



The comparative study of island sign and the spot sign in predicting short-term prognosis of patients with intracerebral hemorrhage



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ABSTRACT

Objectives: It is well known that early hematoma expansion is associated with short-term prognosis of patients with intracranial hemorrhage (ICH). And spot sign is recognized as a reliable computed tomography angiography (CTA) predictor for early hematoma expansion. Recently, island sign is also reported as a novel computed tomography (CT) predictor for early hematoma growth. Here, we compared the predictive abilities of these two signs for short-term outcomes of ICH patients.

Patients and Methods: All the ICH patients were retrospectively identified. Clinical characteristics and radiological parameters were obtained from electronic medical records. Hematoma expansion, spot sign and island sign were assessed by two senior neurologists according to the initial and follow-up CT scans. 3-months prognoses were estimated according to Glasgow outcome scale (GOS). Multivariate logistic regression analyses were employed to explore the associations of short-term prognosis on island sign, spot sign and other clinical variables.

Results: There were 283 ICH patients included. 113 of them presented with early hematoma expansions. 66 of them exhibited island sign, while spot sign occurred in 85 patients. Univariate analyses demonstrated that GCS score at admission (OR: 0.464, 95%CI: 0.395–0.547), hematoma volume (OR: 1.062, 95%CI: 1.041–1.083), interventricular extension (OR: 9.528, 95%CI: 3.915–23.187), island sign (OR: 4.595, 95%CI: 2.404–8.784) and spot sign (OR: 4.052, 95%CI: 2.297–7.147) were correlated with 3-months morbidity. Moreover, multivariate logistic regression analyses further revealed that both spot sign (OR: 3.413, 95%CI: 1.570–7.422) and island sign (OR: 7.564, 95%CI: 2.969–19.273) were strongly associated with 3-months poor outcome and have comparable predictive values (AUC: 0.636 vs. 0.622, $P = .58$). However, spot sign exhibited a superior predictive ability for 3-months mortality compared to island sign (OR: 2.713, 95%CI: 1.570–4.217 vs. OR: 2.362, 95%CI: 1.238–3.899, AUC: 0.700 vs. 0.603, $P < .01$).

Conclusions: Island sign is not just a convenient and reliable predictor for short-term prognosis of ICH patients, but also could be used as an indicator for accurate diagnosis and aggressive treatment.

1. Introduction

Spontaneous Intracerebral hemorrhage (ICH) accounts for approximately 10%–30% of stroke. It is life threatening and carries high incidence of morbidity and mortality [1]. Previously studies reported that early hematoma expansion was occurring in 30% of ICH patients, which could induce poor outcomes and mortality [2,3]. Compared with hematoma size and site, hematoma growth is a potentially modifiable prognostic factor. Consequently, the predictive ability of imaging features for early hematoma expansion has attracted an ocean of attentions in recent years [4]. Some researchers have identified CT angiography (CTA) spot sign as a good predictor for hematoma growth and unfavorable outcome in ICH patients [5–8]. However, in China, CTA remains unavailable to perform within few hours after ICH onset, especially the financial-challenged area. Thus, non-contrast CT (NCCT)

imaging markers are more convenient and reasonable for predicting early hematoma expansion and prognosis up to date. Recently, Li et al. [9] have reported a novel NCCT predictor termed as island sign, which exhibited an excellent predictive ability for early hematoma expansion and poor outcome in 252 patients with ICH. Our previously study evaluated the predictive value of the imaging signs for hematoma expansion [10]. Nevertheless, the different between spot sign and island sign in predicting short-term prognosis has never been explored under the same cohort of patients with ICH. Here, based on the same group of patients with ICH, we evaluated the predictive abilities of both spot sign and the island sign for 3-months mortalities and morbidities of patients with ICH, as well as their predictive efficiency.

