การศึกษาปัจจัยเสี่ยงเพื่อพยากรณ์ผลการรักษาในแง่ภาวะทุพพลภาพและการเสียชีวิตของผู้ป่วยโรคหลอดเลือดสมองอุดตันเฉียบพลันหลังได้รับการรักษาโดยยาละลายลิ่มเลือดทางหลอดเลือดดำภายใน 90 วัน

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บทคัดย่อ

ที่มาของงานวิจัย: ผลการรักษาของผู้ป่วยภาวะโรคหลอดเลือดสมองอุดตันเฉียบพลันที่ได้รับการรักษาด้วยยาละลายลิ่มเลือดทางหลอดเลือดดำขึ้นกับปัจจัยที่แตกต่างกัน การเสียชีวิตและทุพพลภาพคือผลกระทบที่ไม่พึงประสงค์หลังการรักษา การวิจัยนี้เป็นงานวิจัยแรกที่ศึกษาหาปัจจัยเสี่ยงที่มีผลต่อการรักษาในผู้ป่วยกลุ่มดังกล่าวในโรงพยาบาลสรรพสิทธิประสงค์

วัตถุประสงค์: ศึกษาปัจจัยเสี่ยงที่ใช้ทำนายผลของการรักษาและการตายในผู้ป่วยโรคหลอดเลือดสมองตีบเฉียบพลันที่ได้รับยาละลายลิ่มเลือดทางหลอดเลือดดำในช่วงหลังการให้ยาเป็นระยะเวลา 90 วัน

วิธีการศึกษา: ศึกษารวบรวมข้อมูลย้อนหลังโดยดูจากเวชระเบียนผู้ป่วยโรคหลอดเลือดสมองตีบที่ได้รับการรักษาด้วย rt-PA (alteplase) จำนวน 306 คน ตั้งแต่ช่วงระยะเวลา มกราคม 2556 จนถึง ธันวาคม 2562 โดยประเมินทุพพลภาพจากหลอดเลือดสมองตีบ Modified Rankin Scale (MRS) ประเมินหลังการรักษา 90 วัน รวมถึงเก็บข้อมูลการเสียชีวิตร่วมด้วย ใช้สถิติ univariable และ multivariable logistic regression เพื่อวิเคราะห์หา independent prognostic factors เพื่อพยากรณ์ผลหลังการรักษาและการเสียชีวิตใน 90 วัน

ผลการศึกษา: ผลการรักษาดีพบได้ 168 (54.9%) ผลการรักษาปานกลางพบ 77 (23.9%) ผลการรักษาไม่ดีพบ 85 (21.2%) หลังจากวิเคราะห์ด้วยสถิติ multivariable regression analysis พบว่ามี 3 ปัจจัยที่พบความสัมพันธ์ในการพยากรณ์ผลการรักษาอย่างมีนัยยะสำคัญทางสถิติ คือคะแนนประเมินความรุนแรงของภาวะหลอดเลือดสมองตีบ (NIHSS) OR, 2.30 (P-value =0.029, 95% CI: 1.091-4.840) การได้รับยา nicardipine ก่อนได้รับยา rt-PA เนื่องจากความดันสูง OR 2.55 (P-value = 0.013, 95% CI: 1.220-5.335) ภาวะเลือดออกในสมอง 3.5 (P-value = 0.018, 95% CI: 1.977-7.8) ส่วนปัจจัยที่มีผลต่อการพยากรณ์การเสียชีวิตคือ NIHSS เช่นกัน OR 18.75 (P-value = 0.014, 95% CI: 1.799-195.385) และภาวะไตวายเรื้อรัง OR 8.52 (P-value = 0.05, 95% CI: 1.815-89.125)

สรุปผลการศึกษา: คะแนน NIHSS การได้รับยา nicardipineในช่วงความดันขึ้นสูงอาจเป็นปัจจัยที่พยากรณ์ภาวะทุพพลภาพของผู้ป่วยที่มีภาวะโรคหลอดเลือดสมองอุดตันเฉียบพลันหลังการรักษาด้วยยาละลายลิ่มเลือดทางหลอดเลือดดำในช่วง 90 วันหลังการรักษา นอกจากนั้นคะแนน NIHSSแรกรับและภาวะไตวายเรื้อรังยังอาจเป็นปัจจัยพยากรณ์การเสียชีวิตหลังการรักษาในผู้ป่วยลักษณะเดียวกัน ผู้ป่วยที่มีปัจจัยเสี่ยงเหล่านี้ควรได้รับการดูแลและประเมินอาการอย่างใกล้ชิด

