

New models for predicting mortality and poor prognosis after supratentorial intracerebral hemorrhage

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Abstract

Background: The study aimed to determine the multiple related risk factors and their prognostic significance of intracerebral hemorrhage (ICH), and to develop models for predicting poor outcome and mortality.

Methods: We retrospectively analyzed 141 consecutive patients with acute ICH presenting to the neurological department of Tongji Hospital from December 2016 to April 2018. Independent predictors of 6-month prognostic significance were identified by logistic regression, and discriminative performance was assessed by using the area under curve (AUC) of receiver-operating characteristic (ROC). Models of poor prognosis and mortality were developed.

Results: Independent predictors of poor outcome ($mRS \geq 3$) were as follows: NIHSS score, D-Dimer, mixed hematoma density, irregular hematoma shape, ICH volume, cerebral cortical atrophy and midline shift. The sensitivity and specificity of poor prognosis model were 87.5% and 87.4%, respectively. Independent factors associated with 6-month mortality included platelet counts at admission, NIHSS score, eGFR, presence of intraventricular hemorrhage (IVH), third ventricle Sylvian fissure distance. The sensitivity and specificity of the model for mortality were 90.0% and 94.4%, respectively.

Conclusions: Two models for prognostic significance of ICH were developed and could well predict the poor prognosis and mortality.

Background

Intracerebral hemorrhage (ICH) is a common neurological emergency, accounting for 20% of all strokes, and usually leads to severe disability or death. Its mortality rate at 1 month is about 40%, and about 54% in 1 year, only 12–39% of patients achieve permanent functional independence^[1–3]. Therefore, early identification of patients at high risk of ICH is crucial for prognosis.

Previously, a number of prognostic models for mortality and functional outcome after ICH such as the ICH score, the ICH-GS score, the modified ICH score, the FUNC score and ICH index^[4–8] have been established. The variables that they include are GCS score, ICH volume, IVH, ICH location, infratentorial ICH origin, age etc. Recently, some other factors were found to be associated with prognosis including hematoma enlargement, the use of antithrombotic drugs, do-not-resuscitate (DNR) treatment, intense antihypertension^[9–11], and newfound various CT signs (island sign, black hole sign, blend sign, hematoma irregularity and heterogeneity etc.)^[12–15]. Earlier studies on the prognosis of ICH have covered a relatively simple and limited number of factors, and these models do not include newly identified CT signs, the sensitivity and specificity of the models also need to be improved. In our study, we have taken into account those new findings and expected to develop new prognostic models for ICH.

Methods

Patients

From December 2016 to April 2018, patients with spontaneous supratentorial intracerebral hemorrhage hospitalized in the Department of Neurology, Tongji Hospital, Huazhong University of Science and Technology were enrolled. Patients with spontaneous ICH within a week of onset were included. Exclusion criteria were as follows: (1) primary intraventricular hemorrhage; (2) hemorrhage secondary to trauma, tumor, vascular malformations, aneurysm and hemorrhagic transformation of ischemic stroke; (3) patients undergoing hematoma evacuation before admission. Our data were anonymous, the requirement for informed consent was therefore waived^[16].

Data Collecting

Data were retrospectively recorded including: (1) general clinical characteristics: age, gender, general personal information, smoking or drinking history, history of hypertension, diabetes and antithrombotic use, systolic and diastolic blood pressure at admission, body temperature, pulse, duration of hospital stay, levels of consciousness, concomitant diseases. (2) laboratory examination: blood routine at admission, coagulation function, D-Dimer, blood glucose, N/L ratio (by absolute neutrophil count divided by absolute lymphocytes count), the results of the next morning blood test, including: low density lipoprotein (LDL), various indicators of inflammation [high sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate, procalcitonin (PCT), interleukin], albumin, renal function indexes [eGFR, Cysc, ESRD (end-stage renal disease, for glomerular filtration rate < 15 ml/min/1.73 m² or dialysis patients), $eGFR = 186 \times (Scr)^{-1.154} \times (age) - 0.203 \times (0.742 \text{ female patients})$]^[17], SIRS [systemic inflammatory response syndrome, in accordance with the following 2 or more criteria: (1) temperature > 38 °C (100.4°F) or < 36 °C (96.8°F); (2) heart rate (HR) > 90 beats/min; (3) respiration rate (RR) > 20 beats/min or arterial carbon dioxide partial pressure (PaCO₂) < 32 mmHg; (4) white blood cell count > 12,000 / μL or < 4000 / μL or immature cells > 10%]^[18], admission and the fourth day of NT-proBNP.