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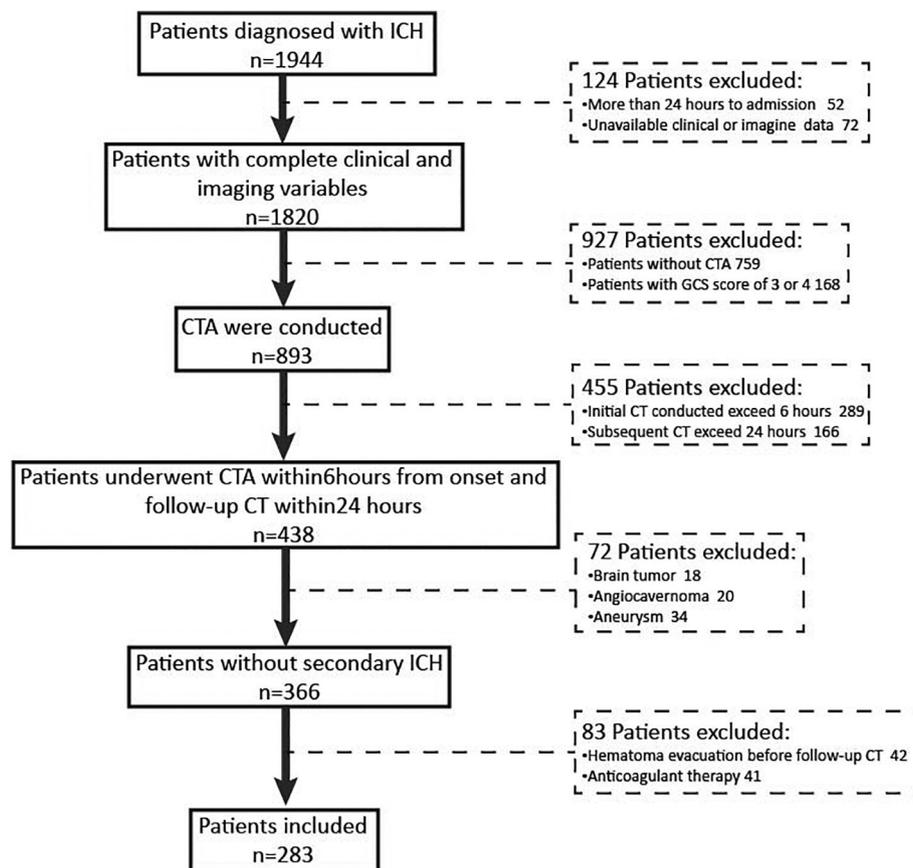


Fig. 1. Flowchart of patient enrollment.

2. Patients and methods

2.1. Patients

This study was conducted based on the ICH patients' follow-up database within the Department of Neurosurgery, West China Hospital. We retrospectively reviewed all the ICH patients that visited to our hospital from January 2015 to December 2017. Patients who meet the following criteria were included into this study: (1) Adult patients (Age > 18 years) with ICH that were confirmed by head CT scan; (2) Primary CT scans and CTA were performed within 6 h after onset of ICH symptoms; (3) The Followed CT scan was performed within 24 h after initial CTA. Patients were ineligible if: (1) the clinical or radiological data is not available; (2) they suffered from secondary ICH induced by trauma, tumor apoplexy, aneurysm, arteriovenous malformation, Moyamoya disease or other cerebrovascular anomalies; (3) surgical treatment such as hematoma evacuation was conducted before follow-up CT scans. (4) the Glasgow Coma Scale (GCS) score of patient is below 5; (5) the anticoagulant treatment has been performed. All this studies are approved by the Ethic Committee of West China Hospital, Sichuan University. And the signed consents were obtained from the patients or their relatives. This study was conducted in accordance with the Declaration of Helsinki and relevant regulations of Sichuan University.

2.2. Clinical variables

The following baseline clinical variables were collected from the electronic medical record system, including age, gender, medical history, smoking history, alcohol abuse, hospitalized blood pressure and GCS score. The laboratory variables including prothrombin time (PT), activated partial thromboplastin time (APTT) and international

normalized ratio (INR). The short-term functional outcomes were assessed by Glasgow Outcome Scale (GOS) at 3 months. The poor outcome was defined as GOS 1 to 3 scores while patients with GOS \geq 4 were considered to have a favorable outcome [11].

2.3. Imaging data

Two senior neurologists independently evaluate the initial CTA and followed CT scans. Any different opinion would be resolved by further discussion of these readers. Imaging features including hematoma site, hematoma volume, intraventricular hemorrhage (IVH), early hematoma expansion, spot sign and island sign, were estimated based on initial CTA scans and followed CT scans. Hematoma volume was calculated by ABC/2 method [12]. Hematoma expansion was defined as a 33% increasing of the volume, or the absolute hemorrhage is above 12.5 ml, which was determined by followed NCCT [3]. Based on the previously definition of island sign, at least 3 small hematomas that all separate from the major hematoma, or > 4 small hematomas that may connect with or separate from the main hematoma should be recognized as typical island sign. The shape of the separated small hematomas should also be suborbicular whereas the shape of small hematomas connecting with major hematoma should be sprout-like or bubble-like [9]. Meanwhile, the spot sign could be also briefly defined as \geq 1 focus of contrast pooling (Hounsfield unit value > 120) within the ICH [5,13].

2.4. Statistical analysis

Clinical characteristics baseline, laboratorial parameters and image data were compared between patients with or without short-term poor outcome. Data was expressed as the mean \pm standard deviation (SD) or median with interquartile range (IQR) or frequency with percentage.

According to different circumstances, results were analyzed by student's *t*-test, Mann-Whitney *U* test, Chi-square test or Fisher's exact test. The variables with a *P* value of < 0.10 identified in univariate analysis were included in a multivariable analysis. The multivariable regression analysis was performed to adjust the associations of island sign and spot sign on poor outcomes. The inter-observer reliability of island sign and spot sign were assessed by K value and Spearman analysis was conducted to assess the correlation. Receiver- operator characteristics analyses (ROC) and area under curves (AUC) were applied to compare the predictive values of island sign and spot sign for short-term outcome in patients with ICH. The variables with a *P* < .05 were considered statistically significant. All statistical analyses were performed by SPSS software (Version 23.0).

