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Intensive care unit admission prediction tool for ischemic stroke patients receiving intravenous thrombolysis: A retrospective cohort study

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Abstract

Background: Some evidence suggests that given the limited healthcare resources, the majority of low-risk stroke patients may not require critical care monitoring. This study aimed to establish a predictive score for identifying post-intravenous thrombolysis (IVT) acute ischemic stroke patients who should be monitored in the intensive care unit (ICU). *Methods:* This was a retrospective cohort study of patients with acute ischemic stroke who underwent IVT at Songklanagarind Hospital, Thailand between January 2010 and December 2019. Baseline characteristics and clinical outcomes were recorded. Systolic blood pressure (SBP) was collected using the first recorded in the emergency department (ED) as well as the National Institutes of Health Stroke Scale (NIHSS). *Results:* Of the 171 patients with stroke, 73 (42.7%) needed ICU care. The median age was 67 years old. The median SBP and NIHSS were 160 mm Hg and 10, respectively. The predicting stroke ICU (PSU) score was developed, with the following points assigned: NIHSS score (1 point if > 9), SBP (1 point if > 170 mmHg), and infarct size greater than 1 lobe (2 points if present). The PSU score achieved an area under the ROC curve of 0.759 (95% confidence interval [CI] = 0.688–0.830). A PSU score ≥ 1 predicted the need for ICU care with a sensitivity of 91.78%.
Conclusions: The PSU score, which is based on the NIHSS score, systolic blood pressure, and infarct size, predicts the need for ICU care after IVT in patients with stroke.

Keywords: Acute ischemic stroke, intensive care unit, intravenous thrombolytic therapy

INTRODUCTION

According to the 2018 American Heart Association /American Stroke Association guidelines, patients should be admitted to specialized stroke care after intravenous thrombolysis (IVT).[1] Patients who receive recombinant tissue plasminogen activator (rt-PA) are usually sent to a stroke unit or the intensive care unit (ICU) for close observation and monitoring of complications, such as worsening stroke, cerebral edema, cerebral herniation, and especially hemorrhagic transformation after reperfusion therapy.[2]

In resource-limited facilities, it is necessary to determine whether patients should be admitted to the ICU or stroke unit after IVT. Unnecessary ICU admission causes overcrowding in the emergency department (ED)[3], as well as an increased risk of ICU-associated infection and delirium.[4,5] In comparison with the general ward, inappropriate admission of patients with stroke to the ICU results in no cost or outcome benefit.[6] On the other hand, inappropriate admission to the ward or delayed transfer to the ICU result in poor outcomes.[7]

A previous study by Faigle *et al*.[8] proposed the intensive care after thrombolysis (ICAT) score for selecting appropriate post-IVT patients to be admitted to the ICU. The score combines the components of male sex, Black race, systolic blood pressure (SBP), and the National Institutes of Health Stroke Scale (NIHSS). The score was developed in a US setting and had a race component that was not validated in low- to middle-income or Asian countries. We hypothesized that some post-IVT patients who do not require critical care would be admitted to a stroke unit or general ward setting. This study aimed to develop a clinical risk prediction score to identify patients needing ICU admission in the

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setting of a Thai population and a resource-limited hospital.

METHODS

Study design

A clinical risk score was developed using a retrospective observational cohort. Data on patients with acute ischemic stroke who received IVT at Songklanagarind Hospital between January 2010 and December 2019 were collected from the hospital database. Patients aged ≥ 18 years with acute ischemic stroke who received IVT with rt-PA were included. Patients who initially underwent mechanical thrombectomy were excluded from this study.

This study was conducted according to the Helsinki Declaration, and it was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC 62-392-14-4). Since this study was retrospective in nature and all data were anonymized, the Ethics Committee has waived informed consent for the study.

