

Comparison of Accuracy among Post-thrombolytic Symptomatic Intracerebral Hemorrhage Predictive Scores in Ischemic Stroke Patients in Khon Kaen Hospital.

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Abstract

Introduction: Post-thrombolytic symptomatic intracerebral hemorrhage (sICH) is one of complications worsening outcome of acute ischemic stroke patients. At this point, we performed a comparison of accuracy among 9 predictive scores using Khon Kaen Hospital patient dataset to assess post-thrombolytic sICH risk.

Methods: Retrospective analytic study of accuracy of predictive scores was conducted from January 2016 to April 2019. The acute ischemic stroke patients who received thrombolytic therapy were included. This study employed patients' information from medical records. Each score system was then calculated. Subsequently, the comparison among these scores were performed using area under receiver operating characteristic curves (ROC). Other baseline characteristics were presented and compared by appropriate statistical methods.

Results: Two hundred and fifty-one patients were recruited. There were 36 (14.34%) patients with post-thrombolytic intracerebral hemorrhage. Of these, 22 (8.76%) patients were symptomatic. Among 9 predictive scores for sICH, DRAGON had the highest predictive power (area under the ROC = 0.74), sensitivity (80.56%) and negative predictive value (91.40%).

Conclusion: Currently, there is no best tool to predict post-thrombolytic ICH. From our result, DRAGON score was best predictor for sICH among others and could be applied to obtain additional information for patient management and bed occupancy consideration of stroke unit.

Keywords: predictive score, post-thrombolytic symptomatic intracerebral hemorrhage (J Thai Stroke Soc. 2020;19(3):17-30)

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การเปรียบเทียบความแม่นยำของเครื่องมือทำนายภาวะเลือดออกในสมองที่แสดงอาการ ในผู้ป่วยโรคหลอดเลือดสมอง หลังได้รับการรักษาด้วยยาละลายลิ่มเลือด ในโรงพยาบาลขอนแก่น

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บทคัดย่อ

บทนำ ภาวะเลือดออกในสมองที่แสดงอาการในผู้ป่วยที่ได้รับยาละลายลิ่มเลือดทางหลอดเลือดดำ เป็นภาวะแทรกซ้อนหนึ่งที่ทำให้การรักษาโรคหลอดเลือดสมองไม่ได้ผลดี การศึกษานี้เป็นการศึกษาเปรียบเทียบความแม่นยำของเครื่องมือที่ใช้ประเมินความเสี่ยงต่อภาวะดังกล่าว

วิธีวิจัย ศึกษาความแม่นยำของวิธีการวินิจฉัยแบบย้อนหลังในช่วงมกราคม 2559 ถึง เมษายน 2562 โดยเก็บข้อมูลผู้ป่วยโรคหลอดเลือดสมองที่ได้รับการรักษาด้วยยาละลายลิ่มเลือดจากเวชระเบียน มาคำนวณคะแนนตามเครื่องมือประเมินความเสี่ยงต่อภาวะเลือดออกในสมอง แล้วใช้วิธีทางสถิติ คำนวณค่าพื้นที่ใต้กราฟ receiver operating characteristic curve เพื่อเปรียบเทียบความแม่นยำ ส่วนข้อมูลพื้นฐานของผู้ป่วย นำเสนอ และวิเคราะห์ข้อมูลด้วยวิธีทางสถิติตามความเหมาะสม

ผลการวิจัย ผู้ป่วยที่ได้รับยาละลายลิ่มเลือด มีจำนวน 251 ราย พบภาวะเลือดออกในสมอง 36 ราย (ร้อยละ 14.34) เป็นภาวะเลือดออกในสมองที่แสดงอาการ 22 ราย (ร้อยละ 8.76) ในเครื่องมือประเมินความเสี่ยงต่อภาวะเลือดออกในสมองที่แสดงอาการ 9 ชนิด DRAGON เป็นเครื่องมือที่มีความสามารถในการทำนายสูงสุด คือ มีพื้นที่ใต้กราฟ 0.74 มีความไวสูงสุด คือ ร้อยละ 80.56 และมีค่าทำนายผลลบสูงสุด คือ ร้อยละ 91.40

