การศึกษาเปรียบเทียบความแม่นยำของการพยากรณ์โรคหลอดเลือดสมองเฉียบพลันโดยใช้คะแนน Full Outline of UnResponsiveness Score Coma Scale, Glasgow Coma Scale และ Glasgow Coma Scale-Pupils Score ในห้องฉุกเฉิน โรงพยาบาลศิริราช

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บทคัดย่อ

บทนำ

คะแนนความรู้สึกตัวสามารถใช้ในการพยากรณ์การเสียชีวิตของผู้ป่วยโรคหลอดเลือดสมองเฉียบพลันได้ดี แต่ยังไม่มีการศึกษาที่เปรียบเทียบระหว่างระบบคะแนน Full Outline of UnResponsiveness (FOUR), Glasgow Coma Scale (GCS) และ Glasgow Coma Scale-Pupils (GCS-P) Score

วัตถุประสงค์

เพื่อเปรียบเทียบความสามารถในการพยากรณ์การเสียชีวิตในโรงพยาบาลระหว่างคะแนนทั้ง 3 ระบบ และวัตถุประสงค์รอง ได้แก่ การพยากรณ์การเสียชีวิตและภาวะทุพพลภาพถาวรที่ 30 และ 90 วัน

วิธีการศึกษา

เป็นการศึกษาเชิงวิเคราะห์แบบไปข้างหน้าของผู้ป่วยโรคหลอดเลือดสมองเฉียบพลันที่เข้ารับการรักษาที่ห้องฉุกเฉิน โรงพยาบาลศิริราช ระหว่าง สิงหาคม 2562 ถึง ตุลาคม 2563 โดยผู้ป่วยจะได้รับการประเมินคะแนนความรู้สึกตัวทั้ง 3 ระบบที่ห้องฉุกเฉิน ก่อนที่จะได้รับการรักษาจำเพาะ หลังจากนั้นผู้วิจัยจะติดตามผู้ป่วยด้วยบทสัมภาษณ์ทางโทรศัพท์ที่ 30 และ 90 วันหลังเกิดโรค

ผลการศึกษา

จากประชากรทั้งหมด 315 ราย พบว่ามีผู้เสียชีวิตในโรงพยาบาล 33 ราย คิดเป็นร้อยละ 10.47 คะแนนความรู้สึกตัวที่สามารถพยากรณ์การเสียชีวิตในโรงพยาบาลได้แม่นยำที่สุด คือ คะแนน GCS-P ซึ่งมีค่าพื้นที่ใต้เส้นโค้ง (AUC) 0.932 (95% CI 0.885-0.976, p<0.001) ในขณะที่ GCS และ FOUR Score มีค่าพื้นที่ใต้เส้นโค้งเท่ากับ 0.930 และ 0.895 ตามลำดับ นอกจากนี้ ยังพบว่าคะแนน GCS-P สามารถพยากรณ์การเสียชีวิตที่ 30 และ 90 วันได้มากที่สุดอีกด้วย (AUC 0.913 และ 0.891) และแม้ว่าคะแนนความรู้สึกตัวทั้ง 3 ระบบจะมีความสัมพันธ์กันกับคะแนน Modified Rankin Scale และ Cerebral Performance Score ในเกณฑ์ต่ำ แต่หากผู้ป่วยมีคะแนน GCS-P, GCS และ FOUR ต่ำลง ก็จะมีโอกาสเกิดภาวะทุพพลภาพถาวรสูงขึ้น

สรุปผลการศึกษา

คะแนนความรู้สึกตัวที่ได้จาก Glasgow Coma Scale–Pupils (GCS-P) score มีความแม่นยำมากที่สุดในการพยากรณ์การเสียชีวิตในโรงพยาบาลและการเสียชีวิตที่ 30 และ 90 วันในผู้ป่วยโรคหลอดเลือดสมองเฉียบพลันในห้องฉุกเฉิน

คำสำคัญ

โรคหลอดเลือดสมองเฉียบพลัน คะแนนความรู้สึกตัว ห้องฉุกเฉิน การพยากรณ์โรค

A Comparison Study of Acute Stroke Prognostication between Full Outline of UnResponsiveness Score Coma Scale, Glasgow Coma Scale and Glasgow Coma Scale-Pupils Score in Emergency Department, Siriraj Hospital

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Abstract

Introduction

The consciousness scoring systems are good predictors for defining mortality in acute stroke. However, there is no study comparing between Full Outline of UnResponsiveness (FOUR), Glasgow Coma Scale (GCS), and Glasgow Coma Scale-Pupils (GCS-P) score.