Data collection

All data used in the analysis were retrieved from electronic medical records, a radiology information system, and standardized stroke fast-track record forms, which were signed by certified neurologists. Baseline clinical characteristics collected included: age, sex, initial NIHSS[9], initial SBP, and diastolic blood pressure which first recorded at the ED, comorbidities, previous medication, initial laboratory findings, stroke lesions, and infarct size on initial brain CT. We retrieved the CT interpretation results, which could only be confirmed by the radiologists. Cerebral infarctions were measured qualitatively using CT scan as normal, lacunar, less than one-half lobe, up to one lobe, and several lobes, as described by Brott *et al*.[10] The clinical outcomes, including hospital length of stay, ICU stay, mortality, and the modified Rankin Scale (mRS) at 30 and 90 days.[11] Only patients' follow-up mRS data were collected using electronic medical records.

End point of interest

The primary endpoint for prediction was compatibility with ICU admission criteria, which were defined previously during ICAT score development.[8,12] The criteria included uncontrolled hypertension requiring intravenous (IV) antihypertensive drugs; use of vasopressors; need for invasive hemodynamic monitoring; respiratory distress resulting in requirement of either continuous bilevel positive airway pressure or mechanical ventilation; anaphylaxis; arterial bleeding requiring blood transfusion; cerebral edema and increased intracranial pressure management; neurosurgical intervention, such as decompressive craniectomy; or symptomatic intracerebral hemorrhage defined as a change in NIHSS score of ≥ 4 points from baseline. The secondary endpoint was a comparison of the discriminating performances of the new and ICAT scores.

Statistical analysis

Sample size estimation for diagnostic test studies was used to calculate the sample size.[13] Estimating that the proportion of post-IVT patients with critical care needs is 25%[8], we calculated that a minimum sample size of 64 would provide 95% confidence level with 80% power to detect a difference of 20% from the presumptive value of 80% sensitivity. Categorical variables are displayed as numbers and percentages. For categorical data, Fisher's exact test or Pearson's chi-square test were utilized. Continuous variables are reported as median and interquartile range (IQR). To ascertain if continuous variables had a normal distribution, the Shapiro–Wilk test was performed. For continuous variable analysis, the Mann–Whitney U test was employed.

Variables were compared between the groups with and without ICU needs. All significant potential predictors were analyzed using univariable logistic regression. Selected variables from simple logistic regression with a P-value < 0.1 were introduced to a multiple logistic regression analysis.

In order to make variables more easily applicable in a practical score, strongly correlated continuous variables were transformed into categorical variables based on clinically and statistically significant subgroups. Each predictor's logistic coefficient was divided by the lowest model coefficient before being rounded to the nearest non-decimal integer. Area under the receiver operating characteristic (ROC) curve (AUC) analysis was used to assess each model's capacity for discrimination.

The Hosmer–Lemeshow test was used to assess the goodness-of-fit of the model calibration. Analysis of the difference between the AUCs of the new and ICAT scores was conducted using the method developed by Delong *et al*.[14] Internal validation was performed with a bootstrapping re-sampling procedure with 1,000 replicates to evaluate the optimism of the model. Statistical significance was set at $P < 0.05$ for all comparisons. All statistical analyses were performed using STATA, version 16 (StataCorp LP, College Station, TX, USA).

RESULTS

Patient flow and recruitment

A total of 197 patients who underwent IVT in the ED were recruited for this study. Twenty-six patients were excluded from the study because they had undergone endovascular thrombectomy. Finally, 171 patients were enrolled in this study. Seventy-three patients (42.7%) were defined as needing ICU care (Figure 1).

Patient characteristics

The baseline characteristics of all patients were classified into two groups: those with and without ICU needs (ICU and non-ICU groups, respectively; Table 1). The median age was 67 years (IQR, 57–75 years), and 63.2% were men. The median NIHSS score at presentation was 10 (IQR, 7–14) and the median SBP was 160 mmHg (IQR, 140–177).

Model development and validation

We collected significant values for seven variables from the baseline characteristics for the univariable and multivariable analyses for ICU care needs, including age, NIHSS, SBP, anticoagulant therapy rate, infratentorial lesion, lacunar infarct, and infarct size > 1 lobe. A multivariable logistic regression model was used until there were three predictors left; namely NIHSS, SBP, and infarct size >1 lobe, which were statistically significant for the adjusted odds ratio (OR) (Table 2).