บทสรุป ปัจจุบัน ยังไม่มีเครื่องมือที่ดีที่สุดที่ใช้ทำนายภาวะเลือดออกในสมองที่แสดงอาการ จากการศึกษา DRAGON อาจเป็นเครื่องมือที่ดีที่สุดในการทำนายภาวะดังกล่าว และเป็นข้อมูลประกอบการดูแลรักษาผู้ป่วย และการบริหารจัดการเตียงของหอผู้ป่วยโรคหลอดเลือดสมอง

คำสำคัญ: เครื่องมือประเมินความเสี่ยง, ภาวะเลือดออกในสมองที่แสดงอาการหลังได้รับการรักษาด้วยยาละลายลิ่มเลือด (J Thai Stroke Soc. 2020;19(3):17-30)

Introduction

Post-thrombolytic symptomatic intracerebral hemorrhage (sICH) is one of the complications worsening outcome of acute ischemic stroke patients after thrombolytic therapy.¹⁻⁵ The incidence is about 2.1–11.1%.^{1-4, 6-9}

There were at least 9 predictive scores (as shown in Table 1) which had been developed to evaluate post-thrombolytic sICH risks. The most recent predictive score was the Symptomatic Intracerebral Hemorrhage Score (SICH score) derived from analytic study in provincial and 4 regional hospitals in the northern part of Thailand.⁹

Several studies had been comparing accuracy of these predictive scores. There were 4 analyses from Asia. The predictive models compared in Taiwan study were Post-thrombolysis Risk Score (PRS), Hemorrhage After Thrombolysis (HAT) score, Safe Implementation of Thrombolysis in Stroke–Symptomatic Intracerebral Hemorrhage (SITS–SICH) score, Glucose Race Age Sex Pressure Stroke Severity score (GRASPS), and Stroke Prognostication using age And NIHSS–100 (SPAN–100) index.¹⁰ The Chinese comparative study used blood Sugar, Early infarct signs and hyperDense cerebral artery sign, Age, and NIHSS (SEDAN) score, SITS–SICH, GRASPS, PRS, and SPAN–100 index.¹¹ One of Thai studies, conducted at Ramathibodi hospital, compared PRS, HAT, Dense cerebral artery pre–stroke modified Rankin scale Age Glucose Onset–to–treatment time NIHSS (DRAGON) score, SEDAN, SITS–SICH and SPAN–100 index.¹² The other Thai study, conducted at Siriraj hospital, compared between DRAGON, HAT, GRASPS, PRS, SEDAN, iScore, SITS–SICH and SPAN–100.⁸ There was no study compared among all 9 score systems.

Here, we performed a comparison of accuracy among 9 predictive scores using Khon Kaen Hospital patient dataset to assess post-thrombolytic sICH risk in Khon Kaen Hospital.

Materials and methods

Data from all acute ischemic stroke patients who received thrombolytic therapy at Khon Kaen Hospital between January 2015 and April 2019 were reviewed. Intracerebral hemorrhage was detected by brain computed tomography (CT) within 36 hours after thrombolytic therapy. Symptomatic intracerebral hemorrhage (sICH) was defined as deterioration of neurologic status (increase in the National Institutes of Health Stroke Score (NIHSS) ≥ 4)^{2,3} within 36 hours. We collected age, gender, race, atherosclerotic risk factors (diabetic mellitus, hypertension, dyslipidemia, smoking, coronary heart disease, previous stroke, peripheral arterial disease), arrhythmia, valvular heart disease, renal disease, antithrombotic agent usage within 1 month, pre–stroke modified Rankin scale (mRS), vital signs, NIHSS, onset–to–IV rt–PA time, weight, rt–PA dosage, usage of antihypertensive agent during thrombolytic therapy, complete blood count, initial capillary blood glucose, glomerular filtration rate (GFR) and brain CT findings.

Statistic methods

The information from patients' medical records were analyzed statistically by Stata Program. Categorical variables were presented as frequency and percentage. Continuous variables were presented as mean \pm SD or median and range depending on the types of data distribution.