3. Results

283 ICH patients from January 2015 to December 2017 were enrolled in current study. There were 199 males and 84 females. Detail information for exclusion was presented in the flowchart (Fig. 1). Mean age of patients was 60.23 ± 10.67 with a range from 26 to 89 years. The average volume of hematoma was 24.99 ± 14.87 ml. Supratentorial hematomas or infratentorial hematomas were observed in 260 and 23 patients, respectively. The baselines of clinical variables are summarized in Table 1. The comparison between patients with or without poor outcomes and the clinical parameters between survivors and deaths were presented in Table 2. There is no significantly difference in gender, hypertension, ischemia, blood pressure, smoking history, alcohol use, PT, APTT or INR. Early hematoma growths were detected in 113 patients with ICH. 66 of them possessed island sign and 85 of them showed a spot sign. There were 41 patients with both spot sign and island sign that experienced early hematoma expansion, and all island sign were observed only at supratentorial area (Table 1). The morbidity rate and mortality rate were 52.6% (149 patients) and 32.2% (91 patients), respectively. 52 individuals had island sign and 64 individuals presented with spot sign over 149 ICH patients with unfavorable outcomes, while only 10 of 134 individuals without poor outcomes presented with island sign, and 21 individuals with spot sign exhibited good outcomes (Table 2). This result indicated that ICH patients with poor outcome had a higher prevalence of spot sign and

island sign than those who with favorable outcome. K value was calculated for evaluating inter-observer reliabilities of both island sign and spot sign, and the results indicated an excellent inter-reader agreement between two senior neurologists as the K values are 92.8% and 90.3% for island sign and spot sign, respectively. Additionally, 13 individuals over 16 patients (81.3%) with island sign and underwent poor outcome, and 25 out of 35 patients (71.4%) with spot sign had unfavorable outcomes. Spearman analysis showed a correlation between spot sign and island sign (correlation coefficient = 0.550, *P* < .001). Univariate analysis showed that GCS score at admission (OR:0.464, 95%CI: 0.395–0.547), hematoma volume (OR:1.062, 95%CI: 1.041–1.083), interventricular extension (OR:9.528, 95%CI: 3.915–23.187), island sign (OR: 4.595, 95%CI: 2.404–8.784) and spot sign (OR: 4.052, 95%CI: 2.297–7.147) were all independently associated with unfavorable outcome (*P* < .01, Table 3). In contrast, elder (OR:1.037, 95%CI: 1.011–1.063), presence of hydrocephalus (OR:2.903, 95%CI: 1.479–5.698), GCS (OR:0.615, 95%CI: 0.546–0.693), hematoma size (OR:1.114, 95%CI: 1.085–1.144), IVH (OR:4.664, 95%CI: 2.479–8.776), island sign (OR:2.982, 95%CI: 1.687–5.272) and spot sign (OR:6.424, 95%CI: 3.672–11.240) were significantly related to mortality at 3-months (*P* < .01, Table 4). Moreover, multivariate logistic regression analyses revealed that GCS score, hematoma size, IVH, island sign and spot island remained as independent predictors for short-term morbidity and mortality (Tables 3 and 4). As expected, both island sign and spot sign also independently predicted early hematoma growth (Table 5).

The sensitivity, specificity and positive/negative values of island sign for predicting poor outcome were 34.9%, 89.6%, 78.8%, 55.3%, respectively. On the other hand, the sensitivity, specificity, PPV and NPV of spot sign were 43.0%, 84.3%, 75.3%, 57.1%, respectively (Table 6). Afterwards, the receiver-operator analysis was also conducted to validate the predictive ability of island sign and spot sign for morbidity and mortality (Fig. 2). The AUC of island sign and spot sign for predicting the poor outcome of ICH patients were 0.622 and 0.636, respectively, and no significantly difference was observed between this two signs (*P* = .58). However, by comparing to that of island sign (0.603, *P* < .01, Fig. 2), spot sign showed a significantly superior accuracy in predicting short-term mortality with an AUC of 0.700. Other than spot, island sign harbored comparable abilities in predicting early

Table 1

Baseline clinical characteristics related to island sign and early hematoma growth in patients with ICH.