A prediction score was developed using the major multivariate clinical factors. Each predictor's logit coefficient served as the weight for the score transformation. A weighted score was assigned to each predictor as follows: NIHSS (1 point if NIHSS > 9), SBP (1 point if SBP > 170 mmHg), and infarct size > 1 lobe (2 points if present) (Table 3).

The prediction score was named the predicting stroke ICU (PSU) score, with the highest sensitivity of 91.78% and the lowest specificity of 30.61% at a cutoff of ≥ 1 point (Table 4). A

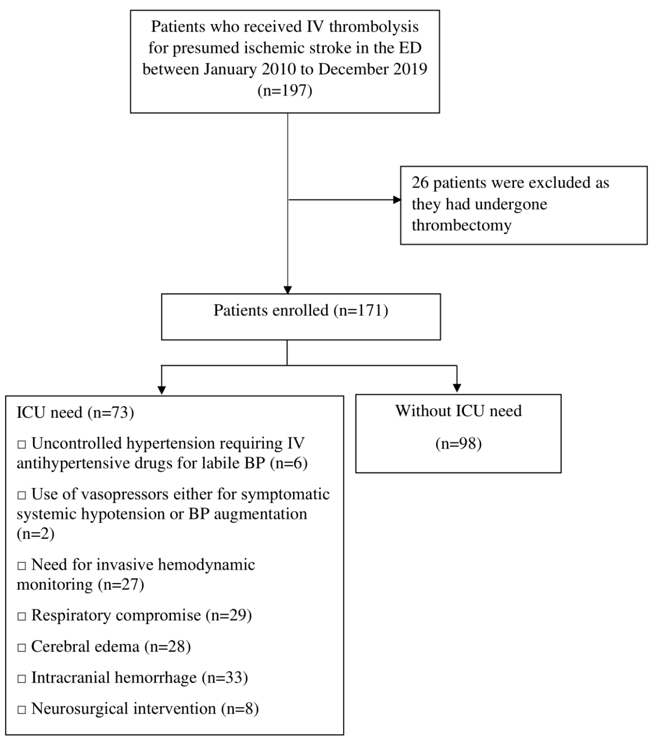

Figure 1. Flow of patients within the study.
Abbreviations: BP, blood pressure; ED, emergency department; ICU, intensive care unit; IV, intravenous.

Table 1: Baseline characteristics of patients

Characteristics	All patients (n = 171)	ICU needs (n = 73)	Without ICU needs (n = 98)	P-value
Age, years	67 (57-75)	70 (59-80.5)	66 (56-73.2)	0.025
Sex, male	108 (63.2)	47 (64.4)	61 (62.2)	0.774
NIHSS	10 (7-14)	11 (9-16.5)	9 (6-12)	0.001
SBP	160 (140-177)	163 (149.5-185.5)	156 (137.8-169)	0.003
DBP	88 (77-100)	89 (79-103.5)	87.5 (76.5-96.5)	0.213
IVT window ≤ 3 h	166 (97.1)	73 (100)	93 (94.9)	0.072
Comorbidities				
HTN	107 (62.6)	56 (76.7)	51 (52)	0.001
DLP	95 (55.6)	41 (56.2)	54 (55.1)	0.890
AF	43 (25.1)	20 (27.4)	23 (23.5)	0.558
DM	33 (19.3)	18 (24.7)	15 (15.3)	0.125
Prior stroke/TIA	28 (16.4)	13 (17.8)	15 (15.3)	0.662
CAD	23 (13.5)	11 (15.1)	12 (12.2)	0.592
Medication				
Antiplatelet	47 (27.5)	25 (34.2)	22 (22.4)	0.087
Anticoagulant	13 (7.6)	2 (2.7)	11 (11.2)	0.038
Statin	61 (35.7)	31 (42.2)	30 (30.6)	0.109
Glucose	111 (100-141)	116 (100.5-150.5)	109.5 (98-131.2)	0.216
Creatinine	1.0 (0.8-1.2)	1.0 (0.8-1.2)	0.9 (0.8-1.2)	0.165
INR	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	0.384
Stroke lesions				
Supratentorial	170 (99.4)	72 (98.6)	98 (100)	0.245
Right hemispheric	78 (45.6)	32 (43.8)	46 (46.9)	0.687
Left hemispheric	101 (59.1)	42 (57.5)	59 (60.2)	0.725
Infratentorial	10 (5.8)	8 (11.0)	2 (2)	0.014
Infarct size				
Normal	4 (2.3)	0 (0)	4 (4.1)	0.081
Lacunar	11 (6.4)	1 (1.4)	10 (10.2)	0.020
< 0.5 lobe	86 (50.3)	31 (42.5)	55 (56.1)	0.077
0.5-1 lobe	23 (13.5)	7 (9.6)	16 (16.3)	0.202
> 1 lobe	47 (27.5)	34 (46.6)	13 (13.3)	< 0.001
Outcomes				
Hospital LOS	6 (4-11)	8 (5-15)	5 (4-7.2)	< 0.001
ICU stay[1]	1 (1-3)	2 (1-4)	1 (1-2)	< 0.001
In-hospital mortality	15 (8.8)	14 (19.2)	1 (1.0)	< 0.001
mRS at day 30[2]	4 (2-5)	5 (3-6)	3 (1-5)	0.001
mRS at day 90[3]	4 (2-6)	5 (2-6)	2 (1-7)	0.006