คำสำคัญ: หลอดเลือดสมองอุดตันเฉียบพลัน การให้ยาละลายลิ่มเลือดทางหลอดเลือดดำ ปัจจัยเสี่ยง ปัจจัยพยากรณ์โรค

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ผู้นิพนธ์ที่รับผิดชอบบทความ: พญ.ทัดดาว วิโรจน์อุไรเรือง หน่วยระบบประสาทวิทยา กลุ่มงานอายุรกรรม โรงพยาบาลสรรพสิทธิประสงค์ ตำบลในเมือง อำเภอเมือง จังหวัดอุบลราชธานี 34000 โทร 045-319200 ต่อ 1450 อีเมล w.thaddao@gmail.com

Introduction

Acute ischemic stroke is one of the common world's most common non-communicable diseases resulting in substantial death and disability. The prevalence of stroke in Thailand is estimated to be 1.88% among adults 45 years and older.[1] Once the patients developed acute ischemic stroke the decline of quality of life would certainly be affected. To date, the standard guideline treatment for acute ischemic stroke within the onset 4.5 hours is intravenous thrombolysis (rt-PA). From numerous the evidence-based studies revealed the efficacy to minimize disability and mortality.[2-4]

The several factors associated with the outcomes after intravenous thrombolysis had been studied such as hypertension[5], age[6], severity of stroke (National Institutes of Health Stroke Scale:NIHSS)[7], renal function[8], time to treatment.[9] Despite, there were limited Thai-based population studies had been studied in risk predicting the outcomes following intravenous thrombolysis in stroke patients.[10-14]

Furthermore, we studied significant risk factors other than from literature reviews that were different from the previous studies in Thailand. For example, the NIHSS score cut point of≥15 which is distinct from other Thai studies.

The aim of this study was to find the independent factors for predicting the disability and mortality in stroke patients at 90-day follow-up after receiving intravenous thrombolysis.

Methods

Study design and study population

This study was conducted using the database of OPD serv software with retrospective recruitment analyzing the calculated sample size of 290 patients according to the prior Thai based population study.[15]

However, we totally collected 326 patients in order to alleviate the effect of missing data. All the patients were clinically and radiologically diagnosed as acute ischemic stroke by neurologists; admitted from January 1, 2013 to December 31, 2019.

Case identification

The inclusion and exclusion criteria consisted of the protocol based on the ASA/AHA guideline for acute ischemic stroke/TIA management, 2014[16]. Additional exclusion criteria are incomplete data, and loss to follow up. During the data collection period, the inclusion criteria had not been modified to meet the updated ASA/AHA guideline for early management in acute stroke, 2019[17]. Furthermore, mechanical thrombectomy was not available in our hospital.

Study design

This study design was a retrospective cohort study conducted in Sanpasitthiprasong Hospital, Ubonratchathani.

Predicting factors

Demographic data, personal and medical history as well as clinical data were obtained through medical record reviews by the investigators. These included ages, sex,

smoking and pre-existing conditions, diabetes, hypertension, dyslipidemia, stroke and coronary artery disease. The severity of stroke was assessed using the National Institute Hospital Stroke Severity (NIHSS) score. We intended to use NIHSS cut point of ≥15 based on the evidence of poor clinical o utcome after thrombolysis at Sanpasitthiprasong Hospital. Disability of stroke patients was assessed by neurologists using the modified Rankin Scale (mRS) on arrival and at the time of thrombolytic treatment being started and 90-day follow-up. Data of post-treatment complications were also collected and these included brain edema, pneumonia, intracerebral hemorrhage[18], and seizure[19]. Laboratory test results including hematocrit, white blood cell count, platelets, INR, serum creatinine, and LDL were collected.[20-22]. Radiographic assessment based on brain CT non-contrast analysis was independently performed by a neurologist and a radiologist and 100% between-raters concordance was observed. The radiological findings consisted of ASPECT score[23], brain edema, and intracerebral hemorrhage.

The definition of outcome

The clinical outcomes that we mainly focus on were the death after intravenous thrombolysis and the unfavorable outcome. The mRS was used to evaluate disability at 90 days. We defined the disability according to the mRS as follows: (1) favorable (mRS 0-1: no significant disability), (2) moderately favorable (mRS 2-3: slight to moderate disability requiring some help but not dependent), and (3) unfavorable (mRS 4-6: severe disability requiring constant nursing care or death).

The death determination was clarified by the death certification in summary discharge in each patient, individually.

