the prediction of substantial hematoma expansion with the use of single-phase CT angiography was 51% in the PREDICT study.(6).The primary aim of this study was to determine the accuracy of the spot sign in the prediction of hematoma expansion in patients with acute ICH by using standardized multiphase CT angiography. This technique enables the demonstration of additional time points from CT angiography by using the same injection of contrast material and very little additional radiation exposure (7)

KEYWORDS

AIMS AND OBJECTIVES

1. To determine the prevalence of the spot sign.
2. To determine the accuracy of using the spot sign to predict the intra-cerebral hemorrhage expansion with standardized multiphase CT angiography.

Spontaneous (i.e., nontraumatic) intracranial hemorrhage (sICH) are second only to trauma as neurologic causes of death and disability. Stroke or "brain attack"—defined as sudden onset of a neurologic event—is a cause of death in industrialized countries and is the most common cause of neurologic disability in adults.

MATERIALS AND METHODS

The study included total 150 patients of intracerebral hemorrhage who reported to the department of medicine, and were referred to the Department of Radio diagnosis to undergo CT scan evaluation of intracranial hemorrhage in a 2900 bed tertiary referral centre from December 2018 to September 2020.

A. Inclusion criteria

Symptomatically and Radiologically confirmed ICH who underwent scanning within 6 hours from symptom onset.

B. Exclusion criteria

1. Secondary causes of ICH
2. Deep coma (GCS 3-5)
3. Renal failure
4. Allergy to iodinated contrast material.
5. Lack of informed consent.

INSTRUMENTATION:

Imaging was done on Philips brilliance iCT 256 slice CT machine

PRE-PROCEDURE CLINICAL EVALUATION:

On admission, relevant demographic characteristics, medical history, clinical presentation, neurologic status (National Institutes of Health Stroke Scale and Glasgow Coma Scales cores), and results of routine laboratory tests were recorded.

ROUTINE INVESTIGATIONS:

- Blood Investigations: CBC, KFT, PT-INR, HIV, HBSAG, Anti-HCV.

METHOD

- Time from symptom onset was defined as time of first symptoms or signs of neurologic deficits or the time the patient was last known to be neurologically intact.
- NIHSS and Glasgow coma score was assessed for each patient for measuring the degree of disability of the patient.

- All patients underwent a standardized acute ICH evaluation that included unenhanced CT followed by multiphase CT angiography at baseline (6 hours) and unenhanced follow-up CT at approximately 24 hours (range, 22–30 hours).
- All CT examinations were performed from the skull base to the vertex with a multi-detector row CT scanner (Philips brilliance iCT 256 slice CT machine).
- Images were acquired with 1.0-mm-thick sections for unenhanced CT and with 0.6-mm-thick sections for multiphase CT angiography.
- Multiphase CT angiography was performed in three automated phases after intravenous injection of contrast material.
- The first phase acquisition was timed to occur during the peak arterial phase, the second during the equilibrium and/or peak venous phase, and the third during the late venous phase.
- The first phase was triggered by monitoring the bolus of contrast material from the descending aorta; scanning started 8 seconds after the CT attenuation value of the aorta reached the threshold value of 120 HU.
- The second phase was acquired after a delay of 4 seconds, and the third phase after a delay of 15 seconds.
- Scanning duration of each phase was 3.5 seconds, with an average dose length product of 300–350 mGy · cm per phase.
- A total of 80 mL of contrast material (370 mg Iodine per mL, Iopromide, Ultravist 370, Bayer Healthcare, US) was injected at a rate of 4 mL/sec; this was followed by a 30-mL normal saline chase at a rate of 4 mL/sec.

Image Analysis-

- ICH volumes were measured by using Formula - $A \times B \times C / 2$ described by Kwak et al. and popularized by Kothari et al.
- A = greatest hemorrhage diameter in the axial plane
- B = hemorrhage diameter at 90° to A in the axial plane
- C = the craniocaudal diameter of the hemorrhage
- ICH location (cerebral lobes, basal ganglia or thalamus, brainstem, or cerebellum), intraventricular extension, and subarachnoid extension were recorded.
- Multiphase CT angiographic scans were interpreted.
- The spot sign was defined according to established criteria.(8)
- Patients who were positive for the spot sign were prospectively categorized into one of four predefined patterns of spot sign presentation.

Table 1 - Various patterns of Spot sign seen in multiphase CT angiography

PATTERN	PHASE 1	PHASE 2	PHASE 3
A	+	-	-
B	+	±	+

C	-	+	-
D	-	-	+

- Patterns of spot sign presentation were prospectively defined; the intent was to represent the dynamic course of spot signs, from spots that resolve quickly to spots that appear late, as observed in studies of dynamic CT angiography.(9,10)

DATA INTERPRETATION :

Collected data was entered into Microsoft Excel spreadsheet. Tables and charts were generated with the help of Microsoft windows 10. Word and excel . Continuous variables were presented as Mean $\pm$ SD. Continuous variables (ICH volume, , absolute hematoma expansion) were compared presence and absence of spot signs by performing independent t-test. Categorical variables were expressed in frequency and percentages. Categorical variables were compared by performing chi-square test. For small number, Fisher exact test was used wherever applicable. Sensitivity, specificity, positive predictive value, Negative predictive value, accuracy and area under curve of three spot sign in three different phases of multiphase angiography for the prediction of absolute hematoma expansion were calculated. Odds ratio and 95% confidence interval were calculated to determine association of spot sign in different phases of CT angiography. $P < 0.05$ was considered as statistical significance. Statistical software STATA version 14.0 was used for data analysis.