The images of baseline CT scan were collected including: the first head CT time from onset, ICH volume, the location of ICH, various CT signs, the midline shift, hemorrhage breaking into ventricles or subarachnoid spaces. The location of cerebral hemorrhage is divided into: lobe, basal ganglia, other (corpus callosum or capsula externa) and multi-site ICH. The ICH volume is calculated by superimposing the area of each bleeding layer and multiplying the total area by the thickness of the section^[19]. Island sign, black hole sign, blend sign, liquid level, satellite sign, hematoma irregularity and heterogeneity are identified referring to previous literatures^[12-15, 20-22]. Two experienced clinicians who were blinded to the clinical profiles of the patients independently assessed all CT signs and discrepancies were determined by an experienced professor. Blend sign, black hole sign, liquid level, hematoma heterogeneity are uniformly defined as mixed hematoma density; island sign, satellite sign, hematoma irregularity are defined as irregular hematoma shape. Midline shift (MLS) was determined by creating a line connecting the anterior and posterior insertions of the falx cerebri, and measuring a perpendicular distance from the

line to the septum pellucidum at the level of the foramen of Monro^[23, 24]. The linear measurement and visual assessment of the contralateral side of ICH were used to determine brain atrophy^[25], linear measurement markers including frontal ratio and third ventricle Sylvian fissure distance. White matter lesion (WML) was graded using the scale described by van Swieten et al^[26]. Lacuna is defined as a circular or oval, subcortical, liquid (like cerebrospinal fluid density) cavity between 3 and 15 mm in diameter, consistent with previous small acute deep cerebral infarction or hemorrhage in the area of perforating branch arteriole^[25].

Different treatments were recorded: conservative treatment, hematoma minimally invasive aspiration, extraventricular drainage (EVD), decompressive craniectomy, and other (hematoma minimally invasive aspiration + EVD + bone flap decompression).

Functional outcome and mortality were evaluated by the modified Rankin scale at 6 months. The mRS were divided into groups with good prognosis ($mRS \leq 2$) and poor prognosis ($mRS \geq 3$); basic recovery group ($mRS \leq 1$), disabled group ($2 \leq mRS \leq 5$) and death group ($mRS = 6$); death and non-death group in univariate analysis. The mRS-9Q method was mainly used to determine the patient mRS score^[27].

Statistical analyses

For univariate analyses, the continuous variables were described by the mean \pm SD values and compared using student's t test and ANOVA analysis. The categorical variables were expressed by frequency and percentage, and chi-square test of four-fold table and row list table, the Bonferroni corrected chi-square test and Fisher exact test were used for comparison between groups.

Multivariate logistic regression analysis was used to investigate the independent factors associated with the prognosis of ICH, those variables that reached $P < 0.2$ (or close to 0.2) in univariate analysis were considered for multivariable analysis, and the stepwise regression was performed backward. Finally, we determined the independent prognostic factors for ICH and developed models for predicting poor outcome and mortality. Univariate and multivariate receiver operating characteristic curve (ROC) analyses were performed, and the Yoden index was used to set up the cut-off value of continuous variables. Statistical analysis was performed with SPSS (version 22.0), and $P < 0.05$ was considered statistically significant.

Results

Of the 141 patients with ICH, the average age was 54.72 ± 10.91 years old, 95 male patients (67.4%), and 46 female patients (32.6%) were admitted. The mean systolic blood pressure was 153.72 ± 26.29 mmHg, the mean diastolic blood pressure was 93.43 ± 19.01 mmHg. 87 patients (61.7%) had a good prognosis, 54 patients (38.3%) had poor conditions. 57 patients (40.4%) had a basic recovery, 69 Patients (48.9%)

had a disability and 15 (10.6%) died. Baseline characteristics of patients are shown in Table 1 and Table 2.

Table 1

Baseline, clinical and imaging characteristics for outcome subgroups (good and poor prognosis)

	Good prognosis (mRS 0–2)	Poor prognosis (mRS 3–6)	P value
Patients, n(%)	87	54	
Gender(male)	57(65.5%)	38(70.4%)	0.584
Age(year)	53.72 ± 11.48	56.33 ± 9.81	0.168
DBP(mmHg)	95.02 ± 20.38	90.87 ± 16.43	0.186
SBP(mmHg)	153.30 ± 27.87	154.39 ± 23.77	0.805
Pulse(times/min)	77.25 ± 9.65	83.80 ± 18.59	0.019
PLT(*10 ⁹ /L)	206.21 ± 61.37	201.76 ± 66.15	0.685
eGFR(ml/min/1.73 m ²)	88.03 ± 29.06	86.62 ± 28.11	0.775
ESRD	4(4.6%)	4(7.4%)	0.482
Antithrombotic use	9(10.3%)	4(7.4%)	0.766
D-Dimer(mg/L)	0.533	0.935	0.157
SIRS	0(0%)	8(14.8%)	< 0.001
IVH	28(32.2%)	26(48.1%)	0.075
SAH	11(12.6%)	13(24.1%)	0.106
N/L ratio	5.97(2.35–11.69)	8.27(2.0-19.4)	0.005
NIHSS score	2.74(0–10)	13.42(9–17)	< 0.001
WBC(*10 ⁹ /L)	9.22 ± 2.94	11.60 ± 4.20	< 0.001
Mixed hematoma density	22(25.3%)	16(29.6%)	0.697
Irregular hematoma shape	21(24.1%)	37(68.5%)	< 0.001

Note: data are n (%), mean ± SD or median. ESRD, end-stage renal disease. SIRS, systemic inflammatory response syndrome. IVH, presence with IVH. SAH, presence with SAH. N/L ratio, absolute neutrophil count divided by absolute lymphocytes count. Mixed hematoma density, including: blend sign, black hole sign, liquid level, hematoma heterogeneity. Irregular hematoma shape, including: island sign, satellite sign, hematoma irregularity. Central cerebral atrophy and cortical cerebral atrophy, determined by visual assessment of the contralateral side of ICH^[24]. WML, white matter lesion, WML grade described by van Swieten scale^[25].