Characteristic	Baseline <i>n</i> = 283	Expanders (<i>n</i> = 113)	Nonexpander (<i>n</i> = 170)	<i>P</i>
Male	199(70.3)	81(71.7)	118(69.4)	0.68
Age (years)	60.23 ± 10.67	61.23 ± 11.72	59.56 ± 9.89	0.19
Systolic blood pressure(mmHg)	165.94 ± 34.10	167.73 ± 29.07	164.75 ± 37.10	0.47
Diastolic blood pressure(mmHg)	94.71 ± 18.37	95.59 ± 16.74	94.12 ± 19.40	0.51
Mean arterial pressure(mmHg)	117.86 ± 22.14	118.14 ± 19.64	117.66 ± 23.71	0.86
Medical history	–	–	–	–
Hypertension	141(49.8)	62(54.9)	79(46.5)	0.16
Diabetes mellitus	26(9.2)	10(8.8)	16(9.4)	0.87
Ischemic stroke	33(11.7)	15(13.3)	18(10.6)	0.49
Smoker	136(48.1)	49(43.4)	87(51.2)	0.19
Alcohol (> 3 drinks per 24 h)	115(40.6)	46(40.7)	69(40.6)	0.98
Hydrocephalus	41(14.5)	18(15.9)	23(13.5)	0.57
Time to initial CTA(hours)	3.63 ± 1.99	2.98 ± 1.73	4.05 ± 2.05	< 0.01*
GCS score on admission	11(8, 14)	8(6, 10)	13(9, 14)	< 0.01*
Hematoma size (ml)	24.99 ± 14.87	37.29 ± 13.35	16.81 ± 11.23	< 0.01*
Presence of IVH	52(18.4)	24(21.2)	28(16.5)	0.31
Supratentorial hematoma	260(91.9)	111(98.2)	151(88.8)	0.02*
PT (seconds)	11.56 ± 2.04	11.56 ± 1.93	11.56 ± 2.12	0.99
APTT (seconds)	28.95 ± 3.24	28.74 ± 2.84	29.10 ± 3.47	0.36
INR	1.24 ± 1.03	1.19 ± 0.94	1.28 ± 1.09	0.47
Island sign	66(23.3)	53(46.9)	13(7.6)	< 0.01*
Spot sign	85(30.0)	65(57.5)	20(11.8)	< 0.01*

Data are described as n(%), mean ± standard deviation, median (interquartile range) as appropriate.

IVH, intraventricular hemorrhage; CTA, CT angiography; GCS, Glasgow coma scale; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio.

Table 2
Baseline clinical characteristics related to 3-month morbidity and mortality in patients with ICH.

Characteristic	Favorable outcome (n = 134)	Poor outcome (n = 149)	P	Survivor (n = 192)	Death (n = 91)	P
Male	94(70.1)	105(70.5)	0.95	137(71.4)	62(68.1)	0.58
Age (years)	60.72 ± 9.95	59.78 ± 11.29	0.46	58.96 ± 10.53	62.89 ± 10.54	< 0.01*
Systolic blood pressure(mmHg)	164.42 ± 35.26	167.31 ± 33.07	0.48	166.66 ± 34.99	164.43 ± 32.28	0.61
Diastolic blood pressure(mmHg)	93.87 ± 17.99	95.46 ± 18.73	0.47	93.79 ± 17.98	96.62 ± 19.11	0.23
Mean arterial pressure(mmHg)	117.39 ± 22.19	118.27 ± 22.15	0.74	117.39 ± 22.38	118.83 ± 21.72	0.61
Medical history	–	–	–	–	–	–
Hypertension	70(52.2)	71(47.7)	0.44	93(48.4)	48(52.7)	0.49
Diabetes mellitus	13(9.7)	13(8.7)	0.77	14(7.3)	12(13.2)	0.11
Ischemic stroke	13(9.7)	20(13.4)	0.33	18(9.4)	15(16.5)	0.08
Smoker	60(44.8)	76(51.0)	0.29	94(49.0)	42(46.2)	0.66
Alcohol(> 3 drinks per 24 h)	50(37.3)	65(43.6)	0.28	74(38.5)	41(45.1)	0.29
Hydrocephalus	15(11.2)	26(17.4)	0.14	19(9.9)	22(24.2)	< 0.01*
GCS score on admission	13(11, 14)	9(6, 9)	< 0.01*	12(9, 14)	7(6, 9)	< 0.01*
Hematoma size (ml)	19.15 ± 12.63	30.24 ± 14.83	< 0.01*	19.18 ± 11.74	37.25 ± 13.31	< 0.01*
Presence of IVH	6(4.5)	46(30.9)	< 0.01*	20(10.4)	32(35.2)	< 0.01*
Supratentorial hematoma	125(93.3)	137(91.9)	0.67	178(92.7)	84(92.3)	0.91
PT (seconds)	11.67 ± 2.17	11.45 ± 1.92	0.38	11.66 ± 2.12	11.35 ± 1.86	0.24
APTT (seconds)	28.96 ± 3.58	28.95 ± 2.90	0.99	29.12 ± 3.46	28.61 ± 2.69	0.22
INR	1.28 ± 1.10	1.21 ± 0.96	0.53	1.28 ± 1.08	1.17 ± 0.92	0.41
Early hematoma expansion	18(13.4)	95(63.8)	< 0.01*	43(22.4)	70(76.9)	< 0.01*
Island sign	14(10.4)	52(34.9)	< 0.01*	32(16.7)	32(37.4)	< 0.01*
Spot sign	21(15.7)	64(43.0)	< 0.01*	33(17.2)	52(57.1)	< 0.01*

Data are expressed as n(%), mean ± standard deviation, median(interquartile range) as appropriate.