OBSERVATION AND RESULTS

Table no. Distribution of cases with presence of spot sign

	NO. OF CASES	PERCENT
WITH SPOT SIGNS	56	37.33%
WITHOUT SPOT SIGNS	94	62.67%

Table no 12. Distribution of cases with spot sign according to different phases.

PHASES	NO. OF CASES	PERCENT
PHASE- I	22	14.67
PHASE-II	26	17.33
PHASE-III	29	19.33

Table no 13. Distribution of cases with spot sign according to pattern.

PATTERN	NO. OF CASES	PERCENT
0	94	62.67
A	4	2.67
B	19	12.67
C	23	15.33
D	10	6.67

Table no 14 .Distribution of cases with spot sign according number of spot signs

NUMBER OF SPOT SIGN	NO. OF CASES	PERCENT
NO	96	64
1	36	24
2	18	12

Comparison of absolute ICH volume expansion with presence of spot signs

The mean absolute hematoma expansion at 24 hours in the study was found to be 2.63 cc. The mean hematoma expansion in patients with spot sign was found to be 5.07 ± 7.02 cc and without spot sign to be 1.68 ± 1.16 cc. The mean absolute hematoma expansion at 24 hours in patients positive for spot sign in phase 1, phase 2, and phase 3 as found to be 8.13 ± 9.86 cc 4.74 ± 4.65 cc and 4.58 ± 3.99 cc respectively

Table no 15. Comparison of ich volume expansion with presence of spot signs

	MEAN ABSOLUTE HEMATOMA EXPANSION
PHASE 1	8.13 ± 9.86 cc
PHASE 2	4.74 ± 4.65 cc
PHASE 2	4.58 ± 3.99 cc

Association of presence of spot signs and absolute expansion.

In the study a significant absolute hematoma expansion (> 6 ml or $> 33\%$) was seen in 18 out of 56 patients with spot sign, while only 3 out of 94 patients without a spot sign showed significant hematoma expansion .18 out of the 21 patients (85.71%) with significant hematoma expansion at 24 hour follow up, were positive for spot sign, while 3 out of 21 (14.29%) were negative for spot sign. 38 out of the

56 patients (67.85%) positive for spot sign did not show significant hematoma expansion. 3 out of 94 patients negative for spot sign showed a significant hematoma expansion on follow up scan.

Table no 16.Association of presence of spot signs and absolute expansion.

ABSOLUTE EXPANSION	WITH SPOT SIGNS		WITHOUT SPOT SIGNS		P-VALUE
	FREQUENCY	PERCENT	FREQUENCY	PERCENT	
>6	18	85.71	3	14.29	<0.0001 ,HS
≤ 6	38	29.45	91	70.55	

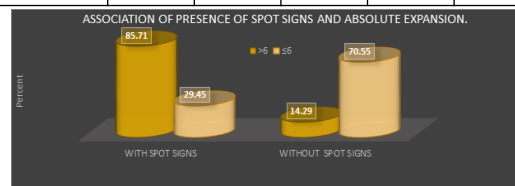


Figure 31 .Association of presence of spot signs and absolute expansion.

Association of presence of spot signs and absolute expansion according to different phases

In the study, 10 patients out of the 22 patients (45.6%) showing spot sign in phase 1 of the multiphase angiography patients, showed an significant hematoma expansion at 24 hour scan .Similarly 11 out of the 26 patients (42.3%) and 10 out of 29 patients (38.9%) in phase 2 and phase 3 respectively showed a significant hematoma expansion .

Table no 17.Association of presence of spot signs and absolute expansion according to different phases.

ABSOLUTE EXPANSION	PHASE-I		PHASE-II		PHASE-III	
	FREQUENCY	PERCENT	FREQUENCY	PERCENT	FREQUENCY	PERCENT
>6	10	45.45	11	42.30	10	34.48
≤ 6	12	54.54	15	57.70	19	65.52
OR 95% C.I.	8.86 (2.71 – 28.24)		8.36 (2.67-25.81)		5.26 (1.72-15.69)	
P-VALUE	<0.0001 ,HS		0.0068,HS		0.0367,S	

Table no 18.Sensitivity, specificity,predictive values,accuracy and area under the curve of spot sign in different phases in prediction of intracerebral hemorrhage expansion.