	Good prognosis (mRS 0–2)	Poor prognosis (mRS 3–6)	P value
The location of ICH			< 0.001
lobe	21(24.1%)	5(9.3%)	
basal ganglia	55(63.2%)	26(48.1%)	
multi-site ICH	8(9.2%)	22(40.7%)	
other	3(3.4%)	1(1.9%)	
ICH volume(ml)	9.86(2.32–21.44)	27.23(11.42–46.44)	< 0.001
Midline shift(mm)	2.21(0.37–3.93)	3.20(1.09–6.93)	< 0.001
Different treatment			< 0.001
conservative treatment	80(92%)	30(55.6%)	
hematoma minimally invasive aspiration	7(8.0%)	22(40.7%)	
other	0(0%)	2(3.7%)	
Frontal ratio	27.2%(22.8%-30.6%)	26.3%(21.2%-29.6%)	0.088
Third ventricle Sylvian fissure distance(mm)	39.23(37.17–41.33)	38.37(35.83–40.37)	0.003
Central cerebral atrophy			0.414
none	40(46.0%)	24(44.4%)	
moderate	35(40.2%)	26(48.1%)	
severe	12(13.8%)	4(7.4%)	
Cortical cerebral atrophy			0.679
none	20(23.0%)	12(22.2%)	
moderate	49(56.3%)	34(63.0%)	

Note: data are n (%), mean ± SD or median. ESRD, end-stage renal disease. SIRS, systemic inflammatory response syndrome. IVH, presence with IVH. SAH, presence with SAH. N/L ratio, absolute neutrophil count divided by absolute lymphocytes count. Mixed hematoma density, including: blend sign, black hole sign, liquid level, hematoma heterogeneity. Irregular hematoma shape, including: island sign, satellite sign, hematoma irregularity. Central cerebral atrophy and cortical cerebral atrophy, determined by visual assessment of the contralateral side of ICH^[24]. WML, white matter lesion, WML grade described by van Swieten scale^[25].

	Good prognosis (mRS 0–2)	Poor prognosis (mRS 3–6)	P value
Severe	18(20.7%)	8(14.8%)	
Lacuna	39(44.8%)	20(37.0%)	0.385
White matter lesion grading			0.813
0	80(92.0%)	49(90.7%)	
1	3(3.4%)	1(1.9%)	
2	2(2.3%)	3(5.6%)	
3	1(1.1%)	0(0%)	
4	1(1.1%)	1(1.9%)	

Note: data are n (%), mean ± SD or median. ESRD, end-stage renal disease. SIRS, systemic inflammatory response syndrome. IVH, presence with IVH. SAH, presence with SAH. N/L ratio, absolute neutrophil count divided by absolute lymphocytes count. Mixed hematoma density, including: blend sign, black hole sign, liquid level, hematoma heterogeneity. Irregular hematoma shape, including: island sign, satellite sign, hematoma irregularity. Central cerebral atrophy and cortical cerebral atrophy, determined by visual assessment of the contralateral side of ICH^[24]. WML, white matter lesion, WML grade described by van Swieten scale^[25].

Table 2

Baseline, clinical and imaging characteristics for outcome subgroups (non-death and death)

	Non-death	Death	P value
Patients, n(%)	126	15	
Gender(male)	84(66.7%)	11(73.3%)	0.774
Age(year)	54.21 ± 11.07	59.0 ± 8.52	0.061
PLT(*10 ⁹ /L)	209.20 ± 62.45	165.07 ± 55.35	0.01
eGFR(ml/min/1.73 m ²)	90.42 ± 25.96	62.89 ± 37.94	0.015
ESRD	4(3.2%)	4(26.7%)	0.005
Pulse(times/min)	78.56 ± 13.08	89.80 ± 18.30	0.035
DBP(mmHg)	93.56 ± 19.46	92.40 ± 15.15	0.790
SBP(mmHg)	153.70 ± 26.59	153.87 ± 24.53	0.980
Albumin(g/L)	42.95 ± 4.25	41.25 ± 4.49	0.181
D-Dimer(mg/L)	0.595	1.673	0.105
SIRS	5(4.0%)	3(20.0%)	0.04
IVH	43(34.1%)	11(73.3%)	0.005
SAH	19(15.1%)	5(33.3%)	0.136
N/L ratio	6.29(1.97–13.87)	8.77(2.04–23.46)	0.107
NIHSS score	5.80(1–13)	14.0(6–18)	0.029
WBC(*10 ⁹ /L)	9.92 ± 3.50	11.86 ± 4.51	0.052
Mixed hematoma density	35(27.8%)	3(20.0%)	0.759
Irregular hematoma shape	47(37.3%)	11(73.3%)	0.011
The location of ICH			0.014
lobe	23(18.3%)	3(20.0%)	
basal ganglia	77(61.1%)	4(26.7%)	
multi-site ICH	22(17.5%)	8(53.3%)	
other	4(3.2%)	0(0%)	
ICH volume(ml)	12.18(2.63–30.85)	27.33(12.40-52.42)	< 0.001
Midline shift(mm)	2.35(0.47–4.87)	3.90(0.78–8.16)	0.083