Objectives

To compare the accuracy of FOUR, GCS-P, and GCS scores for predicting in-hospital mortality. The other objectives are the prognostication of these scores for 30-day and 90-day mortality and poor neurological outcome.

Method

The prospective cohort study was conducted in the emergency department of Siriraj Hospital, between August 2019 and October 2020. Acute stroke patients were evaluated by the scoring systems before definitive treatment. The telephone interview was done at 30 and 90 days after onset of acute stroke.

Results

From 315 participants, 33 (10.47%) were died in the hospital. The best scoring system for predicting in-hospital mortality was the GCS-P score with the area under the curve (AUC) 0.932 (95% CI 0.885-0.976). The AUC of GCS and FOUR scores were 0.930 and 0.895 respectively. GCS-P score was also the best coma score for predicting the 30 and 90-day mortality (AUC of 0.913 and 0.891). Although there was a poor relationship between the Modified Rankin Scale, Cerebral Performance Score, and coma scoring systems, the patients with low GCS-P, GCS, or FOUR scores tended to have poor neurological outcomes.

Conclusion

GCS-P score is the best prognostication for in-hospital, 30-day, and 90-day mortality in acute stroke patients in the emergency department.

Keywords

Acute stroke, Coma scoring system, Emergency department, Prognostication

Introduction

Cerebrovascular accident is a global burden disease. The World Stroke Organization fact sheet 2019 reported a stroke incidence of 185.01 (171.98-198.75) crude rate per 100,000 per year or 13.7 million new strokes yearly[1]. About five million stroke patients die annually. In Thailand, stroke is the second leading cause of death. Although the national management system for acute stroke is implemented, the mortality rate still increased from 43.3 in 2015 to 53.0 per 100,000 population per year in 2019[2]. After the COVID-19 pandemic, there are concerns that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection might be associated with future thrombotic events, including ischemic stroke[3].

A reliable and feasible prognostic tool is essential for treating acute stroke patients because the decision-making might be changed depending on the prognosis[4]. The level of consciousness is one of the commonly used prognostic factors. There are a lot of evidence-based publications that support the value of various coma scoring systems. The Glasgow Coma Scale (GCS) score is a well-known system used for over 40 years. The score has adequate reliability. However, many factors influence its reliability, for example, the observer's experience, the type of stimuli used to stimulate a patient, the type of pathology of a patient, and the confounding effect of intubation[5, 6]. The Full Outline of UnResponsiveness (FOUR) score was created in 2005, aiming to assess the level of consciousness in patients who cannot evaluate the verbal score from the GCS score[7]. The FOUR score was reliable for predicting poor neurological outcomes and mortality in several neurological diseases, including acute stroke[8, 9]. Moreover, in 2018, the GCS-Pupils (GCS-P) scoring system was created and proved the usefulness of the outcome prognostication in traumatic brain patients[10]. The GCS-P score has an additive effect on prognostication to the GCS score[11].

Objectives

Several studies focus on determining the prognostication comparing head-to-head between the GCS and FOUR scores or the GCS and GCS-P scores[12, 13]. However, to date, no study has reported comparing the GCS-P, GCS, and FOUR scores. Therefore, this study aims to define the prognostication abilities of these three scores for mortality and morbidity of acute stroke patients.

Method

The prospective cohort study was conducted in the emergency department (ED) of Siriraj Hospital, a 2,000-bed university hospital in Thailand. Before the data collection, every emergency physician was trained to ensure the validity and reliability of the GCS, FOUR, and GCS-P score ratings. The 30-minute interactive lecture was provided, followed by the post-learning test. Ten videos of stroke patients with different coma scores were used for the evaluation. The physician scoring less than 80% must take the re-training and the remediation exam. The Siriraj Institutional Review Board approved the study with protocol number 396/2562 (EC1), as demonstrated in Appendix 1.