Predictive scores of each patient were calculated using parameters differently based

on different predictive methods. The predictive models were PRS, HAT, SEDAN, Total Health Risks in Vascular Events (THRIVE), GRASPS, SITS-SICH, DRAGON, SPAN-100 and SICH scores. Then specificity and sensitivity of each predictive method were calculated. Ranges of score values obtained by each method were used for determination of area under curve (AUC) values. The AUCs of each predictive score were compared for accuracy of prediction of the symptomatic intracerebral hemorrhage event in patients receiving rt-PA therapy. The level of statistical significance was defined when *P*-value was less than 0.05.

Results

Our study included acute ischemic stroke patients in Khon Kaen Hospital during January 2016 to April 2019. The total number of patients with acute ischemic stroke who received rt-PA treatment was 253. Two of them were excluded on account of no information of pre-thrombolytic brain CT. Finally, the number of patients included in the study was 251. Intracerebral hemorrhage occurred in 36 patients (14.34%). There were 22 patients (8.76%) who had sICH. Risk assessment scores used for post-thrombolytic ICH prediction were shown in Table 1.

Table 1. Description of predictive scores

Score	Parameter	Point	Score	Parameter	Point
SITS-SICH ²²	Aspirin + clopidogrel	3	SICH ⁹	Valvular heart disease	2
	Aspirin monotherapy	2		Aspirin	1.5
	NIHSS \geq 13	2		SBP prior to thrombolysis	
	NIHSS 7-12	1		\geq 140 mmHg	1
	Blood glucose \geq 180 mg/dL	2		NIHSS 11-20	2
	Age \geq 72 years	1		\geq 21	3.5
	SBP \geq 146 mmHg	1		Platelet $<$ 250,000 /mm ³	1
	Weight \geq 95 kg	1		IV antihypertensive	
	Hypertension	1		drug during thrombolysis	1
	Onset-to-Needle time				
\geq 180 minutes	1				
PRS ²³	Age \geq 60 years	1	THRIVE ^{24, 25}	Age 60-79 years	1
	Baseline NIHSS $>$ 10	1		\geq 80 years	2
	Platelet $<$ 150,000/mm ³	1		NIHSS 11-20	2
	Blood Glucose $>$ 150 mg/dL	1		\geq 21	4
		Hypertension		1	
		Diabetes mellitus		1	
SPAN-100 ²⁶	Age (years) + NIHSS		Atrial fibrillation	1	
	\geq 100	Positive			
	$<$ 100	Negative			

Table 1. Description of predictive scores (continued)

Score	Parameter	Point	Score	Parameter	Point
HAT ²⁷	Blood glucose > 200 mg/dl	1	SEDAN ²⁸	Blood glucose	
	NIHSS 15-20	1		145-216 mg/dL	1
	≥ 20	2		> 216 mg/dL	2
	Hypodensity of MCA territory on brain CT			Early infarct sign	1
	No	0		Hyperdense cerebral artery sign	1
	< 1/3	1		Age > 75 years	1
	≥ 1/3	2		NIHSS ≥10	1
GRASPS ²⁹	Age ≤ 60 years	8	DRAGON ³⁰	Hyperdense cerebral artery sign or early infarct sign on brain CT	
	61-70 years	11		No	0
	71-80 years	15		Either	1
	NIHSS 0-5	25		Both	2
	6-10	27		Pre-Stroke mRS ≤ 1	0
	11-15	34		>1	1
	16-20	40		Age < 65 years	0
	> 20	42		65-79 years	1
	SBP < 120 mmHg	10		≥ 80 years	2
	120-149 mmHg	14		Blood glucose ≤ 144 mg/dL	0
	150-179 mmHg	18		> 144 mg/dL	1
	≥ 180 mmHg	21		Onset-to-Needle time ≤ 90 minutes	0
	Blood glucose			> 90 minutes	1
	< 100 mg/dl	2	NIHSS 0-4	0	
	100-149 mg/dl	6	5-9	1	
	≥ 150 mg/dl	8	10-15	2	
	Race Non-Asia	0	> 15	3	
	Asia	9			
	Gender Female	0			
	Male	4			