	Non-death	Death	P value
Different treatment			0.015
conservative treatment	99(78.6%)	11(73.3%)	
hematoma minimally invasive aspiration	27(21.4%)	2(13.3%)	
other	0(%)	2(13.3%)	
Frontal ratio	26.8% (22.1%-30.3%)	27.2% (22.8%-30.4%)	0.883
Third ventricle Sylvian fissure distance(mm)	38.98(36.67–41.15)	38.23(36.1-39.84)	0.121
Central cerebral atrophy			1.000
none	57(45.2%)	7(46.7%)	
moderate	54(42.9%)	7(46.7%)	
severe	15(11.9%)	1(6.7%)	
Cortical cerebral atrophy			0.804
none	28(22.2%)	4(26.7%)	
moderate	75(59.5%)	8(53.3%)	
Severe	23(18.3%)	3(20.0%)	
Lacuna	55(43.7%)	4(26.7%)	0.273
White matter lesion grading			0.084
0	117(92.9%)	12(80.0%)	
1	4(3.2%)	0(0%)	
2	3(2.4%)	2(13.3%)	
3	1(0.8%)	0(0%)	
4	1(0.8%)	1(6.7%)	
<p>Note: data are n (%), mean±SD or median. ESRD, end-stage renal disease. SIRS, systemic inflammatory response syndrome. IVH, presence with IVH. SAH, presence with SAH. N/L ratio, absolute neutrophil count divided by absolute lymphocytes count. Mixed hematoma density, including: blend sign, black hole sign, liquid level, hematoma heterogeneity. Irregular hematoma shape, including: island sign, satellite sign, hematoma irregularity. Central cerebral atrophy and cortical cerebral atrophy, determined by visual assessment of the contralateral side of ICH[24]. WML, white matter lesion, WML grade described by van Swieten scale[25].</p>			

Univariate Analysis

Good prognosis group (mRS ≤ 2) and poor prognosis group (mRS ≥ 3)

The pulse rate, presence with systemic inflammatory response syndrome (SIRS), N/L ratio, NIHSS score, white blood cell count, irregular hematoma shape, ICH volume, midline shift, third ventricle Sylvian fissure distance, the location of ICH and conservative treatments were associated with poor prognosis (Table 1).

Basic recovery group (mRS 0–1), disability group (mRS 2–5) and death group (mRS 6)

Compared with the basic recovery group and the disability group, the pulse rate, the proportion of end-stage renal disease (ESRD), IVH and irregular hematoma shape, the presence of the island sign, the ratio of N/L was higher in the death group, glomerular filtration and PLT counts were lower. The proportion of patients with SIRS and subarachnoid hemorrhage, white blood cell count were lowest in the basic recovery group (Table I in the online-only Data Supplement).

Death and non-death group

The pulse rate, presence with ESRD, SIRS, IVH and irregular hematoma shape, NIHSS score, ICH volume, PLT count, glomerular filtration rate, the location of ICH and conservative treatments were associated with mortality (Table 2).

Multivariate Analysis

The multivariate logistic regression analysis showed that NIHSS score, D-Dimer, mixed hematoma density, irregular hematoma shape, ICH volume, cortical brain atrophy and midline shift independently predicted poor prognosis. Factors associated with mortality of ICH include: platelet count at admission, NIHSS score, IVH, third ventricle Sylvian fissure distance. Inflammation signs (elevated white blood cell count and N/L ratio) may increase the risk of mortality ($P = 0.05, 0.093$), and hematoma minimally invasive aspiration may reduce the risk of mortality ($P = 0.053$) (Table 3).

Table 3. Multivariable analysis of poor outcome (mRS ≥ 3) and mortality

Poor outcome			
Variable	OR	95% CI	P value
NIHSS score	1.496	1.271-1.761	0.000
D-Dimer	1.204	1.010-1.436	0.038
Irregular hematoma shape	5.654	1.315-24.303	0.020
Mixed hematoma density	0.189	0.043-0.832	0.028
Midline shift(1.43-2.42mm)	10.526	1.615-68.602	0.014
ICH volume	1.125	1.041-1.216	0.003
Severe cerebral cortical atrophy	18.440	1.734-196.115	0.016
Mortality			
Variable	OR	95% CI	P value
NIHSS score	1.454	1.055-1.995	0.027
platelet counts	0.974	0.950-0.999	0.038
eGFR	0.925	0.875-0.978	0.006
IVH	33.841	1.460-784.514	0.028
white blood cell count	1.735	1.000-3.021	0.050
hematoma minimally invasive aspiration	0.028	0.001-1.053	0.053
third ventricle Sylvian fissure distance ≥ 38.93 mm	0.071	0.005-0.924	0.043
the frontal lobe ratio ≥ 0.289	0.064	0.002-2.270	0.131
The location of ICH			0.106
N/L ratio			0.093

Abbreviation: CI, confidence interval. IVH, presence of intraventricular hemorrhage.