SPOT SIGN POSITIVITY	SENSITIVITY(%)	SPECIFICITY(%)	PPV(%)	NPV(%)	ACCURACY	AUC
PHASE-I	57.14	92.25	54.54	92.96	87.11	0.7473
PHASE-II	52.38	85.27	42.30	91.93	80.67	0.6883
PHASE-III	52.38	86.05	37.93	92.36	81.33	0.6921

Correlation of pattern of spot signs with absolute hematoma expansion.

In my study, 3 patients out of the 4 patients (75%) showing pattern A of spot sign in multiphase angiography patients, showed an significant hematoma expansion at 24 hour scan .Similarly 10 out of the 19 patients (52.6%) , 4 out of 23 patients (17.4%) and 1 out of 10 patients (10%) in showing pattern B,C and D respectively showed a significant hematoma expansion .

Table no 19.Correlation of pattern of spot signs with absolute hematoma expansion.

ABSOLUTE HEMATOMA EXPANSION	PATTERN OF SPOT SIGNS							
	A		B		C		D	
	FREQUENCY	PERCENT	FREQUENCY	PERCENT	FREQUENCY	PERCENT	FREQUENCY	PERCENT
>6	3	75	10	52.6	4	17.4	1	10
≤ 6	1	25	9	41.4	19	82.6	9	90
P-VALUE	<0.001 ,HS		<0.001 ,HS		0.610,NS		1.000,NS	

DISCUSSION

In this study of 150 patients of intraparenchymal hemorrhage, most common age group was 51-60 years (36.6%). Mean age of presentation was 57.62 ± 10.19 years. There were only 8 cases below the age of 40 years.

In this study, 56 (37.3%) patients out of the 150 patients show presence of spot sign in at least one phase while spot sign was not seen in any phase in remaining 94 (62.6%) patients. The prevalence of spot sign in

the study population was 37.3%. The spot sign was seen more frequently in the later phases of multiphase CT Angiography: 22 of 150 patients (14.6%) in phase 1, 26 of 150 (17.3%) in phase 2, and 29 of 150 (19.3%) in phase 3. ($P < .001$). Pattern A was observed - in 4 of the 56 patients with the spot sign in at least one phase (7%); pattern B in 19 (33.9%); pattern C in 23 (41.1 %); and pattern D 10 (17.8 %).

Among the 150 patients included in the hematoma expansion analysis, 56 (37.3 %) had a spot sign in at least one phase and 21 (26.3%) experienced substantial hematoma expansion (6 mL or .33%).

Substantial hematoma expansion occurred more frequently in patients with spot sign in phase 1 (10 of 12 patients [45.45%] $P < .0001$), phase 2 (11 of 26 patients [42.3] ($P = .0068$), and phase 3 (10 of 29 patients [38.48] ($P = .0367$), than in patients without spot sign in these phases 3 of 94 patients (3.2%).

The highest positive predictive value was observed in phase 1 (54.54%) 10 of 22 patients), negative predictive values were consistently high in all phases; the negative predictive value was highest in phase 1 (92.25% [patients]) of multiphase CT angiography. The association of spot sign presence in phase 1 (odds ratio, 8.86; 95% confidence interval: 2.7-28.24), phase 2 (odds ratio, 8.36; 95% confidence interval: 2.67-25.81), and phase 3 (odds ratio, 5.26; 95% confidence interval: 1.72-15.69), with the primary outcome remained significant in separate adjusted multiple logistic regression models.

The mean absolute hematoma growth at 24 hours was 1.6 mL. The presence of the spot sign was associated with higher absolute hematoma growth in phase 1 (8.13 ± 9.86 mL), phase 2 (4.71 ± 4.65 mL) and phase 3 (4.58 ± 3.99 mL) as well in any of the three phases (5.07 ± 7.02 mL) vs (1.68 ± 1.16 mL compared with patients without the spot sign (Bonferroni adjusted $\alpha = .0125$). Absolute hematoma growth analysis revealed a hierarchical pattern of spot sign presentation and hematoma growth, as follows: pattern A > pattern B > pattern C > pattern D > no spot sign.

SUMMARY

In this study of 150 patients of intraparenchymal hemorrhage who underwent multiphase CT angiography spot sign was seen in 37.3% patients in at least one of the phases of multiphase CT angiography. The spot sign was seen in phase I in 22 (14.6%) patients, in phase 2 in 26 (17.3%) patients and in 29 (19.3%) patients in phase 3 of the multiphase protocol. Substantial hematoma expansion (>6ml or 33%) was seen in 21 (26.3%) patients with hematoma expansion more frequently in patients with spot sign in phase 1, phase 2 and phase 3 than in patients without spot sign. Presence of spot sign in predicting significant hematoma expansion was false positive in 67.85% cases and false negative in 3.19% patients. Median absolute hematoma growth at 24 hours was 1.6 ml. Presence of the spot sign was associated with higher absolute hematoma growth in phase 1, phase 2 and phase 3 as well in any of the three phases compared with patients without the spot sign. Absolute hematoma growth analysis revealed a hierarchical pattern of spot sign presentation and hematoma growth, as follows: pattern A > pattern B > pattern C > pattern D > no spot sign.

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