The sample size calculation

The objective of this study was to find the influencing factors to predict the disability and death in stroke patients who underwent intravenous thrombolysis. According to this, we used this following formula to calculate the sample size.[24]

$$n_1 = \left[\frac{z_{1-\frac{\alpha}{2}} \sqrt{\bar{p}\bar{q}\left(1+\frac{1}{r}\right)} + z_{1-\beta} \sqrt{p_1 q_1 + \frac{p_2 q_2}{r}}}{\Delta} \right]^2$$

$$r = \frac{n_2}{n_1}, q_1 = 1 - p_1, q_2 = 1 - p_2$$

$$\bar{p} = \frac{p_1 + p_2 r}{1+r}, \bar{q} = 1 - \bar{p}$$

Sample size determination for the present study was based on a research question “what are factors associated with risk of disability in patients with acute ischemic stroke receiving intravenous thrombolysis treatment. According to data from a previous study in a Thai population by Pornpatr A. et al, 53% of ischemic stroke patients without a history of hypertension later developed severe degree of disability (p1=0.53), meanwhile 69% of the patients with a history of hypertension developed severe disability (p2=0.69). At 95% confidence level and 80% power, 290 patients were required. A sample size was inflated to 326 to account for 0.61% missing data and/or loss of follow-up.

Data analysis

Baseline characteristics in particular NIHSS were analyzed and presented as mean for continuous variables and as percentage for dichotomous variables. The association between the selected variables and the functionally clinical outcome were divided into 3 groups: good (0-1 mRS) moderate (2-3 mRS) poor (4-6 mRS) those were tested by univariable logistic regression models. Multivariable logistic regression models were finally established to calculate adjusted odds ratios, as well as 95% confidence intervals for the predictive effect of multiple variables of the outcome. Similarly, the association between the chosen variables and death were also analyzed by univariable logistic regression and multivariable logistic regression.

Result

The sample size 326 was calculated and collected data. However, some were excluded by additional exclusion criteria 0.61%. (Figure 1) The final sample size used to define outcome was 306 patients. The‰male gender patients were 54.2 %, mean aged was 63.72 ± 13.496, the mean m RS on admission and after discharge 90 days was 3.45 ± 0.989 and 1.86 ± 1.71, respective ly. (Table 1) The patients were divided into 3 groups depend on mRS. The mRS 0-1 was no disability or favorable outcome; 168 cases (54.9%), mRS 2-3 was moderate favorable outcome meaning requires some help but not totally dependent; 73 cases (23.9%). mRS 4-6 was defined as unfavorable outcome which needed help and totally dependent; 65 patients (21.2%).

The incidence of death in our study was 3.9% in 90 days.