N/L ratio, absolute neutrophil count divided by absolute lymphocytes count.

Establishment of models of poor prognosis and mortality

Poor outcome model

Based on the results of multivariate logistic regression, a poor prognosis model was developed, with all the variables of the model as follows:

- X_1 , D-Dimer count
- X_2 , NIHSS score
- X_3 , irregular hematoma shape population
- X_4 , ICH volume count
- X_5 , MLS as 1.43-2.42mm population
- X_6 , MLS as 2.42-4.13mm population
- X_7 , $MLS \geq 4.13$ mm population (the reference value of MLS is 0-1.43mm)
- X_8 , mixed hematoma density population
- X_9 , mild brain atrophy population
- X_{10} , severe brain atrophy population

$$P_1 = 1 / [1 + e^{-K_1}]$$

$$K_1 = -8.715 + 0.186X_1 + 0.403X_2 + 1.732X_3 + 0.118X_4 + 2.354X_5 - 0.686X_6 - 0.228X_7 - 1.668X_8 + 0.612X_9 + 2.915X_{10}$$

P_1 is the probability of 6-month poor outcome. The ROC curve analysis shows that the AUC area of the model is 0.942, and the corresponding threshold value P is 0.422 according to the Yoden index. When $P_1 > 0.422$, the sensitivity and specificity of the patient's poor prognosis are 87.5%, 87.4% (Fig. 1).

Mortality model

The variables of the mortality model were as follows:

X_1 , PLT count

X_2 , eGFR value

X_3 , presence with IVH

X_4 , white blood cell count

X_5 , NIHSS score

X_6 , hematoma minimally invasive aspiration population (conservative patients are reference values)

X_7 , third ventricle Sylvian fissure distance ≥ 38.93 mm population

X_8 , the frontal lobe ratio ≥ 0.289 population

$X_{9(1)}$, lobe hemorrhage population

$X_{9(2)}$, basal ganglia hemorrhage population

$X_{9(3)}$, multi-site hemorrhage [other (capsula externa or corpus callosum hemorrhage) as reference values]

$X_{10(1)}$, $4.15 \leq N/L$ value < 6.6 population

$X_{10(2)}$, $6.6 \leq N/L$ value < 10.86 population

$X_{10(3)}$, N/L value ≥ 10.86 population (patients with N/L value < 4.15 are reference values)

$$P_2 = 1 / [1 + e^{-K_2}]$$

$$K_2 = -8.574 - 0.027X_1 - 0.078X_2 + 3.522X_3 + 0.553X_4 + 0.372X_5 - 3.57X_6 - 2.645X_7 - 2.755X_8 + 12.369X_{9(1)} + 8.967X_{9(2)} + 12.664X_{9(3)} - 1.295X_{10(1)} - 5.031X_{10(2)} - 5.865X_{10(3)}$$

P_2 is the probability of 6-month mortality. The ROC curve analysis shows that the AUC area of the model is 0.949, and the corresponding threshold value P is 0.229 according to the Yoden index. When $P_2 > 0.229$, the sensitivity and specificity of determining the patient's death are 90.0%, 94.4% respectively (Fig.2).

Discussion

We conducted a system for prediction of poor outcome and mortality in patients with ICH. Independent predictors of poor prognosis were NIHSS score, D-Dimer, CT imaging features (hematoma mixed density, irregular hematoma shape, ICH volume, brain atrophy, and midline shift). Decreased platelet count at admission, high NIHSS score, IVH, and third ventricle Sylvian fissure distance less than 38.93 mm can increase mortality. Other factors that may increase mortality include white blood cell count, N/L ratio, hematoma minimally invasive aspiration.

Based on the risk factors above, the sensitivity and specificity of models of poor prognosis (sensitivity 87.5%, specificity 87.4%) and mortality (sensitivity 90.0% specificity 94.4%) were higher than the predictive value of single factor (e.g. ICH volume, d-dimer, NIHSS score) (sensitivity varied from 66.7–87.5%, specificity varied from 55.2–89.7%) (Figure I in the online-only Data Supplement).

NIHSS score at admission was independent predictors of poor prognosis of ICH and associated with high risk of hematoma enlargement (HE)^[28–30]. In the risk score for predicting the 1-year functional outcome after ICH (ICH-FOS)^[31], as the NIHSS score increased by 1 point, the risk of poor prognosis increased to 1.1 times. We also found that NIHSS score was independently associated with long-term poor outcome and increased mortality. The ROC curve and the Yoden index showed that the cut-off value of NIHSS score for predicting poor ICH prognosis was 9.5 points, with sensitivity and specificity of 87.5% and 75.9%, respectively.