SITS-ICH = safe implementation of treatments in stroke symptomatic intracerebral hemorrhage

PRS = post-thrombolysis risk score

SPAN-100 = stroke prognostication using age and NIHSS-100 index

HAT = hemorrhage after thrombolysis

SICH = Symptomatic Intracerebral Hemorrhage Score

THRIVE = Total Health Risks in Vascular Events

SEDAN = blood Sugar Early infarct signs and hyperDense cerebral artery sign Age and NIHSS

GRASPS = Glucose Race Age Sex Pressure Stroke Severity score

DRAGON = Dense cerebral artery prestroke modified Rankin scale Age Glucose Onset-to-treatment time
NIHSS

NIHSS = National Institute of Health Stroke Scale

SBP = systolic blood pressure

MCA = middle cerebral artery

CT = computed tomography

IV = intravenous

mRS = modified Rankin Scale

The patient's baseline characteristics were presented in Table 2. The age of patients was 66.76 ± 12.34 years old. Majority of them was 143 (56.97%) males. The patient's body weight was 61.75 ± 13.00 kilograms. There were 111 (44.22%) patients with hypertension, 88 (35.06%) patients with diabetes mellitus, 80 (31.87%) smokers, 41 (16.33%) patients with dyslipidemia and 9 (3.59%) patients with diagnosis of chronic kidney disease. Despite cardioembolic-related underlying diseases, there were 74 (29.48%) patients with atrial fibrillation and 9 (3.59%) patients with valvular

heart disease. There were 39 (15.54%) aspirin usage. The patients' pre-stroke mRS was 1.05 ± 0.30 . Systolic and diastolic blood pressures were 158.95 ± 28.16 and 90.93 ± 18.79 mmHg, respectively. The number of patients who received intravenous antihypertensive drug was 43 (17.13%). From brain CT findings, there were 38 (15.14%) patients presented with hyperdense cerebral artery signs, 72 (28.69%) patients with early infarct signs, 26 (10.36%) and 9 (3.59%) patients with hypodensity $< 1/3$ and $\geq 1/3$ of MCA territory, respectively.

Table 2. Baseline characteristics

Baseline characteristics	Mean \pm SD or N (%)
Male	143 (56.97)
Age (years)	66.76 ± 12.34
Weight (kg)	61.75 ± 13.00
Hypertension	111 (44.22)
Diabetes mellitus	88 (35.06)
Dyslipidemia	41 (16.33)
Chronic kidney disease	9 (3.59)
Liver disease	1 (0.40)
Coronary artery disease	13 (5.18)
Atrial fibrillation	74 (29.48)
Valvular heart disease	9 (3.59)
Aspirin usage	39 (15.54)
Smoking	80 (31.87)
Alcoholic drinking	75 (29.88)

Bivariate analysis demographics and baseline characteristics of patients with and without sICH were presented in Table 3. These 2 groups had similar sex, age, weight, medication usage, and underlying disease except dyslipidemia in which, all 41 (17.90% *P*-value = 0.03) of them were in the non-sICH group. The baseline NIHSS were significantly higher in sICH group (15.86 ± 5.66 vs 12.06 ± 6.34 *P*-value < 0.01). There was statistically significant difference of brain CT findings between 2 groups.

The hypodensity ≥ 1/3 of MCA territory was found more in sICH group (27.27% vs 1.31% *P*-value < 0.01). Moreover, early infarct sign was found more in sICH group (72.73% vs 24.45% *P*-value < 0.01) On the contrary, hypodensity < 1/3 of MCA territory was found less in sICH (1.31% and 27.27% *P*-value < 0.01). All 9 predictive scores were higher in sICH group but only HAT, SICH, THRIVE, SEDAN and DRAGON scores achieved statistical significance.