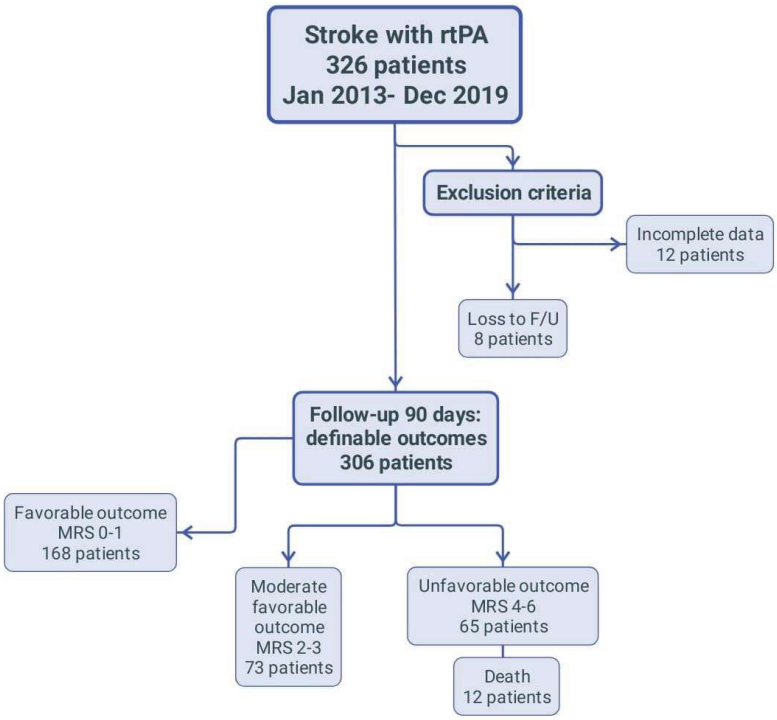

Figure.1 Study flow

Variables		Number	%
Age (Mean ± SD)		63.72 ± 13.496	
Sex			
	Male	166	54.2
	Female	140	45.8
	Seizure	3	1
	Intracranial hemorrhage	35	11.4
	Post thrombolytic brain edema	15	4.9
	Post thrombolysis pneumonia	18	5.9
Atrial fibrillation		56	18.3
Coronary artery disease		10	3.3
Diabetes mellitus		90	29.4
Hypertension		156	51
Dyslipidemia		116	37.9
Chronic kidney disease		25	8.2
Previous stroke/TIA		34	11.1
Statin use		68	22.2
SSRI/TCA use		7	2.3
Use of nicardipine before thrombolysis in hypertension (≥185/110 mmHg)		44	14.4

Table. 1 Baseline characteristics of stroke patients who received thrombolytic treatment

Variables	Mean± SD
SBP	150.8 ± 28.311
DBP	85.45 ± 17.33
NIHSS on arrival	10.52 ± 4.73
mRS on arrival	3.45 ± 0.989
mRS at 90-day follow-up	1.86 ± 1.71
Door to needle (min)	70.18±27.418
Onset to treat (min)	196.75 ±54.23
Hematocrit	45.65 ± 53.96
WBC	9380.32 ± 8546.62
Platelet (Mean ± SD)	248514.18 ± 74945.5
INR (Mean ± SD)	1.03 ± 0.42
LDL (Mean ± SD)	117.03 ± 40.39
ASPECT score (Mean ± SD)	7.98±1.505

Table 1 : Baseline characteristics of stroke patients who received thrombolytic treatment

The study aimed to find the prognostic factors to predict the functional outcome and death at 90-day follow-up in those who were diagnosed acute ischemic stroke (AIS) after treated with intravenous thrombolysis. Comparison of demographic and clinical factors of patients with acute ischemic stroke, If those factors were continuous data, the one-way ANOVA was precisely selected to analyze. Whereas, the categorical data we used Chi square test.

The study found that the significant predictive risk factors for outcome were NIHSS on arrival ≥ 15 P-Value <0.001, 95% CI: 1.823-5.447, mRS on arrival P-value < 0.001, 95% CI: 1.488-2.526, ASPECTS score P-value < 0.001, 95% CI: 0.617-0.840, Hematocrit P-value = 0.049, 95% CI: 1.00-1.007, LDL P-value =0.018, 95% CI: 1.001-1.012, High blood pressure with nicardipine used P-value < 0.001, 95% CI: 1.605-5.291 and ICH P-value < 0.001, 95% CI: 1.732-7.066 (Table 2). The statistically significant predictive risk factors for the death in 90 days were NIHSS on arrival ≥ 15 P-value < 0.001, 95% CI: 2.680-29.256, mRS on arrival P-value = 0.021, 95% CI: 1.142-5.301, ASPECTS score P-value = 0.016, 95% CI: 0.539-0.939, diabetes mellitus P-value = 0.034, 95% CI: 1.099-11.529, chronic renal failure P-value = 0.004, 95% CI: 1.808-23.370 and post thrombolysis pneumonia P-value = 0.011, 95% CI: 1.520-25.297. (Table 3)

Factors	Functional outcome			P-Value
	Favorable (N=168)	Moderate favorable (N=73)	Unfavorable (N=65)	
Age (year)	63.89 ± 14.09	62.53±12.13	64.62±13.49	0.973
Gender Male N(%)	94 (56.6)	40 (24.1)	32 (19.3)	0.411
NIHSS on arrival ≥15	18 (32.1)	16 (28.6)	22 (39.3)	< 0.001
mRS on arrival	3.23 ±1.021	3.49 ± 0.872	3.98 ± 0.82	< 0.001
Door to needle time (min)	69.11 ± 27.65	73.97±30.25	68.69±23.18	0.702
SBP at admission	149.19±26.80	154.26±30.84	151.06±29.25	0.398
ASPECTS score	8.28±1.43	7.92±1.54	7.29±1.44	< 0.001
Onset to treat(min)	195.95±58.57	198.08±48.41	197.31±49.09	0.803
Platelet count x 10^9/L	251850.75±81109.59	255513.89±62745.18	232136.92±69203.71	0.169
LDL mmol/L	112.16±35.57	121.46±41.69	124.65±48.70	0.018
INR	1.06±0.56	0.9696±0.08	1.03±0.13	0.469
Hematocrit	38.72±23.04	56.97±81.22	51.06±69.49	0.049
Serum creatinine	1.85±7.84	0.94±0.33	2.93±14.14	0.63
Diabetes mellitus N(%)	42 (46.7)	24 (26.7)	24 (26.7)	0.053
Hypertension N(%)	87 (55.8)	33 (21.2)	36 (23.1)	0.96

