A Study of CT-Angiography Spot sign as a predictor of Hematoma expansion in patients with primary intracerebral Haemorrhage

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Abstract
Background: Primary intracerebral haemorrhage occurs in 10-30% of patients with stroke and is the deadliest and disabling type of stroke. Early hematoma expansion is an independent predictor of neurologic worsening and mortality. Early hematoma expansion can be found out by spot sign in CT-Angiography done within 24 hrs. Hematoma expansion and poor outcome is correlated with the size and location of the initial bleeding. Deep haemorrhages are associated with high mortality rates. The spot sign is defined as 1mm to 2mm foci of enhancement within the hematoma on CTA source images typically located in the periphery of the hematomas and suggest the likelihood of expansion. The pathologic basis remains unclear but may represent primary vessel pathology such as micro aneurysms.

Objectives
1) To find out the predictive value of CT-Angiography spot sign with hematoma expansion.
2) To find clinical profile and its relationship with development of spot sign.

Materials and Methods: A prospective study was conducted after obtaining institutional ethical committee clearance. Patients having primary intracerebral haemorrhage were included and analysed according to the Performa. CT angiography spot sign was assessed within in 24 hours after ictus and evaluated for hematoma expansion.

Results: 52 study subjects were enrolled in the study predominantly males around age group of 40-60 years. There was significant association between Hematoma expansion and Spot sign with (P value <0.001) with positive predictive value of 88 % and specificity of 70%. Calculated Kappa value was 76.71 showed it is a relative good tool for assessment. There was no significant association with any other variables of hematoma expansion except hematoma volume which showed Linear by linear association with p value <0.05. Spot sign frequency seen with moderate to large hematomas.

Conclusion: As in previous studies CT Angiography spot sign was a good independent predictive tool for accessing hematoma expansion with good sensitivity and specificity. In our study spot sign in CT-Angiography was found to be helpful in moderate to large hematomas which are life threatening and require close monitoring of patient condition. However, absence of Spot sign doesn’t rule out hematoma expansion.
Introduction

Intracerebral haemorrhage is one of the major causes for disability in 15% of stroke pathology which has a high one-month mortality rate of 30% - 50%. It can cause sudden death in 48 hours. Intense close monitoring is required during initial period of admission to prevent mortality. Hematoma expansion can occur within a period 6 hour to 48 hours. Hence prediction of hematoma expansion is of great importance by Clinicoradiological methods.

Non-contrast CT is the basic initial investigation tool for diagnosing intra cerebral haemorrhage. Hypertension is found to be one of the leading cause for non-traumatic ICH. The incidence increased progressively with degree of hypertension. The typical location of hypertensive ICH is (basal ganglia, thalamus, cerebellum and pons). Studies demonstrated secondary vascular lesions even in typical hypertensive haemorrhages location. CT-Angiography is a non-invasive technique to find out such pathology. DSA (Digital Subtraction Angiography) is more sensitive in identifying aneurysmal lesions.

Study by Becker et al.1999 examined the role of iodinated contrast administration in primary intra cerebral haemorrhage. CT-Angiography spot sign has been with increased risk of hematoma expansion in prospective as well as retrospective studies. The other parameters that will predict the poor outcome in intra cerebral haemorrhage includes age, blood glucose levels, Glasgow comma scale and haemorrhage location, size of the hematoma and intraventricular extension.

Methods

Patient Selection

Our institutional Ethical committee approval was obtained and prospective study has been conducted with patients admitted through emergency department. Only patient’s demonstrated intra cerebral haemorrhage in CT scan were only included the study. Patient was excluded if ICH was shown by history and diagnostic workup to be secondary to trauma, aneurysm, vascular malformation, haemorrhagic infarcts, vasculitis or brain tumour. Hematoma expansion which is considered an increase in ICH volume of more than 6 ml or 30% from the baseline ICH volume, CT-Angiogram was performed within 24 hrs after admission. The two largest clinical trials use >33% or >12.5 ml INTERACT2and ≥ 33%ATACH II as their dichotomized definition of hematoma expansion.