Table 3. Bivariate analysis demographics and baseline characteristics of patients with and without symptomatic intracerebral hemorrhage

Baseline characteristics	sICH (N=22)	Non-sICH (N=229)	<i>P</i> -value
Male	12 (54.55)	131 (57.21)	0.81
Age (years)	63.44 ± 10.88	67.08 ± 12.33	0.15
Weight (kg)	62.99 ± 14.62	61.63 ± 12.86	0.67
Hypertension	7 (31.82)	104 (45.41)	0.22
Diabetes mellitus	4 (18.18)	84 (36.68)	0.10
Dyslipidemia	0	41 (17.90)	0.03
Chronic kidney disease	2 (9.09)	7 (3.06)	0.18
Liver disease	0	1 (0.44)	> 0.90
Coronary artery disease	1 (4.55)	12 (5.24)	> 0.90
Atrial fibrillation	6 (27.27)	68 (29.69)	0.81
Valvular heart disease	2 (9.09)	7 (3.06)	0.18
Aspirin usage	3 (13.64)	36 (15.72)	> 0.90
Smoking	10 (45.45)	70 (30.57)	0.15
Alcoholic drinking	10 (45.45)	65 (28.38)	0.09
Pre-stroke mRS	1.05 ± 0.38	1.05 ± 0.29	0.93
Baseline NIHSS	15.86 ± 5.66	12.06 ± 6.34	< 0.01
SBP prior to thrombolysis (mmHg)	151.18 ± 24.79	159.69 ± 28.40	0.14
DBP prior to thrombolysis (mmHg)	94.27 ± 15.61	90.61 ± 19.06	0.31
Actual rt-PA dose (mg/Kg)	0.899 ± 0.001	0.899 ± 0.006	0.97
IV anti-hypertensive drugs during thrombolysis	3 (13.64)	40 (17.47)	> 0.90
Onset-to-needle time (minutes)	202.45 ± 53.33	206.48 ± 51.28	0.74
Platelet count (/mm ³)	255,636.40 ± 77,238.37	248,401.70 ± 86,589.01	0.68

Table 3. Bivariate analysis demographics and baseline characteristics of patients with and without symptomatic intracerebral hemorrhage (*continued*)

Baseline characteristics	sICH (N=22)	Non-sICH (N=229)	P-value
GFR (ml/min)	75.29 ± 28.51	74.80 ± 24.56	0.94
Initial capillary blood glucose (mg/dL)	164.06 ± 67.15	149.80 ± 72.68	0.35
Brain CT with hyperdense cerebral artery sign	6 (27.27)	32 (13.97)	0.10
Brain CT with early infarct sign	16 (72.73)	56 (24.45)	< 0.01
Brain CT with hypodensity			
< 1/3 of MCA territory	4 (18.18)	22 (9.61)	< 0.01
≥ 1/3 of MCA territory	6 (27.27)	3 (1.31)	
SITS-ICH	5.91 ± 1.57	5.29 ± 1.54	0.08
PRS	2.00 ± 0.76	1.64 ± 0.92	0.07
SPAN100 positive	1 (4.55)	16 (6.99)	0.66
HAT	1.82 ± 1.40	0.75 ± 0.92	< 0.01
SICH	5.80 ± 2.59	4.32 ± 2.78	0.02
THRIVE	8.05 ± 1.73	7.10 ± 1.75	0.02
SEDAN	2.68 ± 0.95	1.70 ± 1.23	< 0.01
GRASPS	84.55 ± 7.59	81.76 ± 9.18	0.17
DRAGON	6.36 ± 1.26	5.28 ± 1.67	< 0.05

NIHSS = National Institute of Health Stroke Scale

mRS = modified Rankin Scale

SBP = systolic blood pressure

DBP = diastolic blood pressure

IV = intravenous

CT = computed tomography

SITS-ICH = safe implementation of treatments in stroke symptomatic intracerebral hemorrhage