Note: Data are presented as median (interquartile range) or n (%)
[1]n = 146, 25 patients were admitted to the non-ICU wards
[2]n = 151, missing value = 20
[3]n = 136, missing value = 35
Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease; DBP, diastolic blood pressure; DLP, dyslipidemia; DM, diabetes mellitus; HTN, hypertension; ICU, intensive care unit; INR, international normalized ratio; IVT, intravenous thrombolysis; LOS, length of stay; mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; TIA, transient ischemic attack.

Table 2: Univariable and multivariable analyses for the need for ICU care

Variables	OR	95% CI	P-value	Adjusted OR	95% CI	P-value
Age	1.03	1.00-1.05	0.028	1.00	0.97-1.03	0.999
NIHSS	1.13	1.06-1.22	< 0.001	1.11	1.03-1.22	0.007
SBP	1.02	1.01-1.03	0.003	1.02	1.01-1.04	0.002
Anticoagulant therapy	0.22	0.48-1.03	0.056	0.21	0.03-1.29	0.091
Infratentorial	5.91	1.21-28.71	0.028	9.09	1.26-65.49	0.028
Lacunar infarct	0.12	0.01-0.97	0.048	0.26	0.03-2.29	0.214
Infarct size > 1 lobe	5.70	2.71-11.98	< 0.001	5.53	2.37-12.92	< 0.001

Abbreviations: CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SBP, systolic blood pressure.

Table 3: Best multivariable clinical predictors and assigned item scores

Predictors	OR	95% CI	P-value	β	Score
NIHSS					
≤ 8	1.00	Reference	-	-	0
> 9	2.83	1.31-6.15	0.008	1.01	1
SBP					
≤ 170	1.00	Reference	-	-	0
> 170	2.81	1.31-6.06	0.008	1.08	1
Infarct size > 1 lobe			-	-	
No	1.00	Reference			0
Yes	6.47	2.87-14.60	< 0.001	1.92	2
Infratentorial					
No	1.00	Reference			
Yes	4.77	0.83-27.3	0.079	-	-
Constant	0.14	0.07-0.31	-	-	-

Abbreviations: β, logistic regression beta coefficient; CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SBP, systolic blood pressure

Table 4: Sensitivity and specificity of the PSU score by cutoff point

PSU score cutoff point	Sensitivity	Specificity	Correctly classified	LR+	LR-
≥ 1	91.78	30.61	42.69	1.32	0.27
≥ 2	67.12	72.45	70.18	2.43	0.45
≥ 3	41.10	94.90	71.93	8.05	0.62
≥ 4	13.70	98.98	62.57	13.42	0.87

Abbreviations: LR+, positive likelihood ratio; LR-, negative likelihood ratio; ICU, intensive care unit; PSU, predicting stroke ICU

higher score cutoff point leads to less sensitivity but greater specificity. We determined that a cutoff of 1 point had the highest sensitivity for ruling out ICU need conditions.