Studies on the effect of d-dimer on prognosis of ICH demonstrated that elevated baseline D-Dimer levels in the blood were independent risk factors for mortality and poor prognosis^[32–34]. We also found that elevated D-Dimer levels can affect functional prognosis at 6 months, and the cut-off value of D-Dimer was 0.565 mg/L. Sensitivity and specificity were respectively 66.7% and 55.2%. The possible mechanism is that elevated D-Dimer may reflect disturbance of the coagulation and fibrinolysis pathways^[33]. Chih-Wei Chen et al found that dynamically-altered D-Dimer in cerebrospinal fluid (CSF) help to predict hematoma enlargement and poor prognosis, d-dimer in CSF is derived from clot lysis caused by elevated fibrinolytic activity in CSF, and is a more accurate indicator of intraventricular hemolysis than that in blood^[35].

ICH volume is one of the best predictors of poor prognosis and the cut-off values of volume vary^[5, 6, 36, 37]. Studies have found that the incidence of 30-day mortality and cerebral herniation are as high as 90%

when basal ganglia hematoma volume ≥ 30 ml, even if the hematoma is removed by surgery within 24 hours after onset^[38]. In our study, the ROC curve and the Yoden index showed that the threshold for hematoma volume for predicting poor prognosis was 23.725 ml, and the sensitivity and specificity were 64.6% and 89.7%, respectively.

Previous studies on CT signs of ICH can be roughly divided into two categories: hematoma density and hematoma shape. Li Qi et al^[22] proposed that black hole sign can predict hematoma enlargement, and is related to the prognosis of dysfunction (OR, 8.19; 95%CI: 2.44–27.49; $p = 0.001$) at 3 months^[15]. Blend signs, liquid levels are also found to be associated with poor prognosis of ICH^[20, 39, 40]. Barras et al^[13] evaluated hematoma irregularity and heterogeneity with a 5-point scale, and reported that heterogeneity can independently predict HE. Li Qi et al also contended that the island sign is a special hematoma with extremely irregular shape, which is associated with early hematoma enlargement (OR, 31.89; 95%CI, 8.67–117.29; $P < 0.001$) and poor functional prognosis (OR, 3.51; 95%CI, 1.26–9.81; $P = 0.017$)^[14]. In our study, mixed hematoma density includes black hole sign, blend sign, liquid level, hematoma heterogeneity, and irregular hematoma shape contains island sign, satellite sign, hematoma irregularity, both are independent influencing factors for the prognosis. Due

to the low positive rate and small sample size, the results of mixed hematoma density are not completely consistent with the previous studies. It is necessary to expand the sample size for verification.

In previous study, the midline shift (MLS) was found to be associated with the early neurological deterioration^[41]. Kiphuth et al. used transcranial duplex sonography (TDS) to measure the midline shift within 2 weeks after ICH, and reported when MLS exceeded 4.5–7.5 mm, the mortality of ICH increased significantly. When MLS exceeded 12 mm, all had poor conditions^[42]. We calculated specific values and classified MLS into quartiles, the result showed that patients with MLS of 1.43–2.42 mm have a higher risk of poor prognosis compared with MLS of 0–1.43 mm. We failed to find a direction correlation between poor prognosis and greater MLS, which may be explained by the small sample size.

We adopted linear measurements and visual presentation template methods to evaluate brain atrophy^[24], and found that severe cortical brain atrophy was independently associated with the prognosis, cortical brain atrophy may be more sensitive than central brain atrophy. Patients with the third ventricle Sylvian fissure distance less than 38.93 mm had a higher risk of death. Previous studies have found that severe WML and brain atrophy are associated with 90-day mortality or major disability^[25]. Other studies have also confirmed that brain atrophy is an independent predictor of poor prognosis (OR = 1.09; CI: 1.05–1.1; $P < 0.001$), due to the presence of brain damage in patients with brain atrophy, which can lead to degenerative diseases such as dementia or subcortical vascular encephalopathy^[43]. Contrary to expectation, we found no significant relationship between lacunes, WML and prognosis, owing to the smaller sample size, the younger age of the study subjects and the lower positive rate of lacuna and WML.

Other factors such as thrombocytopenia also can increase the mortality of ICH. As for the relationship between white blood cell count, N/L ratio, hematoma minimally invasive aspiration and prognosis of ICH (P values were 0.05, 0.093, 0.053, respectively), more clinical results are needed to support.

The strength of this study is to focus on the multiple prognostic factors associated with ICH, innovatively develops new poor prognosis and mortality models of ICH, and both models have high sensitivity and specificity, the variables included in the analysis are relatively comprehensive.