PRS = post-thrombolysis risk score

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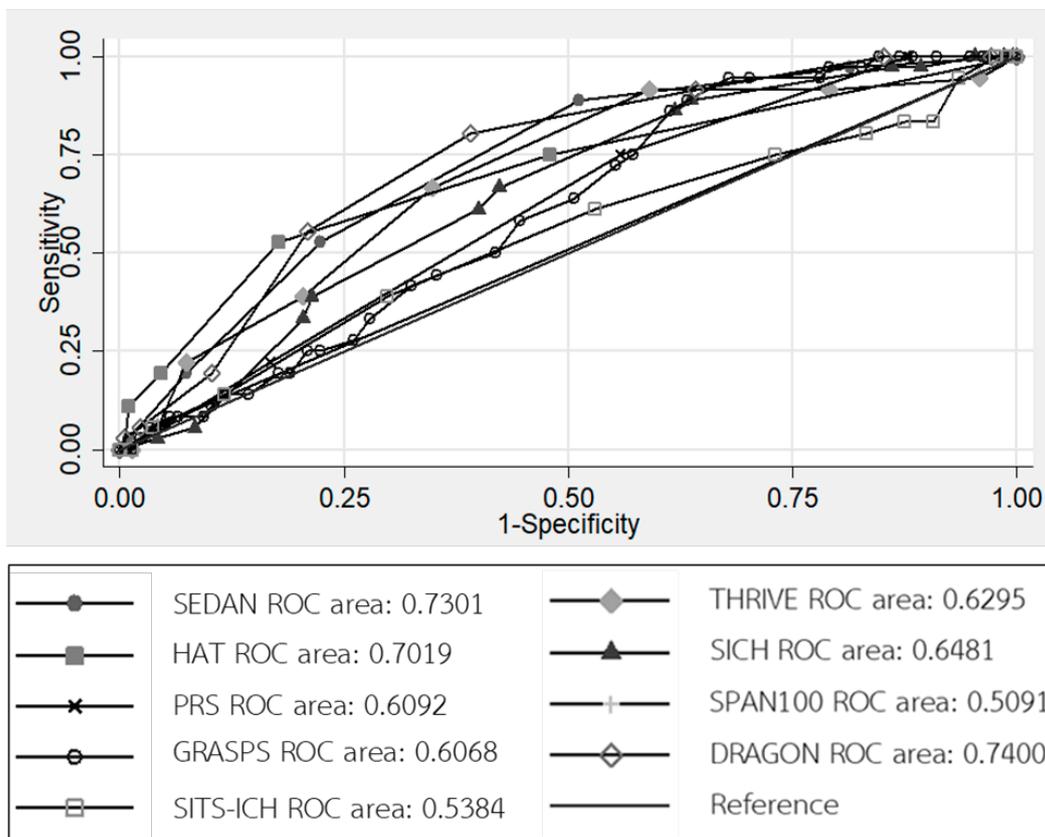
GRASPS = Glucose Race Age Sex Pressure Stroke Severity score

DRAGON = Dense cerebral artery prestroke modified Rankin scale Age Glucose Onset-to-treatment time NIHSS

The highest predictive power of the DRAGON score was reported by the Receiver Operating Characteristic (ROC) curves,

comparing to others as shown in figure 1. Its area under the curve (AUC) was 0.74.

Figure 1. ROC curves and AUC comparison



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Table 4 showed the analysis of sensitivities, specificities, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio and proportion of correctly classified subjects according to the optimal cut-point which represented the maximum value of a trade-off between sensitivities and specificities and

maximize summation of sensitivities and specificities. The accuracy was corresponding to these optimal cut-points. The optimal cut-points were 5 on SITS-ICH score and DRAGON score, 2 on PRS score, 1 (which represented for positive value) on SPAN100, 1 on HAT score, 3.5 on SICH score, 4 on THRIVE score, 3 on SEDAN score and 80 on GRASPS

score. Dragon score had the highest sensitivity (80.56%) and negative predictive value (91.40%). HAT score had the highest positive predictive value (59.06%). SPAN100 score had the highest

specificity (93.49%), negative likelihood ratio (0.98) and proportion of correctly classified subjects (81.27%). The highest positive likelihood ratio was found in SEDAN score (2.36).