Table 2 : Comparison of demographic and clinical factors of patients with acute ischemic stroke by degree of disability at 90-day follow-up measured using the MRS

Factors	Functional outcome			P-Value
	Favorable (N=168)	Moderate favorable (N=73)	Unfavorable (N=65)	
Dyslipidemia N(%)	68 (58.6)	27 (23.3)	21 (18.1)	0.254
Atrial fibrillation N(%)	26 (46.4)	14 (25.0)	16 (28.6)	0.111
Coronary artery disease N(%)	6 (60.0)	3 (30.0)	1 (10.0)	0.588
Chronic renal failure N(%)	12 (48.0)	6 (24.0)	7 (28.0)	0.392
Previous stroke N(%)	18 (52.9)	9 (26.5)	7 (20.6)	0.883
Statin use N(%)	39 (57.4)	15 (22.1)	14 (20.6)	0.688
SSRI/TCA use N(%)	3 (42.9)	2 (28.6)	2 (28.6)	0.515
Nicardipine used in high BP ≥ 185/110 mmHg (N(%)	14 (31.8)	13 (29.5)	17 (38.6)	< 0.001
Post thrombolysis brain edema N(%)	8(53.3)	1 (6.7)	6 (40.0)	0.423
Post thrombolysis pneumonia N(%)	11 (61.1)	2 (11.1)	5 (27.8)	0.864
ICH N(%)	13 (7.7)	4 (5.5)	18 (27.7)	< 0.001

Table 2 : Comparison of demographic and clinical factors of patients with acute ischemic stroke by degree of disability at 90-day follow-up measured using the mRS

Factors	Death		P-Value
	No (N=294)	Yes (N=12)	
Age (year)	63.95±13.35	58.08±16.38	0.144
Gender Male N(%)	158 (95.2)	8 (4.8)	0.384
NIHSS score on arrival ≥ 15	40 (85.1)	7 (14.9)	< 0.001
mRS on arrival	3.43 ± 0.993	4.08 ± 0.669	0.021
Door to needle time (min)	70.05±27.05	73.33±36.62	0.684
SBP at admission	150.91±27.79	147.92±40.48	0.719
ASPECTS score	8.03±1.49	6.92±1.62	0.016
Onset to treat(min)	196.66±24.2	198.92±65.54	0.887
Platelet count x 10^9/L	247838.99±74837.97	265000±79033.94	0.436
LDL mmol/L	116.55±39.57	128.75±57.94	0.305
INR	1.03±0.43	1.11±0.18	0.511
Hematocrit	46.06±55.02	35.68±4.4	0.588
Serum creatinine	1.87±8.93	1.77±1.34	0.969

Table 3: Comparison of demographic and the death of patients with acute ischemic stroke by degree of disability at 90-day follow-up

Factors	Death		P-Value
	No (N=294)	Yes (N=12)	
Diabetes mellitus N(%)	83 (92.2)	7 (7.8)	0.034
Hypertension N(%)	150 (96.2)	6 (3.8)	0.945
Dyslipidemia N(%)	113 (97.4)	3 (2.6)	0.354
Atrial fibrillation N(%)	54 (96.4)	2 (3.6)	0.881
Coronary artery disease N(%)	9 (90.0)	1 (10.0)	0.336
Chronic renal failure N(%)	21 (84.0)	4 (16.0)	0.004
Statin use N(%)	64 (94.1)	4 (5.9)	0.351
SSRI/TCA use N(%)	6 (85.7)	1 (14.3)	0.19
Nicardipine use in severe HT(≥185/110mmHg) N(%)	42 (95.5)	2 (4.5)	0.822
Post thrombolysis brain edema N(%)	13 (86.7)	2 (13.3)	0.076
Post thrombolysis pneumonia N(%)	15 (83.3)	3 (16.7)	0.011
ICH N(%)	32 (91.4)	3 (8.6)	0.147

Table 3: Comparison of demographic and the death of patients with acute ischemic stroke by degree of disability at 90-day follow-up