From August 2019 to October 2020, adult patients diagnosed with acute stroke in the emergency room were enrolled in the study. World Health Organization definition, which is the abrupt onset of a focal neurological deficit secondary to a vascular event lasting more than 24 hours, was used for diagnosis and enrollment. If the patients were later diagnosed with other diseases or had ophthalmic diseases that might affect the pupillary response, for example, post-ophthalmic surgery, they would be excluded from the study.

Intervention

After the consent, the emergency physician, who isn't involved with the study, would rate and record the FOUR, GCS, and GCS-P coma scores. The scoring process must not interfere with the standard management and must be done before giving the definite treatment. The neurologist or neurosurgeon would decide the treatment modality according to the standard hospital guideline.

The primary objective of this study is to determine which coma score is the best prognostication tool to determine the in-hospital death of acute stroke patients. The in-hospital mortality data was gathered from the in-patient documentation by the researchers.

The secondary purpose is the predictive ability of the GCS-P, GCS, and FOUR scores to predict the 30 and 90-day mortality and neurological outcome. After the hospital discharge, at 30 and 90 days after the stroke onset, the investigator would call the patient or the relative to interview to identify the mortality and neurological status. The permanent disability is defined when the patient has the Modified Rankin Scale (MRS) of 4-6[12] and the Cerebral Performance Category (CPC) between 3-5[14, 15]. If the researcher couldn't be contacted for the telephone

follow-up, the data would be addressed missing. The script for the telephone interview for determining the outcome is modified from the structured interview for the Modified Rankin Scale (2002) by Lindsay Wilson of the University of Stirling, United Kingdom (supplemental material section). The validity test by the Modified Delphi method was done by 3 emergency physicians who have experience for more than 5 years to ensure an accurate relationship between the interview questions and scores.

From the previous study with the same faculty, the accuracy of the FOUR and GCS scores for predicting mortality in acute stroke patients were 100 and 92%, respectively[16]. There is no exact data about the GCS-P score, but from the Murray GD study[11], the researcher hypothesizes that the GCS-P has a higher accuracy than the GCS score. Therefore, the expected accuracy of the coma scores in the study is more than 92%. With the 95% confidence interval (95% CI) of 3, the calculated sample size is 315.

Spearman's rank-order correlation was calculated to determine the relationship between the coma score and outcome. The prognostic performance of each coma score was reported with the sensitivity, specificity, positive predictive value, and negative predictive value. Additionally, the mortality and permanent disability prognostication were defined by the area under the curve (AUC) after plotting the receiver operating characteristic (ROC) curve. All analyses were done by using the IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0 Armonk, NY: IBM Corp.

Results

From 332 participants, 17 patients were excluded. Nine patients were diagnosed with the transient ischemic attack, while eight patients received definite treatment before the physician could rate the coma score. There were 315 acute stroke patients in the study with a median age of 65 (IQR 56-75) years old, and the top common underlying diseases were hypertension, dyslipidemia, and diabetes, respectively (Table 1). The median time from the ED arrival to the coma score evaluation or "time to scoring" was 3 (IQR 0-5) minutes. Duration from the onset of stroke or the last seen normal to the ED arrival was about 4 hours (IQR 120-450 minutes).

The majority of the population was ischemic stroke (73.97%). The common locations of ischemia are left middle cerebral artery territory (12.45%), basal ganglion (7.72%), and right middle cerebral

Table 1 The characteristics of the total populations, the in-hospital death, and the survival.

	Total N=315, No (%)	In-hospital death N=33, No (%)	Survival N=282, No (%)	p-value
Age (years old); Median (IQR)	65 (56-75)	73 (64-82)	64 (55-73)	0.003
Male	174 (55.23)	17 (51.52)	157 (55.67)	0.651
Hypertension	230 (73.02)	26 (78.79)	204 (72.34)	0.431
Dyslipidemia	109 (34.60)	11 (33.33)	98 (34.75)	0.872
Diabetes	102 (32.38)	13 (39.39)	89 (31.56)	0.364
Coronary artery disease	28 (8.89)	4 (12.12)	24 (8.51)	0.492
Atrial fibrillation	35 (11.11)	5 (15.15)	30 (10.64)	0.437
Cerebrovascular accident	51 (16.19)	3 (9.09)	48 (17.02)	0.243
Time to scoring (minutes); Median (IQR)	3 (0-5)	5 (0-6.5)	3 (0-5)	0.705
Onset or last seen normal to ED arrival (minutes); Median (IQR)	240 (120-450)	300 (135-520)	240 (120-442)	0.992
Ischemic stroke	233 (73.97)	13 (39.39)	220 (78.00)	<0.001
Hemorrhagic stroke	82 (26.03)	20 (60.61)	62 (21.99)	<0.001