IVH, intraventricular hemorrhage; GCS, Glasgow coma scale; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio.

Table 3
Associations of clinical values on admission with 3 month functional outcome in patients with ICH.

Characteristic	Crude		Adjusted (island sign) ^a		Adjusted (Spot sign) ^b	
	OR(CI)	P	OR(CI)	P	OR(CI)	P
GCS score on admission	0.464(0.395–0.547)	< 0.01	0.486(0.407–0.580)	< 0.01	0.782(0.699–0.875)	< 0.01
Hematoma size (ml)	1.062(1.041–1.083)	< 0.01	1.022(1.013–1.088)	< 0.01	1.045(1.018–1.073)	< 0.01
Presence of IVH	9.528(3.915–23.187)	< 0.01	5.890(1.713–20.259)	< 0.01	5.382(1.480–19.570)	0.01
Island sign	4.595(2.404–8.784)	< 0.01	7.564(2.969–19.273)	< 0.01	–	–
Spot sign	4.052(2.297–7.147)	< 0.01	–	–	3.413(1.570–7.422)	< 0.01

CI, confidence interval; OR, odds ratio; CTA, CT angiography; GCS, Glasgow coma scale.

^a Adjustment by alcohol consumption, time to CTA, supratentorial organ, GCS score, hematoma volume, island sign.

^b Adjustment by alcohol consumption, time to CTA, supratentorial organ, GCS score, hematoma volume, spot sign.

hematoma (island sign VS spot sign 0.696, 0.729, *P* = .25, Fig. 3 and Table 7).

4. Discussion

We compared the predictive value of island sign and spot sign for short-term prognosis in patients with ICH patients. This study indicated that island sign exhibited comparable predictive efficiency with CTA spot sign for poor functional outcome in the same cohort. Meanwhile,

both of them have satisfactory predictive abilities for hematoma expansion. However, the spot sign showed a better predictive accuracy than island sign for mortality at 3 months.

The island sign, black hole sign and blend sign from NCCT, as well as CTA spot sign were initially developed as radiological predictors for hematoma expansion. Afterward, mounts of studies found that they also have close relationship with the prognosis of ICH patients [9,14,15]. Nevertheless, up to date, few evidences were put in demonstrating their predictive abilities in ICH patients with poor clinical prognosis. As

Table 4
Associations of clinical values on admission with 3-month mortality in patients with ICH.

Characteristic	Crude		Adjusted (island sign) ^a		Adjusted (Spot sign) ^b	
	OR(CI)	P	OR(CI)	P	OR(CI)	P
Age	1.037(1.011–1.063)	< 0.01	0.999(0.961–1.038)	0.94	0.997(0.960–1.036)	0.89
Hydrocephalus	2.903(1.479–5.698)	< 0.01	2.310(0.664–8.035)	0.19	2.295(0.752–7.002)	0.14
GCS score on admission	0.615(0.546–0.693)	< 0.01	0.544(0.412–0.681)	< 0.01	0.681(0.593–0.783)	< 0.01
Hematoma size (ml)	1.114(1.085–1.144)	< 0.01	1.091(1.048–1.181)	< 0.01	1.111(1.078–1.146)	< 0.01
Presence of IVH	4.664(2.479–8.776)	< 0.01	2.954(1.235–6.443)	< 0.01	3.620(1.435–9.132)	< 0.01
Island sign	2.982(1.687–5.272)	< 0.01	2.362(1.238–3.899)	< 0.01	–	–
Spot sign	6.424(3.672–11.240)	< 0.01	–	–	2.713(1.570–4.217)	< 0.01

CI, confidence interval; OR, odds ratio; CTA, CT angiography; GCS, Glasgow coma scale.

^a Adjustment by alcohol consumption, time to CTA, supratentorial organ, GCS score, hematoma volume, island sign.

^b Adjustment by alcohol consumption, time to CTA, supratentorial organ, GCS score, hematoma volume, spot sign.

Table 5
Associations of clinical values on admission with hematoma expansion in patients with ICH.

Characteristic	Crude		Adjusted (island sign) ^a		Adjusted (Spot sign) ^b	
	OR(CI)	P	OR(CI)	P	OR(CI)	P
Supratentorial hematoma	3.429(1.135–10.363)	0.03	0.515(0.082–3.241)	0.48	1.998(0.478–8.350)	0.26
Time to CTA	0.734(0.636–0.846)	< 0.01	0.931(0.752–1.147)	0.49	0.887(0.723–1.089)	0.24
GCS score on admission	0.672(0.607–0.744)	< 0.01	0.685(0.596–0.788)	< 0.01	0.719(0.629–0.822)	< 0.01
Hematoma size (ml)	1.172(1.132–1.213)	< 0.01	1.136(1.094–1.180)	< 0.01	1.157(1.114–1.201)	< 0.01
Island sign	10.668(5.428–20.965)	< 0.01	3.596(1.432–9.028)	< 0.01	–	–
Spot sign	14.019(7.414–26.509)	< 0.01	–	–	4.233(1.570–8.248)	< 0.01

CI, confidence interval; OR, odds ratio; CTA, CT angiography; GCS, Glasgow coma scale.