Table 4. Validity testing for predictive scores

Predictive scores	Sensitivity	Specificity	PPV	NPV	LR+	LR-	Proportion of correctly classified subjects
SITS-ICH	50.00%	58.14%	54.43%	53.76%	1.19	0.86	56.97%
PRS	75.00%	44.19%	57.34%	63.87%	1.34	0.57	48.61%
SPAN100	8.33%	93.49%	17.65%	85.90%	1.28	0.98	81.27%
HAT	75.00%	52.09%	59.06%	65.75%	1.57	0.48	55.38%
SICH	69.44%	59.53%	21.88%	88.24%	1.72	0.51	60.96%
THRIVE	55.56%	59.53%	18.69%	88.89%	1.37	0.75	58.96%
SEDAN	52.78%	77.67%	28.36%	90.76%	2.36	0.61	74.10%
GRASPS	50.00%	55.81%	15.93%	86.96%	1.13	0.90	54.98%
DRAGON	80.56%	60.93%	30.77%	91.40%	2.06	0.32	63.75%

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PPV = positive predictive value

NPV = negative predictive value

LR+ = positive likelihood ratio

LR- = negative likelihood ratio

Discussion

This study was conducted to compare the accuracy of 9 assessment methods for predicting of the event of cerebral hemorrhage from rt-PA therapy. One of them was SICH score from the Thai-northern study⁹.

In our study ICH occurred in 36 patients (14.34 %) after IV rtPA treatment. There were 22 patients (8.76%) who had symptomatic intracerebral hemorrhage which were not

different from the prevalence of 2.1-11.1% in previous studies.^{1-4, 6-9}

The patients with dyslipidemia were found only in non-sICH group. There was no obvious relation between dyslipidemia and post-thrombolytic ICH.¹³ Though some previous studies reported that there was inverse association between LDL level and ICH.¹⁴ In our study, we did not specify LDL level due to insufficient data.

The baseline neurological deficits, assessed by NIHSS, was part of all predictive scores. It was higher in the sICH group than the other (15.86 ± 5.66 vs 12.06 ± 6.34). The more severe in stroke severity (higher in NIHSS), the higher risk of post-thrombolytic ICH.

The early infarct signs and MCA territory hypodensity of brain CT were significantly found more in sICH than non-sICH patients. These CT signs might increase risks of post-thrombolytic ICH¹⁵ and are parts of SEDAN, HAT and DRAGON scores in which were statistically significantly different between the 2 groups.

As previous comparisons, DRAGON, SEDAN and HAT scores had more predictive power than the others.^{8-11, 16-18} The highest predictive power was found in DRAGON score reported by the Receiver Operating Characteristic curves (0.74). The second, the third and the fourth highest predictive power were found in SEDAN (0.7301), HAT (0.7019) and SICH (0.6418) scores, respectively. The THRIVE score was also significantly higher in sICH group than the others. From the studies in Asian patients, the best predictive score was HAT,^{8, 10, 12} SITS-ICH⁹ and PRS¹¹ which was different from our results.^{8, 10} The reasons might be because of the different cut-point for AUC calculation, definition of sICH and characteristics of factors in each scoring system. All statistically significant risk factors of sICH in our study were in DRAGON score. Race or ethnicity might not be associated with the predictive power although cerebral microbleeds was more common among Asian.¹⁹⁻²¹

The highest sensitivity predictive score, DRAGON, might be applied for screening for risk of sICH among the post-thrombolytic patient. Higher sICH risk should not be

contraindication of thrombolytic therapy but patient with high sICH risk should receive closer monitoring in post-thrombolytic care resulting in early detection of sICH and immediate treatment in sICH patient.

Limitation

In this study, the serum glucose was replaced by capillary blood glucose. This was due to the practical and convenient screening process of hypoglycemia or hyperglycemia.

Generally, the possibility of the technical or human errors were well aware. As the patients' clinical information was obtained during normal hospital operation, therefore, there were many clinical specialists involved in producing and evaluating clinical data which might consequently cause some variations. Those clinical data, for examples, time of onset and NIHSS.

Conclusion

Currently, there is no best tool to predict post-thrombolytic ICH. From our study, DRAGON had higher predictive power and sensitivity and may be initially used to provide the additional information for the patients and their relatives to understand ICH risk before thrombolytic decision. Furthermore, those with high risk of sICH should be closely monitored leading to early detection and prompt treatment of sICH.

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