The PSU score had an AUC of 0.759 (95% CI = 0.688-0.830), showing that the PSU score model was predictive of the need for ICU care for acute ischemic stroke patients after receiving IVT (Figure 2). The model calibration was confirmed with Hosmer–Lemeshow goodness-of-fit statistics that showed a non-significant P-value of 0.588, and the calibration plot of predicted risk versus

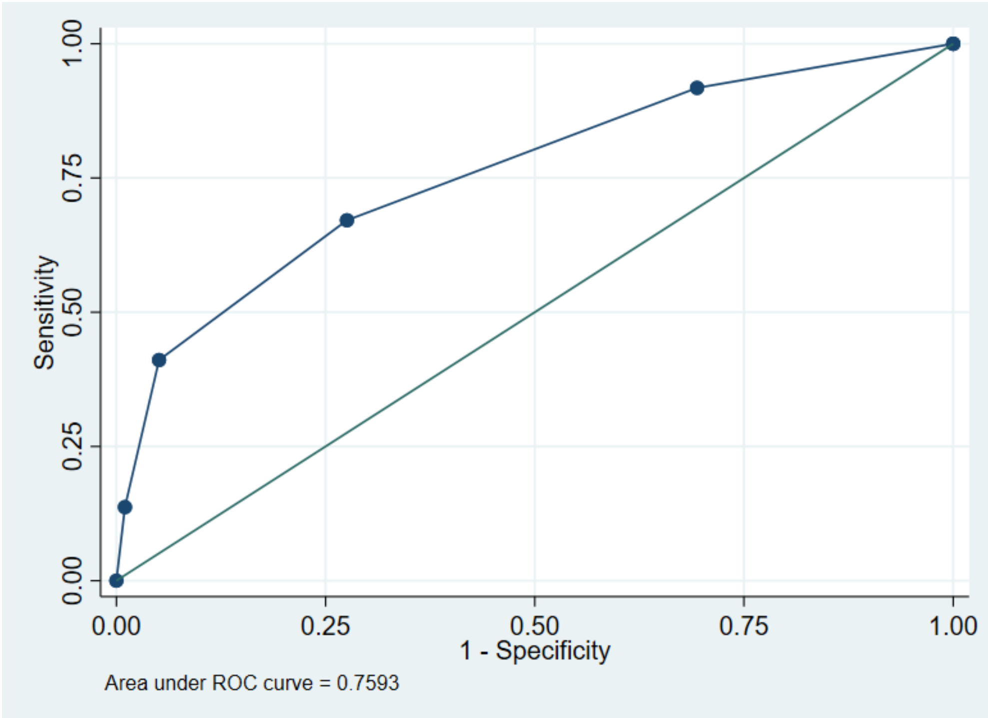

Figure 2. ROC curve for the score model predicting the need for ICU care with an AUC of 0.759.
Abbreviations: AUC, area under the receiver operating characteristic curve; ICU, intensive care unit; ROC, receiver operating characteristic

observed risk of the need for ICU care was also assessed (Figure 3).

The PSU score was compared with the ICAT score in discriminating the need for ICU care. The AUCs of the PSU and ICAT scores were 0.759 and 0.665, respectively (Figure 4).

We performed internal validation of the PSU score via non-parametric ROC with 1,000 bootstrap samples, and the results were acceptably predictive (AUC, 0.658; 95% CI = 0.57–0.74).

DISCUSSION

In the current study, we identified factors associated with ICU admission following IVT in stroke patients. Based on the severity of the stroke as determined by the NIHSS, SBP, and infarct size, we developed and validated a simplified risk assessment score known as the "PSU score." Each element of the score is easily accessible and assessed in clinical practice. An increasing NIHSS score is a risk factor for hemorrhagic complications[15] and hemorrhagic transformation in patients with ischemic stroke.[16] Patients with an NIHSS score of ≥ 10 had a 7.7 times greater chance of needing ICU resources than those with an NIHSS score of < 10.[12] Similar to the PSU score developed in the current study, the NIHSS score is an independent predictor of the need for ICU care. To calculate the PSU score, the NIHSS was divided into two groups: mild (8 points) and moderate-to-severe (> 9) for ease of use.