^a Adjustment by alcohol consumption, time to CTA, supratentorial origin, GCS score, hematoma volume, island sign.

^b Adjustment by alcohol consumption, time to CTA, supratentorial origin, GCS score, hematoma volume, spot sign.

Table 6
Studies concerning imaging predictors for poor clinical outcome in ICH patients.

Study(first author, year of publication)	Imaging predictors	Sensitivity	Specificity	PPV	NPV	AUC
Peter 2017 [24]	Black hole sign	23.1	97.4	92.3	48.7	–
Peter 2017 [24]	Blend sign	31.7	94.9	89.2	51	–
Peter 2017 [24]	Spot sign	34.6	96.2	92.3	52.4	–
Li 2017 [9]	Blend sign	24.2	91.2	75	52.5	–
Han 2014 [14]	Spot sign	86.9	46	43.8	87.9	–
Our study	Island sign	34.9	89.6	78.8	55.3	0.622
Our study	Spot sign	43	84.3	75.3	57.1	0.636

uHG, ultraearly hematoma growth; HDH, hematoma density heterogeneity; PPV, positive predictive value; NPV, negative predictive value; AUC, area under curves.

mentioned above, spot sign was recognized as a robust marker of early hematoma growth in previous retrospective studies [5,6,16]. Recent multicenter studies revealed that spot sign could predict both hematoma expansion and poor prognosis in patients with ICH [17]. Although

there is still controversial for the predictive abilities of spot sign in prognosis of ICH patients, but it is well documented that spot sign is one of the most reliable predictor for early hematoma growth and prognosis until now [2,7,10,14,17–22]. Other than that, Wada et al [16] demonstrated that the sensitivity and specificity of spot sign were 91% and 89% for hematoma growth, respectively. In contrast, a relatively lower sensitivity (77.9%) and higher specificity (93.2%) of spot sign were also reported [23]. Meta-analysis from 18 cohort studies indicated that the sensitivity of spot sign was 53% and specificity was 88%, which is consistent with our current results (sensitivity 57.5%, specificity 88.2%, PPV 76.5%, NPV 75.8%, Table 7) [6]. Overall these conclusions, spot sign showed a relatively weaker role in predicting poor prognosis by comparing with the predictive ability for hematoma expansion. In addition, Peter et al. [24] observed that the sensitivity and specificity of spot sign were 34.6% and 96.2%, respectively. There results were also similar to our results (sensitivity 43.0% and specificity 84.3%). However, Han et al. [14] revealed higher sensitivity (86.9%) and lower specificity (46.0%) for predicting poor outcome in ICH patients. In regarding with this difference, we believe that other potential factors between two studies might not be consistent, including hematoma volume, time interval from onset to initial CTA, setting of CTA, as well as