Image Acquisition

NCCT and contrast CT-A was performed according to department protocol on 128 slice CT scan. NCCT examination was performed using axial technique with 120-140 VP 340 ma and slice thickness reconstitution. Contrast 0.7 mL/kg (maximum 90 ml) of non-ionic iodinated contrast material using power injection at 4-5 ml/ second into an anterior cubital vein.

Image Analysis

The non-contrast CT was reviewed by radiologist to determine the ICH location (lobar, deep grey matter or infratentorial). Subsequently the axial CT Angiogram were independently reviewed for spot windows to determine the presence and scoring of spot sign. Volume of the haemorrhage in millimetres by using ABC/2 method where A is the greatest diameter of haemorrhage on CT section with largest area of haemorrhage, B is the diameter perpendicular to A, and C is the number of sections with haemorrhage multiplied by the section thickness.30ml is selected as a threshold to distinguish between small and large hematomas as done in prior studies.
**Figure:** Shows hyperdense spot sign within and periphery of hematoma during contrast CT- Angiogram study which is discontinuous from the vasculature.

**Spot sign criteria**
- >1 focus of contrast pooling within the ICH
- Attenuation >120 HU
- Discontinuous from normal or abnormal vasculature adjacent to ICH

**Analysis**
Sample size: 54

|          | Males | Females |
|----------|-------|---------|
| Spot sign frequency (%) | Poor outcome (%) |

| Admission MAP (No) | Spotted frequency (%) | Poor outcome (%) |
|-------------------|-----------------------|------------------|
| < 100 (23)        | 3(33)                 | 7(30)            |
| 101-120 (18)      | 4(22)                 | 6(32)            |
| >120 (13)         | 5(40)                 | 4(34)            |

| admission GCS(No) | Spotted frequency (%) | Poor outcome (%) |
|-------------------|-----------------------|------------------|
| <8 (16)           | 5(33)                 | 10(65)           |
| 9-12 (9)          | 3(33)                 | 10(65)           |
| >13 (13)          | 4(15)                 | 3(29)            |

| Blood Glucose >170 (No) | Spot sign frequency (%) | Poor outcome (%) |
|-------------------------|-------------------------|------------------|
| Yes (14)                | 4(31)                   | 7(50)            |
| No (39)                 | 8(20)                   | 10(25)           |

| ICH site: (No)         | Spotted frequency (%) | Poor outcome (%) |
|------------------------|-----------------------|------------------|
| Lobar (30)             | 7(23)                 | 8(29)            |
| Deep grey matter (19)  | 5(25)                 | 6(33)            |
| Infratentorial (5)     |                       | 3(37)            |

| ICH Volume(No)         | Spotted frequency (%) | Poor outcome (%) |
|------------------------|-----------------------|------------------|
| 0.2 -29.9 ml (33)      | 5(15)                 | 5(15)            |
| 30-59.9 ml (10)        | 1(25)                 | 6(35)            |
| >60 ml(11)             | 6(46)                 | 8(74)            |

**Statistical Analysis**
The various statistical analysis used are Chi square test, Chi square test for trend, Sensitivity, Specificity, Kappa statistics, Positive predictive value P value <0.05 is considered as statistically significant. Analysis was performed in SPSS 24.
Temporal Association Hematoma expansion with Spot sign

Table 1

| SPOT SIGN | HEMATOMA | EXPANSION | TOTAL |
|-----------|----------|-----------|-------|
| NO        | 37       | 5         | 42    |
| %         | 88.1%    | 11.9%     | 100%  |
| YES       | 0        | 12        | 12    |
| %         | 0.0%     | 100%      | 100%  |
| TOTAL     | NUMBER   | 37        | 17    |
| %         | 68.5%    | 31.5%     | 100%  |

Chi $^2 = 33.580$ $P< 0.001$
Kappa = 76.71 Good assessment
Sensitivity 37/37 x 100 = 100 %
Specificity 70%
Positive predictive value 37/42 x 100 = 88%

Association of Hematoma volume with hematoma expansion ($P< 0.005$)

Table 2

| ICH -0.2-29 ml | HEMATOMA | EXPANSION | TOTAL |
|----------------|----------|-----------|-------|
| 27             | 6        | 33        |
| 81.8%          | 18.2%    | 100%      |
| ICH-30-59 ml   | 6        | 4         | 10    |
| 60%            | 40%      | 100%      |
| ICH->>60 ML    | 7        | 4         | 11    |
| 36.4%          | 63.6%    | 100%      |
| TOTAL          | 37       | 17        | 54    |
| 68.5%          | 31.5%    | 100%      |