Based on information from 30 research studies, hypertension is the most common risk factor for stroke and has been identified in about 64% of stroke patients.[17,18] Attaining an early and consistently low SBP of < 140 mmHg, even as low as 110–120 mmHg, within the first 24 hours, is associated with better outcomes in acute ischemic stroke patients who underwent thrombolysis.[19] In the current study, the median baseline SBP of all patients was 160 mmHg. We selected a cutoff SBP of 170 mmHg for our model based on the best Youden index.

In individuals with moderate-to-large infarcts, infarct volume was directly related to a lower likelihood of having a favorable outcome.[20] In models with adjustments, infarct volume was a strong predictor of the requirement for ICU care (OR 1.027 per mL increase in volume, 95% CI 1.002-1.052). With 81.3% sensitivity and 66.7% specificity, an infarct volume larger than 3 mL was indicative of critical care treatment requirement.[21] However, non-contrast CT infarct volume needs

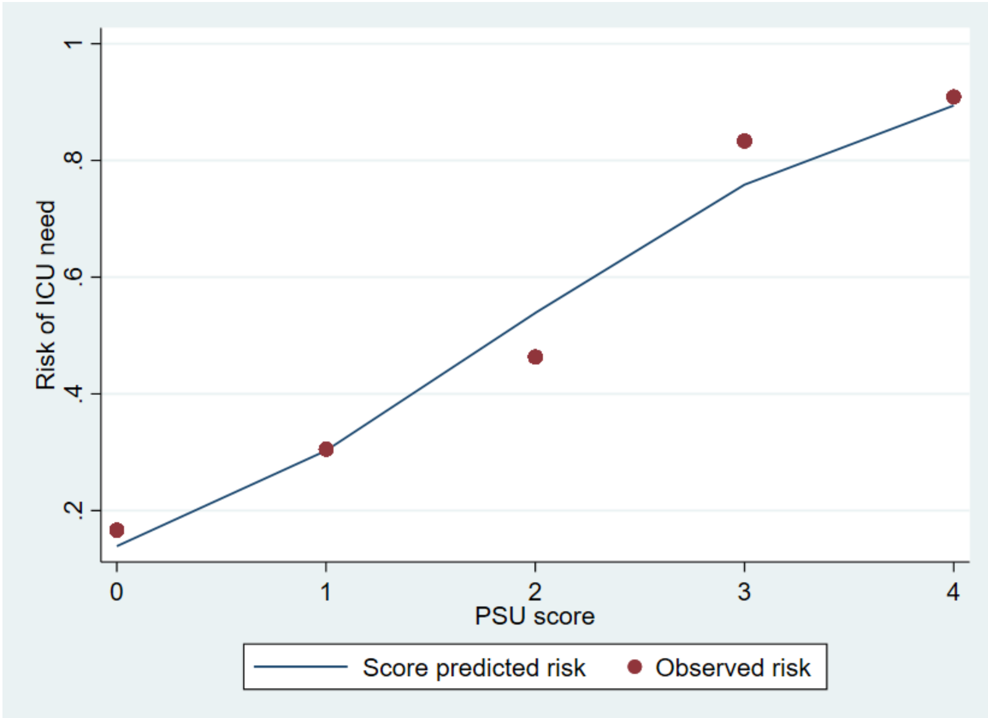

Figure 3. Calibration plot of score predicted risk versus observed risk of ICU admission.
Abbreviations: ICU, intensive care unit