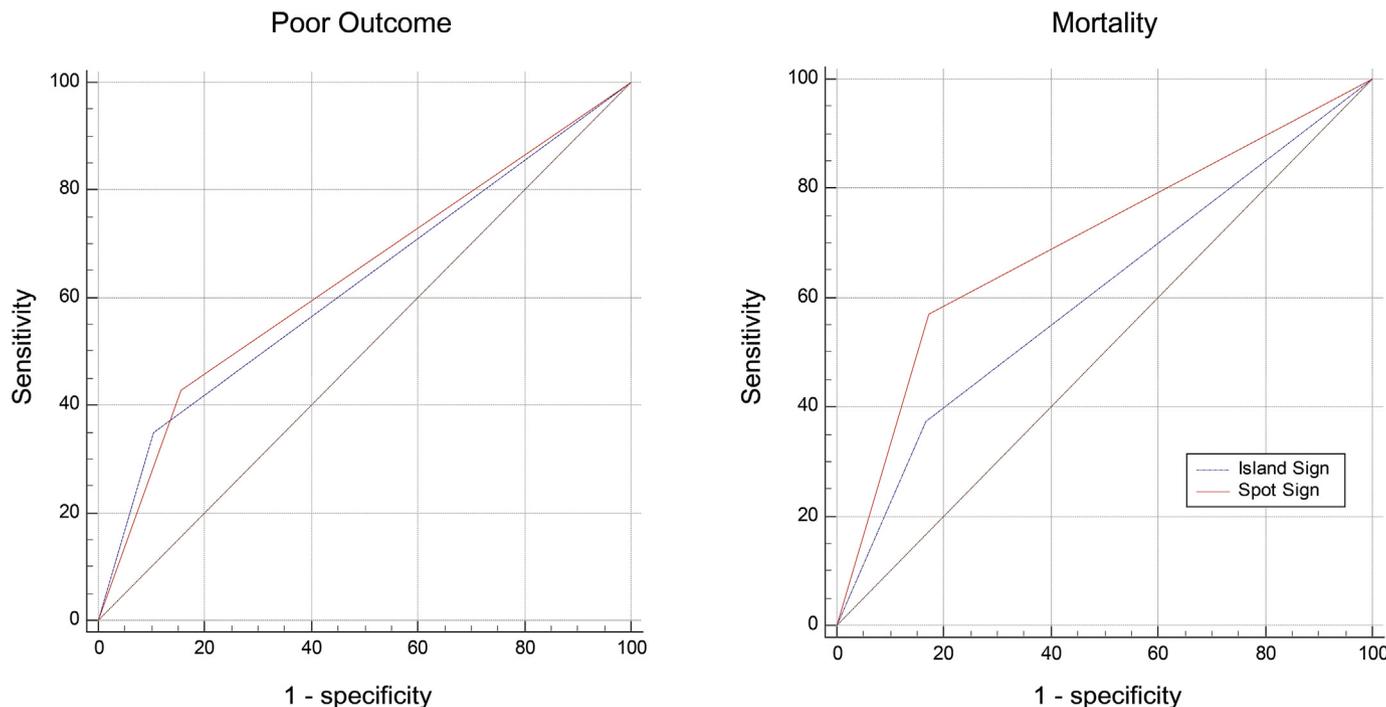


Fig. 2. Receiver operating characteristic curves (ROC) of island sign and spot sign for 3-month morbidity and mortality. Island sign showed a comparable predictive value to spot sign in predictive 3-month poor outcome (AUC 0.622 vs 0.636, $P = .58$) while the spot sign exhibited a better ability in predicting 3-month mortality (AUC 0.700 vs. 0.603, $P < .01$).

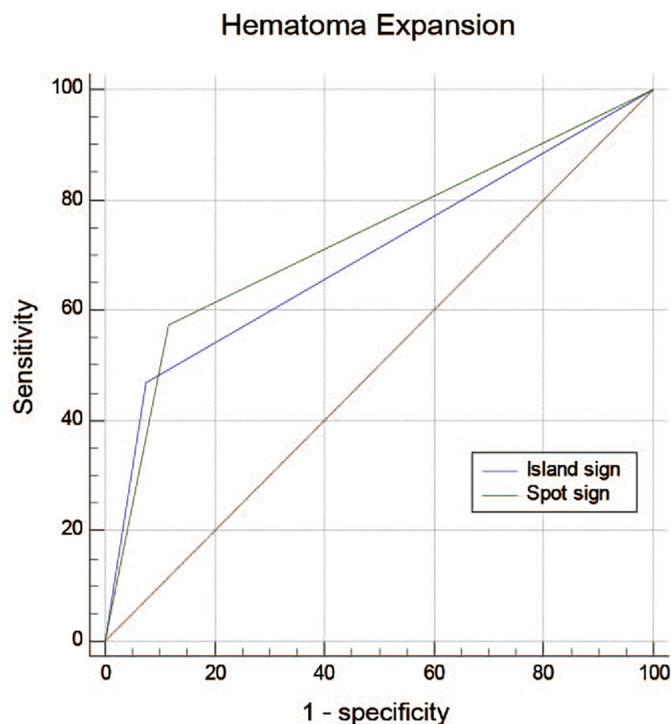


Fig. 3. Receiver operating characteristic curves (ROC) of island sign and spot sign. The AUC is 0.696 for NCCT island sign and 0.729 for CTA spot sign.

Table 7
Studies concerning imaging predictors for hematoma growth in Chinese population.

Study(first author, year of publication)	Imaging predictors	Sensitivity	Specificity	PPV	NPV	AUC
Yu 2017 [29]	HDH grade(> 3)	55.9	70.9	39.8	83	0.677
Yu 2017 [29]	uHG(> 4.7 ml/h)	76.5	57.3	37.1	88.1	0.669
Yu 2017 [29]	Hypodensities	59.0	76.0	44.0	85.0	0.673
Yu 2017 [19]	Black hole sign	43.8	84.5	48.3	82.1	0.641
Yu 2017 [29]	Black hole sign	44.0	83.0	45.0	82.0	0.633
Li 2017 [30]	Black hole sign	33.9	90.2	57.9	77.4	0.62
Li 2016 [26]	Black hole sign	31.9	94.1	73.3	73.2	0.656
Li 2015 [27]	Blend sign	39.3	95.5	82.7	74.1	0.674
Zheng 2017 [20]	Blend sign	50	83	49	83	0.663
Li 2017 [30]	Blend sign	43.1	89	60.9	79.7	0.66
Yu 2017 [21]	Spot sign	62.2	87.1	60.5	87.8	0.746
Yu 2017 [19]	Spot sign	59.4	88.7	63.3	86.9	0.74
Li 2017 [9]	Island sign	44.7	98.2	92.7	77.7	0.715
Our study	Island sign	46.9	92.4	80.3	72.4	0.696
Our study	Spot sign	57.5	88.2	76.5	75.8	0.729

uHG, ultraearly hematoma growth; HDH, hematoma density heterogeneity; PPV, positive predictive value; NPV, negative predictive value; AUC, area under curves.