We recognized several limitations in this study. First, our study was a single-center retrospective study with small sample size. Prospective studies are necessary to validate established poor outcome and mortality models. Second, other prognostic factors such

as various inflammatory markers (hypersensitive C-reactive protein, interleukin, procalcitonin etc.), BMI, the admitted and the fourth day of NT-proBNP had a certain rate of loss. Third, the standardization of the sample was not enough. Finally, patients with cerebral small vascular disease only underwent CT without MRI, which might reduce the predictability. We aim to conduct a large sample prospective study in the future to overcome these limitations.

Conclusions

Two models for prognostic significance of ICH was developed and could well predict the poor prognosis and mortality.

Abbreviations

sICH
Spontaneous Intracerebral hemorrhage
SIRS
Systemic inflammation Response syndrome
ESRD
End stage renal disease
eGFR
Estimated glomerular filtration
GCS
Glasgow coma scale
NIHSS
National institutes of health stroke scale
EVD
Extraventricular drainage
IVH
Intraventricular hemorrhage

WML

White matter lesion

Declarations

Ethics approval and consent to participate

All measurements were performed at Tongji Hospital, Huazhong University of Science and Technology and were approved by Medical Ethical Committee and Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. As our data were anonymous, the requirement for informed consent was therefore waived.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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None

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors contribution

Prof. SBX put forward the protocol and provided the paper guidance. LLC participated in the writing of the thesis. CP is the first co-author. He participated in the topic setting, research, literature review and paper revision. HW assisted in recording and analyzing the data. Prof. ZPT helped to complete the final revision of the article. All authors have read and approved the manuscript.

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Additional Files

Additional file 1. Clinical, laboratory and imaging data for outcome subgroups (basic recovery, disability and death) after ICH. Compared with the basic recovery group and the disability group, the pulse rate, the proportion of end-stage renal disease (ESRD), IVH and irregular hematoma shape, the presence of the island sign, the ratio of N/L was higher in the death group, glomerular filtration and PLT counts were lower. The proportion of patients with SIRS and subarachnoid hemorrhage, white blood cell count were lowest in the basic recovery group.