The multivariable logistic regression analysis was performed to eliminate the confounding factors. The results revealed the independent factors to predict the outcome were NIHSS on arrival≥15 OR, 2.30 P-value =0.029, 95% CI: 1.091-4.840, nicardipine use with severe high blood pressure (≥185/110mmHg), OR 2.55 P-value = 0.013, 95% CI: 1.220-5.335, ICH OR 3.5 P-value = 0.018, 95% CI: 1.977-7.8. NIHSS on arrival was also the significant independent risk to predict death, OR 18.75 P-value = 0.014, 95% CI: 1.799-195.385. Moreover, we found that the co-morbidity, CRF was a statistically significant risk factor for the death with OR 8.52 P-value = 0.05, 95% CI: 1.815-89.125. (Table 4,5,6)

Factors	Crude OR	P-Value	95 % CI of Crude OR		Adjusted OR	P-Value	95 % CI of Adjusted OR	
			Lower	Upper			Lower	Upper
Age (year)	1.000	0.973	0.984	1.017				
Gender Male	0.834	0.411	0.541	1.285				
NIHSS ≥15	1.215	< 0.001	1.823	5.447	1.217	0.000	1.158	1.280
mRS on arrival	2.554	<0.001	1.488	2.526	0.910	0.814	0.413	2.005
DTN (min)	1.001	0.702	0.994	1.009				
SBP	1.003	0.398	0.996	1.011				
ASPECTS score	0.720	< 0.001	0.617	0.840	0.905	0.276	0.756	1.083
Onset to treat	1.001	0.803	0.996	1.005				
White blood cell	1.000	0.368	0.999	1.000				
Platelets	0.593	0.240	0.248	1.418				
LDL	1.006	0.018	1.001	1.012	1.001	0.582	0.995	1.008
INR	0.718	0.469	0.293	1.760				
Hematocrit	1.004	0.049	1.000	1.007	1.003	0.059	0.998	1.007
Serum creatinine	1.007	0.630	0.980	1.034				
Diabetes mellitus	1.584	0.053	0.994	2.526				
Hypertension	1.010	0.960	0.657	1.556				
Dyslipidemia	0.771	0.254	0.492	1.206				
Atrial fibrillation	1.560	0.111	0.902	2.696				
Coronary artery disease	0.713	0.588	0.210	2.426				
Chronic renal failure	1.401	0.392	0.647	3.035				
Previous stroke	1.523	0.883	0.535	2.071				
Statin use	0.898	0.688	0.532	1.517				
SSRI/TCA use	1.583	0.515	0.398	6.302				
Nicardipine used	2.914	< 0.001	1.605	5.291	2.874	0.002	1.452	5.690
Post thrombolysis brain edema	1.535	0.423	0.538	4.377				
Post thrombolysis pneumonia	0.918	0.864	0.348	2.424				
ICH	3.499	< 0.001	1.732	7.066	0.520	0.189	0.196	1.389

Table 4: Factors associated with high degree of disability at 90-day follow-up in patients with acute ischemic stroke receiving intravenous thrombolysis at Sanpasitthiprasong Hospital using univariable and multivariable logistic regression

Factors	Crude OR	P-Value	95 % CI of Crude OR		Adjusted OR	P-Value	95 % CI of Adjusted OR	
			Lower	Upper			Lower	Upper
Age (year)	0.97	0.144	0.931	1.011	0.924			
Gender Male N(%)	1.72	0.384	0.507	5.842	4.429			
NIHSS score at 1st ≥ 15	1.516	0.543	0.397	5.789	0.656			
Door to needle time	1.004	0.684	0.985	1.024	1.018			
SBP at admission	0.996	0.719	0.975	1.018	0.999			
ASPECTS score	0.711	0.016	0.539	0.939	0.605	0.028	0.386	0.948
Onset to treat(min)	1.001	0.887	0.990	1.012	1.003			
Platelet count x 10^9/L	1.0003	0.436	1.000	1.000	1.000			
LDL	1.006	0.305	0.994	1.020	1.015			
INR	1.27	0.511	0.619	2.625	2.799			
Hematocrit	0.974	0.588	0.886	1.071	0.99			
Serum creatinine	0.998	0.969	0.931	1.072	0.864			
Diabetes mellitus	3.56	0.034	1.099	11.529	3.774	0.188	0.522	27.267
Hypertension	0.96	0.945	0.303	3.045	2.094			
Dyslipidemia	0.54	0.354	0.142	2.014	0.106			
Atrial fibrillation	0.889	0.881	0.189	4.174	0.529			
Coronary artery disease	2.88	0.336	0.335	24.763	6.79			
Chronic renal failure	6.5	0.004	1.808	23.370	27.096	0.009	2.321	316.381
Statin use	1.797	0.351	0.524	6.158	0.519			
SSRI/TCA use	4.363	0.19	0.483	39.420	6.72			
Nicardipine used	1.195	0.822	0.253	5.648	1.257			
Post thrombolysis brain edema	4.32	0.076	0.858	21.775	0.068			
Post thrombolysis pneumonia	6.2	0.011	1.520	25.297	95.787	0.029	1.587	5780.345
ICH	2.73	0.147	0.702	10.604	2.714			