sample size of two studies. All those factors would affect the predictive ability of spot sign in ICH patients [17,19,24]. Furthermore, spot sign is also an illustration of the continuous bleeding from surrounding vessels [5]. It is well documented that the leaking of contrast from surrounding vessels (active contrast extravasation) resulted in the presence of spot sign in the hematoma [13]. All the evidences above make us believe that spot sign represents an excellent predictor for poor outcome and early hematoma expansion.

Due to the emergency situation of the patients and limitations of the hospital conditions, CTA could not be performed on all the patients with ICH. Thus, NCCT based predictive features, including blend sign,

black hole sign and hypodensities were recently used to predict the hematoma expansion and prognostic outcomes [8,25–30]. And more recently data also indicated that irregularly shaped hematoma revealed the growth of hematoma in ICH patients [31,32]. As the latest NCCT image marker, island sign was first proposed by Li et al. and was described as an extremely irregularly shaped hematoma since 2017 [9]. In a study containing 252 patients with ICH, island sign was identified as a predictor for hematoma expansion and poor outcome [9]. Here, we found 66 patients with island sign over 113 patients with early hematoma growth. The satisfying sensitivity was 46.9% with a highly specificity of 92.4% for hematoma expansion (Table 7). Moreover, island sign was an independent predictor for poor outcome with a sensitivity of 34.9% and a specificity of 89.6% (Table 6). Similar with spot sign, this novel imaging sign was assumed to reflect multifocal active bleeding from adjacent arterioles as well [9]. We further confirmed that island sign was correlated with CTA spot sign. This finding further supports the hypothesis above. Moreover, this predictive factor was an easy-to-use tool for clinical practice due to several merits. Firstly, it harbors a comparable predictive ability for poor outcome (island sign vs. spot sign: AUC 0.622 vs 0.636) and hematoma expansion (island sign vs. spot sign: AUC 0.696 vs 0.729) to spot sign. In addition, island sign exhibits an outstanding PPV among the above imaging features for hematoma expansion (Table 7). Furthermore, the island sign can be performed in emergency situation, and/or the CTA was unavailable. Simultaneously, the highly interrater reliability ensures that both physician and surgeons can easily handle this new neuroimaging sign during clinical routine. In considering the predictive role and high PPV of island sign for poor clinical outcome and hematoma growth, respectively, we would take it as an efficient and economic indicator for guiding the aggressive treatment of ICH patients, such as hematoma evacuation. Overall, further study will be done for providing more evidences to support our view.

In this study, we compared the predictive ability of spot sign and island sign for clinical outcome. The spot sign showed the trends to have higher sensitivity, lower specificity and better AUC for poor outcomes. These results indicated that island sign exhibited a compared predictive value for 3-month unfavorable outcome than spot sign. But spot sign showed a better predictive power for mortality than island sign. Therefore, spot sign is a plausibly better prognostic factor for clinical outcome in patients with ICH. And island sign also exhibits a satisfying predictive accuracy and remains an acceptable predictor for short-term prognosis if CTA is not available in emergent condition or contraindications of contrast administration occur (eg. progressed renal dysfunction or allergic reaction).

Other than that, our study also confirmed that age, hydrocephalus, GCS, hematoma volume and IVH were correlated with short-term mortality of ICH patients by performing univariate analysis. After adjusting for confounding factor, admission GCS scores and hematoma size were further confirmed to independently associate with 3-month poor outcome and mortality, which were consistent to previous conclusions [33,34].

There are several limits in this study. Firstly, our retrospective cohort research was performed in single medical center, which may lead to a potential selection bias. Following, hematoma size was assessed by ABC/2 methods, which is a less accurate way than CT technology. Furthermore, as the largest general hospital in west region of China, our academic hospital usually recruited individuals who were in worse clinical conditions by comparing the patients admitted to other hospitals at the same region.

5. Conclusion

Our results revealed that both spot sign and island sign have strong predictive abilities for 90-day poor functional outcome and early hematoma growth. Other than spot sign, island sign is also an excellent predictor for both hematoma expansion and poor clinical prognosis of

ICH patients. But spot sign exhibited a superior ability than island sign in predicting mortality at 3 months. However, NCCT based island sign is more convenient to be applied to predict poor outcome and hematoma expansion than CTA based spot sign, thus could be used much easier and wider in clinical practices.

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Conflict of interest

No conflict of interest was reported.

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