Association of Spot sign with Hematoma volume ($P<0.05$)
Chi $^2 = 8.468$

Table 3

| ICH 0.2 –29 ml | NO : | 28 | 5 | 33 |
|----------------|------|----|---|----|
| %              | 84.8%| 15.2%| 100% |
| ICH 30- 59 ml  | NO:  | 9  | 1 | 10 |
| %              | 90%  | 10% | 100% |
| ICH > 60 ML    | NO:  | 6  | 5 | 11 |
| %              | 45.5%| 54.5%| 100% |
| TOTAL          | NO:  | 42 | 12| 54 |
| %              | 77.8%| 22.2%| 100% |

Linear by Linear association with hematoma volume ($P<0.05$)

| Chi $^2$ | P value |
|----------|---------|
| Linear by linear association | 8.158 | 0.004 |
Results
52 study subjects were enrolled in the study predominantly males around age group of 40-60. There was significant association between Hematoma expansion and Spot sign with (P value <0.001) with positive predictive value of 88 % and specificity of 70%. Kappa value was 76.71 suggestive it as a relative good tool for assessment. There was no significant association with any other variables with hematoma expansion except hematoma volume which showed Linear by linear association with p value (<0.05). Spot sign frequency was significantly seen more with moderate to large hematomas.

Discussion
In our study we demonstrated that CTA Spot sign can be used reliably with good predictive value for identification of hematoma expansion in primary ICH. It has good accuracy in predicting in hospital mortality and poor outcome Becker et al9. Km et al10Wada et al11. Spot sign criteria similar to have proposed by Thompson et al12. Patient population with highest mean spot sign have medium initial ICH volume, moderate depression in consciousness at admission with high mean BP with involvement of deep structures are likely to detoriate.

It has been already known that initial haemorrhage volume is not static but will progress within early hours after ictus. The growth occurred 38% subjects within 6 hours of symptom onset 2. The risk factors associated with hematoma expansion are hypertension, anti-coagulation, hyperglycæmia. Hematomaproxression has been defined as increase in size of volume between 33 % and 50% or change in volume 12.5 ml to 20 ml. However, post traumatic ICH expansion of 5 ml predict the need for surgical management13. Timing and Frequency of hematoma expansion is also important. If the patient had undergone scanning within 3 hours of symptom onset the degree of expansion is around 73 % and significant hematoma expansion seen in 1/3 rd of cases. In later time frames chances of detecting significant expansion are down low by 11%.

A brief review is necessary to understand the probable mechanism of hematoma expansion. It was initially described by Charcot and Bouchard 14 implicated that the development of hypertensive ICH in 1868, the aneurysm reported measure up to 2 mm. They occur in deep brain structures including basal ganglia and thalami. Possibilities suggest rare form of adherent clots or pseudoaneurysm, more recently vascular tortuosity and coiling give appearance of aneurysm 15. Recent computational model of hematoma showed avalanche model of hematoma expansion rather than a single bleeder vessel, which again explains the spot sign phenomenon as predictor of hematoma expansion. Contrast enhancement can be due to primary or secondary haemorrhage due to torn perforators, with underlying history of hypertension it is reasonable to speculate these spots represents pseudo aneurysm.

Un identifying the underlying cause of haemorrhage will further lead on to detoriation of the course of illness. Studies have shown even in typical hypertensive location there are chances of 2-4 % in existence of AVM which can cause re-haemorrhage in first year3. In a study done by Yeung et al16 prevalence of secondary lesions in the basal ganglia identified by DSA is around 4%. Outcome: The mortality rate will rise 5% with every 10% increase in hematoma volume and 7 % likely they shift from independence to dependence measured by modified Rankin scale. Early surgical intervention did not show favoured outcome as in STICH trial. However, in STICH 2 trial lobar haemorrhages which are 1cm from the cortex without IVH may be beneficial.