Table 5: Factors associated with death at 90-day follow-up in patients with acute ischemic stroke receiving intravenous thrombolysis at Sanpasitthiprasong Hospital using univariable and multivariable logistic regression

Variables	Odd Ratio	95%CI		p-value
		Lower	Upper	
Predictive risk for outcome at 90 days				
NIHSS score admit ≥ 15	2.30	1.091	4.840	0.029
mRS at D/C	3.53	< 0.001	2.697	4.609
Nicardipine use	2.55	1.220	5.335	0.013
ICH	3.50	1.977	7.800	0.018
Predictive risks for death at 90 days				
NIHSS on arrival ≥ 15	18.75	1.799	195.385	0.014
CRF	8.52	1.815	89.125	0.05

Table 6: Factors associated with high degree of disability and death at 90-day follow-up in patients with acute ischemic stroke receiving intravenous thrombolysis at Sanpasitthiprasong Hospital using multivariable logistic regression

Discussion

The administration of intravenous thrombolysis in acute ischemic stroke patient is the current standard guideline therapy in selected cases. However, the unfavorable outcomes are inevitable in some cases. The current study found that NIHSS on arrival ≥ 15, High blood pressu re with Nicardipine used and ICH were associated with disability at 90 days following up. Whereas the NIHSS on arrival ≥ 15 and CRF were significant risk factors for the death.

The results of our study presented that the unfavorable outcome 90-day rate occurred 45.09%. The 90-day fatality rate was 3.9%. The recent study[25] reported 49% disability and death. The evidences from other studies reported death rate were different in the range of 7.2-11.4%.[26] The mortality and morbidity including intracerebral hemorrhage are important consequences after treatment which the physicians have to be ultimately concerned.

The unfavorable outcome in our study was defined as MRS 2-6 which the patients were dependent and require help in performing activity of daily living or death. There are several stroke thrombolytic predictive instruments (TPI) to predict functional outcome such as DRAGON scores[27], SNARL[28], SVM scores[29], THRIVE scores.[30]Nevertheless, the parameters in these models are diverse and some models have low sensitivity, specificity including limited evidence of external validity.[31] Currently, there are no single standard model to predict outcome in acute ischemic stroke patient being treated with intravenous thrombolysis.

Although, the cut point values of NIHSS in each trial were different however, we intentionally used the cut point of NIHSS 15 because in the practical we noticed that most of the patients in this group after thrombolysis in our hospital they still had disabilities. The result revealed the NIHSS ≥15 on arrival was an independent factor to predict functional outcome which was consistent with other previous studies. In Thai based elderly population study[15] reported that NIHSS> 15 was independent factor to predict outcome in stroke patient after treated with alteplase which was concordant with our current study. Contrarily, another study showed that NIHSS> 12 on arrival was the predictor of outcome in 3 months[32] which was not consistent with our study. This could be explained by this study included only anterior circulation stroke but excluded posterior circulation stroke whereas our study had been included all stroke subtypes. Severity of stroke were standardly evaluated by NIHSS and widely accepted that higher NIHSS was associated with deteriorated stroke.[33-35]

High blood pressure had been widely recognized as one significant risk of poor outcome and death after stroke due to brain edema, increased intracranial pressure and intracerebral hemorrhage.[5] Use of nicardipine is indicated in BP≥185/110 mmHg prior to rt PA prescription in stroke[17]. We revealed high BP with using intravenous nicardipine was the independent factor to predict poor outcome in AIS after being given rtPA 90 days.

The patients with renal dysfunction can possibly have poor functional outcome from natural course of disease and the risk of bleeding after thrombolysis.[36]There were several studies reported that renal dysfunction related to poor outcome and symptomatic ICH in stroke with thrombolytic patients which was coherent with this study.[37]

The NIHSS had been showed in several previous studies in the aspect of effective predicting mortality in acute ischemic stroke[33-35].

In our study we found the congruent results that indicated the NIHSS was the independent risk factor of the death as well.