Figures

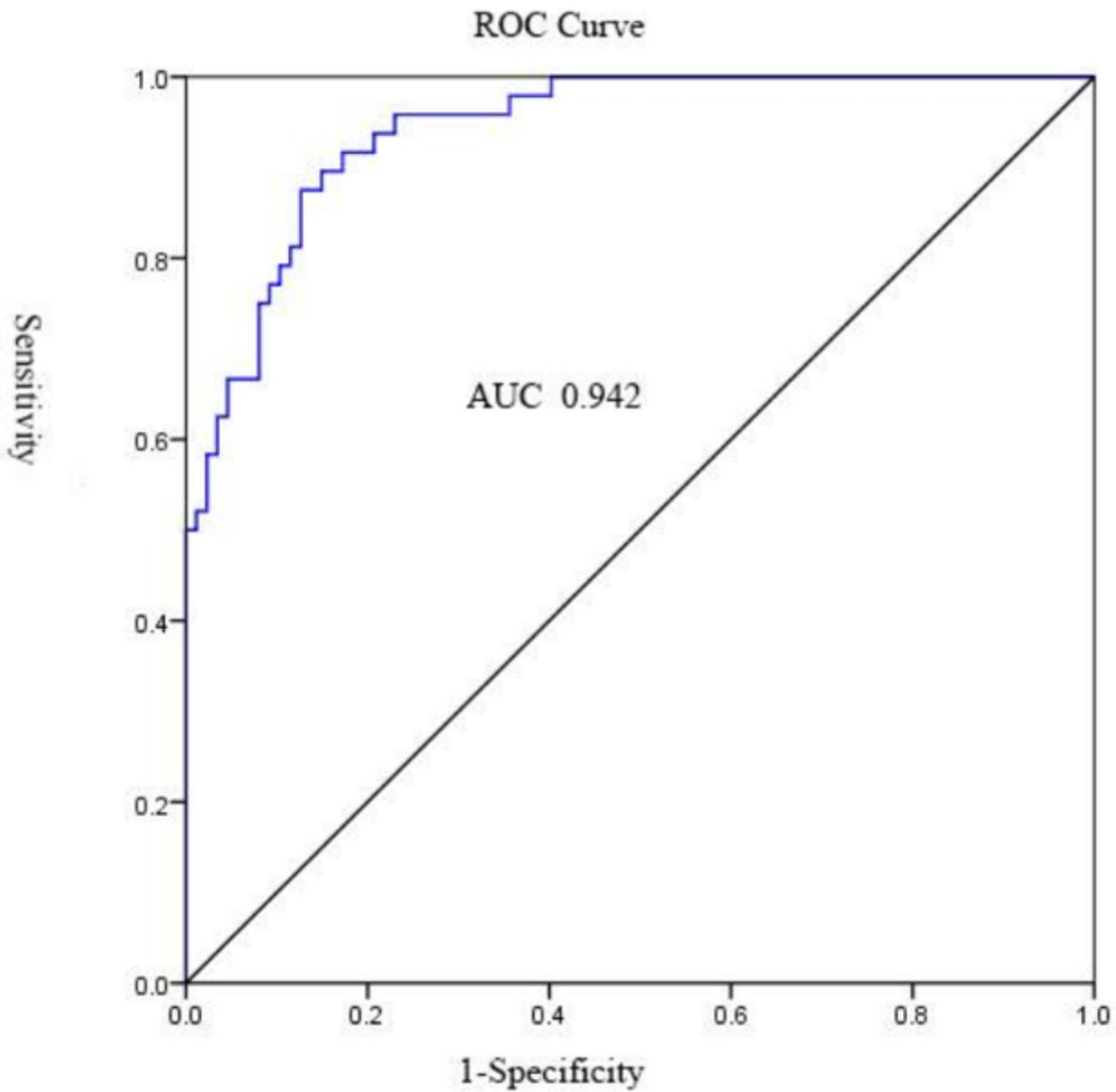


Figure 1

ROC curve used for predicting 6-month poor outcome after ICH. AUC, area under curve; ROC, receiver operating characteristic

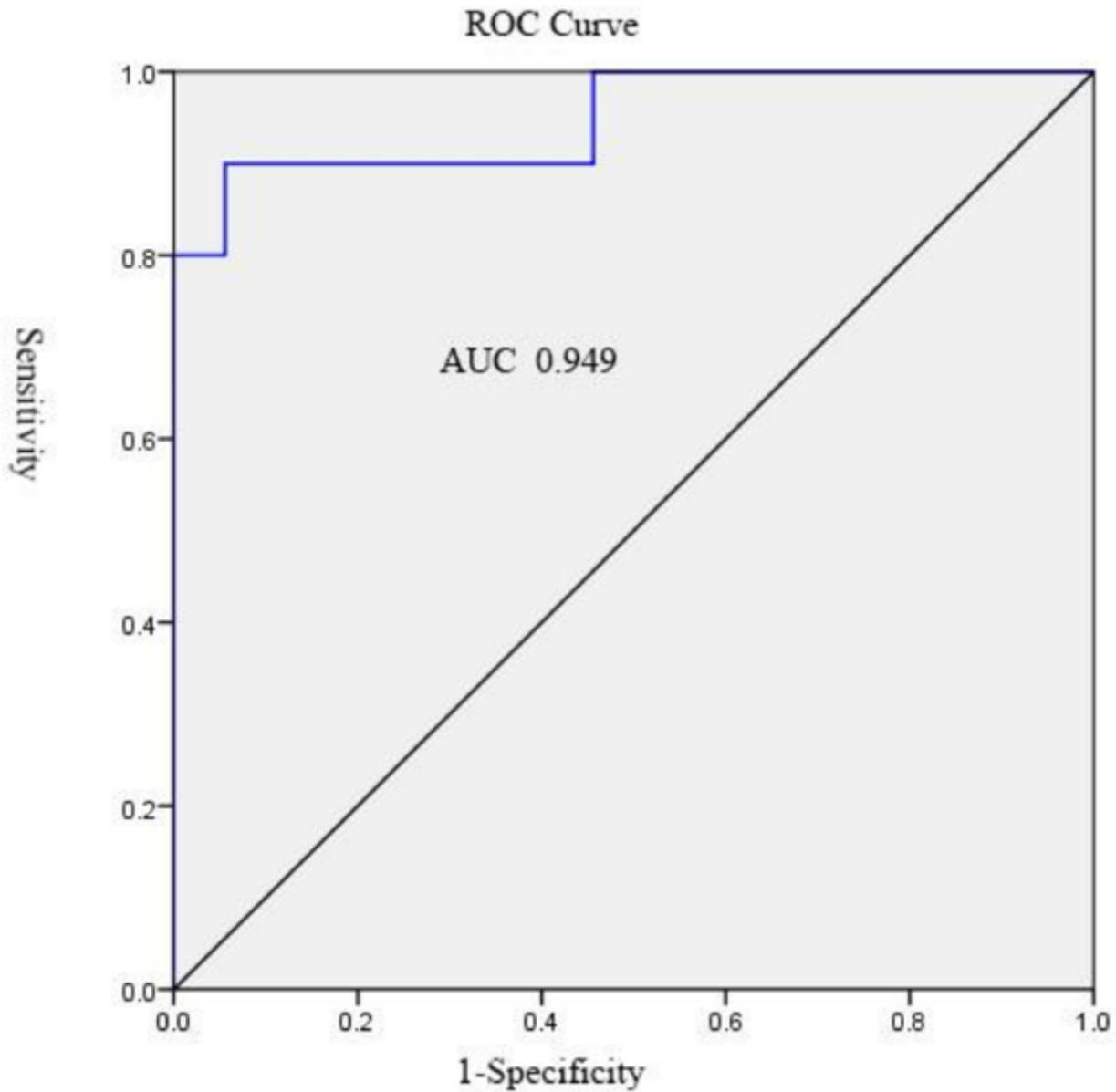


Figure 2

ROC curve used for predicting 6-month poor outcome after ICH. AUC, area under curve; ROC, receiver operating characteristic

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