Conclusion
CT Angiography spot sign is a good independent predictive tool for accessing hematoma expansion with good sensitivity and specificity. In our study spot sign in CT-Angiography is found to be helpful in moderate to large hematomas which are
life threatening and may signal close monitoring of patient condition. The major challenge is its relatively low sensitivity of 51% in the recent prospective PREDICT trial which highlights the considerable number of patients who will suffer expansion despite the absence of a spot sign on CTA.

References

1. Broderick, J. P., et al. (1999). "Guidelines for the management of spontaneous intracerebral haemorrhage: A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association." Stroke 30(4): 905-915.

2. Brouwers HB, Falcone GJ, McNamara KA, Ayres AM, Oleinik A, Schwab K, et al: CTA spot sign predicts hematoma expansion in patients with delayed presentation after intracerebral hemorrhage. Neurocrit Care 012;17: 421–428.

3. Zia, E., et al. (2007). "Blood pressure in relation to the incidence of cerebral infarction and intracerebral hemorrhage. Hypertensive hemorrhage: debated nomenclature is still relevant." Stroke 38(10): 2681-268.

4. Kim J, Smith A, Hemphill JC, Smith WS, Lu Y, Dillon WP, Wintermark M. Contrast extravasation on CT predicts mortality in primary intracerebral hemorrhage. American Journal of Neuroradiology. 2008 Mar 1;29(3):520-5.

5. Becker KJ, Baxter AB, Bybee HM, Tirschwell DL, Abouelsaad T, Cohen WA. Extravasation of radiographic contrast is an independent predictor of death in primary intracerebral hemorrhage. Stroke. 1999 Oct 1;30(10):2025-32.

6. Qureshi AI, Palesch YY, Barsan WG, Hanley DF, Hsu CY, Martin RL, Moy CS, Silbergleit R, Steiner T, Suarez JJ, Toyoda K. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. New England Journal of Medicine. 2016 Sep 15;375(11):1033-43.

7. Qureshi AI, Palesch YY. Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) II: design, methods, and rationale. Neurocritical care. 2011 Dec 1;15(3):559-76.

8. Kazui S, Minematsu K, Yamamoto H, Sawada T, Yamaguchi T. Predisposing factors to enlargement of spontaneous intracerebral hematoma. Stroke. 1997 Dec 1;28(12):2370-5.

9. Becker K, Tirschwell D. Intraparenchymal hemorrhage, bleeding, hemostasis, and the utility of CT angiography. International Journal of Stroke. 2008 Feb;3(1):11-3.

10. Kim J, Smith A, Hemphill JC, Smith WS, Lu Y, Dillon WP, Wintermark M. Contrast extravasation on CT predicts mortality in primary intracerebral hemorrhage. American Journal of Neuroradiology. 2008 Mar 1;29(3):520-5.

11. Wada R, Aviv RI, Fox AJ, Sahlas DJ, Gladstone DJ, Tomlinson G, Symons SP. CT angiography “spot sign” predicts hematoma expansion in acute intracerebral hemorrhage. Stroke. 2007 Apr 1;38(4):1257-62.

12. Thompson AL, Kosior JC, Gladstone DJ, Hopyan JJ, Symons SP, Romero F, Dzialowski I, Roy J, Demchuk AM, Aviv RI, PREDICT/Sunnybrook ICH CTA Study Group. Defining the CT angiography ‘spot sign’in primary intracerebral hemorrhage. Canadian Journal of Neurological Sciences. 2009 Jul;36(4):456-61.

13. Chang EF, Meeker M, Holland MC. Acute traumatic intraparenchymal hemorrhage: risk factors for progression in the early post-injury period. Neurosurgery. 2006 Apr 1;58(4):647-56.

14. Charcot JM, Bouchard C. Nouvelle recherches sur la pathogenie del’
hemorrhagie cerebrale. Arch Physiol Norm Pathol. 1868;1:643–645.

15. Challa VR, Moody DM, Bell MA. The Charcot-Bouchard aneurysm controversy: impact of a new histologic technique. Journal of neuropathology and experimental neurology. 1992 Mar 1;51(3):264-71.

16. Yeung R, Ahmad T, Aviv RI, de Tilly LN, Fox AJ, Symons SP. Comparison of CTA to DSA in determining the etiology of spontaneous ICH. Canadian Journal of Neurological Sciences. 2009 Mar;36(2):176-80.