ICH was one another significant risk to predict death in our study. In the prior study[38] reported the correlations between ICH and death or disability. Meanwhile, we were unable to detect the relation of disability and ICH. Despite, the definition of ICH, the interval between intravenous thrombosis and ICH were different in individual studies[39]. The result from the previous study revealed the publication of the European Co-operative Acute Stroke Study-II (ECASS-II)[40] defined symptomatic ICH had the largest independent impact. Whereas, We used Canadian stroke network definition to detect clinically irrelevant ICH after thrombolysis. The definition of any parenchymal hemorrhage was the definition that we used according to Canadian stroke network had low sensitivity and specificity.[39] In comparison with ECASS-II considered ICH correlated with neurological decline.

The differences may relate to the differences in the criteria used to define ICH.

The limitation of our study was as the following; first: the data collection derived from retrospective chart computer-based review that could have missing data and potential confounding effects. Second, cause of death determination was difficult to distinguish between the causation of death from stroke after thrombolysis and death from other causes: for example; co-morbidities. Since, the determination of death was collected from the summary chart review and death certification, this was limited to clarify from retrospective design. Third, the sample size was small that could reflect to underpower and alpha error. Fourth, the study was single center hospital based thus the lack of generality and external validity were the limitations. It requires further studies to optimize impact of significance.

Our study is the first study conducted to evaluate various risk factors among the Northeastern Thai population to predict outcome in stroke after thrombolysis in 90 days. Since, the effectiveness of thrombolysis is time dependent. Screening the patients who might be at risk of poor outcome furthermore lead to death are considerable. We postulated that the prognostic factors found in this study could be used to develop the optimal guideline management or prognostic predicting model screening to evaluate the outcome of stroke following thrombolysis. Additionally, this might be beneficial for the ER team or ICU team to properly manage emergency conditions in cases of having these risks. Finally, the prognostic model to predict functional outcome or adapted clinical practice guideline in our hospital could possibly be developed in the future. However, the future prospective trials with more sample size would be more practical.

Conclusion

In our present study, we found that NIHSS, high blood pressure and nicardipine use could be independent predictive outcome in stroke patient who is treated with intravenous thrombolysis. Moreover, the NIHSS on arrival was the predictor for the death in similar setting patients.

This finding may be useful for the physicians to early detect and close monitoring in the high risk of deteriorated stroke patients after intravenous thrombolysis.

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Potential risk factors predicting functional outcome and mortality at 90-day follow-up in patients with acute ischemic stroke receiving intravenous thrombolysis at Sanpasitthiprasong Hospital

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ABSTRACT

Background: Clinical outcomes of intravenous thrombolysis depend on various factors. Disability and death are the major unfavorable consequences after treatment. This is the first study conducted to evaluate the risk factors related to the outcomes at Sanpasithiprasong Hospital.

Objective: To examine predictors of disability and mortality in stroke patients who received intravenous thrombolysis at 90-day follow-up at a referral tertiary hospital.

Methods: In this retrospective cohort study, sociodemographic and clinical data of 306 stroke patients treated with recombinant tissue plasminogen (rt-PA/Alteplase) from January 2013 to December 2019 were obtained through medical record reviews. Outcomes included death and disability measured by the Modified Rankin Scale (MRS) at 90 days after intravenous thrombolysis treatment. Univariate and multivariate logistic regression was used to examine factors associated with mortality and outcome after 90 days.

Results: Favorable outcome had been observed 168 (54.9%), moderate unfavorable outcome was 72 (23.9%), unfavorable outcome was seen 85 (21.2%). Significant outcome prognostic factors according to multivariable regression analysis were NIHSS (OR 2.30, P-value=0.029, 95% CI: 1.091-4.840), Nicardipine use in high blood pressure (OR 2.55, P-value=0.013, 95% CI: 1.220-5.335), and intracerebral hemorrhage (ICH) (OR 3.5 P-value=0.018, 95% CI: 1.977-7.8). The predictive factors for the death were NIHSS (OR 18.75, P-value = 0.014, 95% CI: 1.799-195.385) and chronic renal failure (CRF) (OR 8.52, P-value=0.05, 95% CI: 1.815-89.125).

Conclusion: The NIHSS, high blood pressure with nicardipine use could be independent factors predictive outcome in stroke patients who had been treated with thrombolysis. Moreover, the high NIHSS on arrival and CRF possibly were the predictors for the death in similar setting patients. These factors should be evaluated and closely monitored.

Keywords: Stroke, thrombolysis, outcome, risk factors, prognostic factors

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