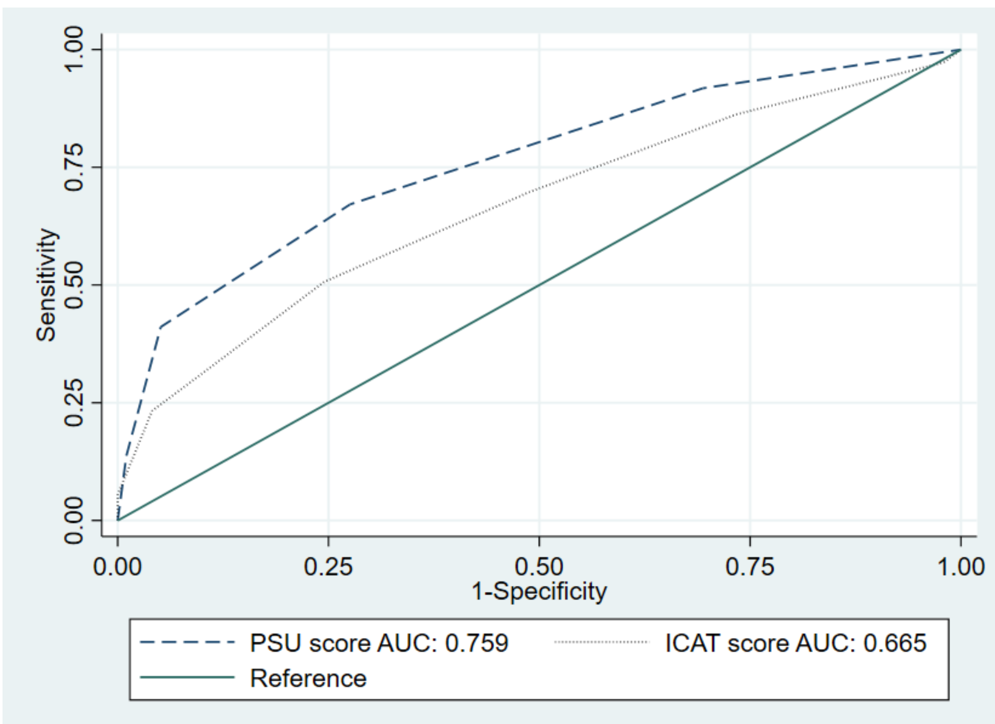

Figure 4. Comparison of AUCs between the PSU and ICAT scores.
Abbreviations: ICAT, intensive care after thrombolysis; ICU, intensive care unit; PSU, predicting stroke ICU

to be interpreted carefully; thus, we decided to use the number of lobes affected by the infarction to calculate our score.

Compared with the ICAT score, the PSU score demonstrated superior diagnostic performance when assessing the need for critical care after IVT in patients with stroke. However, the Black race component of the ICAT score was omitted from the calculation because of the lack of African American patients in our cohort. Patient characteristics were quite different between the two studies. Stroke severity was higher in our patients than in those in the ICAT study (median NIHSS score, 10 vs. 7). Only 24.8% of the patients in the ICAT study required ICU care, which was lower than the rate in our study (42.7%). The most common ICU complication in the ICAT study was uncontrolled hypertension requiring titration of IV antihypertensive drugs (51.4%), whereas in our study, it was intracranial hemorrhage (45.2%).

To the best of our knowledge, this is the first study to report the predictive value of the PSU score in Thai patients who underwent IVT. This new score may provide valuable information for assessing disease severity. Patients with a PSU score ≥ 1 may require more intensive care.

Our study had several limitations. First, we did not include race in our score. Although the Black race affected clinical outcomes in the ICAT score study, we cannot apply this component in Thailand or other Asian countries. Second, different institutions throughout the world may have different criteria of admittance to the ICU. We used the same indication from a previous model study to compare the two scores. Third, we did not include individuals who received endovascular treatment following IVT. Our findings can only be utilized in patients undergoing IVT without subsequent endovascular treatment. Fourth, we could not retrieve the mRS information during the follow-up visit since it was missing. All we could obtain from the electronic medical records was information on who was there. Finally, this study examined a small sample of patients from a single center over a period of 10 years in a retrospective approach. Owing to the limited generalizability to larger populations, further validation of our score using an external dataset is required.

In conclusions, The PSU score, which combines the NIHSS score, SBP, and infarct size, predicts the need for ICU care after IVT in patients with ischemic stroke and may be useful in triaging such patients to the appropriate environment, thus reducing the cost burden of healthcare facilities, which is of significant value especially considering the limited resources of the healthcare system.

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DISCLOSURE

Ethics: This study approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC 62-392-14-4). Since this study was retrospective in nature and all data were anonymized, the Ethics Committee of the Faculty of Medicine, Prince of Songkla University has waived informed consent for the study.

Availability of data: The data from this study are available from the corresponding author upon request.

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Conflict of interest: None

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