IQR, inter-quartile range; ED, emergency department.

artery territory (6.44%) respectively. Thrombolytic therapy was given in 18 patients (7.73%), and thrombectomy was performed in 26 patients. (11.16%)

Meanwhile, bleeding are commonly seen in the basal ganglion (35.37%), thalamus (21.95%), and brainstem (6.10%). The CT scan revealed 20.73% of intraventricular hemorrhage, 10.98% of obstructive hydrocephalus, and 8.54% of brain herniation. There were about 20% of the hemorrhagic patients (15 patients) had undergone surgery.

Thirty-three stroke patients (10.47%) died in the hospital. At 30 and 90 days after the stroke onset, the mortality increased to 40 and 43 patients. When compared to the patients who were able to be discharged home, the in-hospital death was significantly older (p 0.003).

Table 2 The median coma scores of total populations, in-hospital, 30-day, and 90-day mortality.

Coma score	Total, Median (IQR)	In-hospital mortality, Median (IQR)	30-day mortality, Median (IQR)	90-day mortality, Median (IQR)	p-value
GCS score	15 (12-15)	7 (5-10)	8 (5.25-10)	8 (6-10)	<0.001
GCS-P score	15 (12-15)	6 (3-10)	7.5 (4-10)	8 (4-10)	<0.001
FOUR score	16 (15-16)	9 (5-13)	11 (5-13)	11 (5-14)	<0.001

IQR, Inter-quartier range; GCS, Glasgow Coma Scale; GCS-P, Glasgow Coma Score-Pupil; FOUR, Full Outline of UnResponsiveness.

However, the CT scan outcomes of the hemorrhagic stroke, which were the location of disease and complications, were not different (p-value 0.75 and 0.11 respectively) between the in-hospital death and the survival to discharge patients. There was also no significant difference in the definite treatment modality between the survival and the death group.

The median (IQR) GCS, GCS-P, and FOUR coma scores in the study were 15 (12-15), 15 (12-15), and 16 (15-16) respectively. (Table 2) The patient who died in the hospital had a significantly lower coma score (p<0.001). When comparing the location and complication of disease (CT scan result) between the low and high levels of 3 coma scores, there were no significant differences. Only the FOUR score of 9 and lower had a significantly higher rate of obstructive hydrocephalus with a p-value of 0.017.

With the cut-off standard value, the FOUR scores showed the highest specificity for predicting in-hospital mortality, while the other scores had higher sensitivity. (Table 3) For the in-hospital mortality prognostication, the GCS-P score had the highest area under the curve (AUC), which was 0.932 (95% CI 12.68-13.42, p<0.001), while the GCS and FOUR scores had the AUC of 0.93 and 0.895 respectively. (Figure 1) The AUC for predicting the 30- and 90-day mortality showed similar results. The GCS-P score had the highest AUC of 0.913 and 0.891, respectively.

The number of lost to follow-up at 30 and 90 days was 21. The distribution of the MRS and CPC scores of the remaining population was scattered, as demonstrated in the supplemental material section. The 30 and 90-day neurological outcomes had a moderate relationship with the coma

Table 3 Sensitivity, Specificity, positive predictive value, and negative predictive value of Glasgow Coma Scale, Glasgow Coma Scale-Pupil, and Full Outline of UnResponsiveness score for in-hospital mortality prognostication.

Score	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
GCS <8	60.61 (42.14-77.09)	96.10 (93.13-98.04)	64.52 (48.91-77.54)	95.42 (93.17-96.96)
GCS-P <8	60.61 (42.14-77.09)	95.74 (92.68-97.78)	62.50 (47.32-75.57)	95.41 (93.15-96.95)
FOUR <9	51.52 (33.54-69.20)	99.29 (97.46-99.91)	89.47 (67.26-97.24)	94.59 (92.49-96.14)

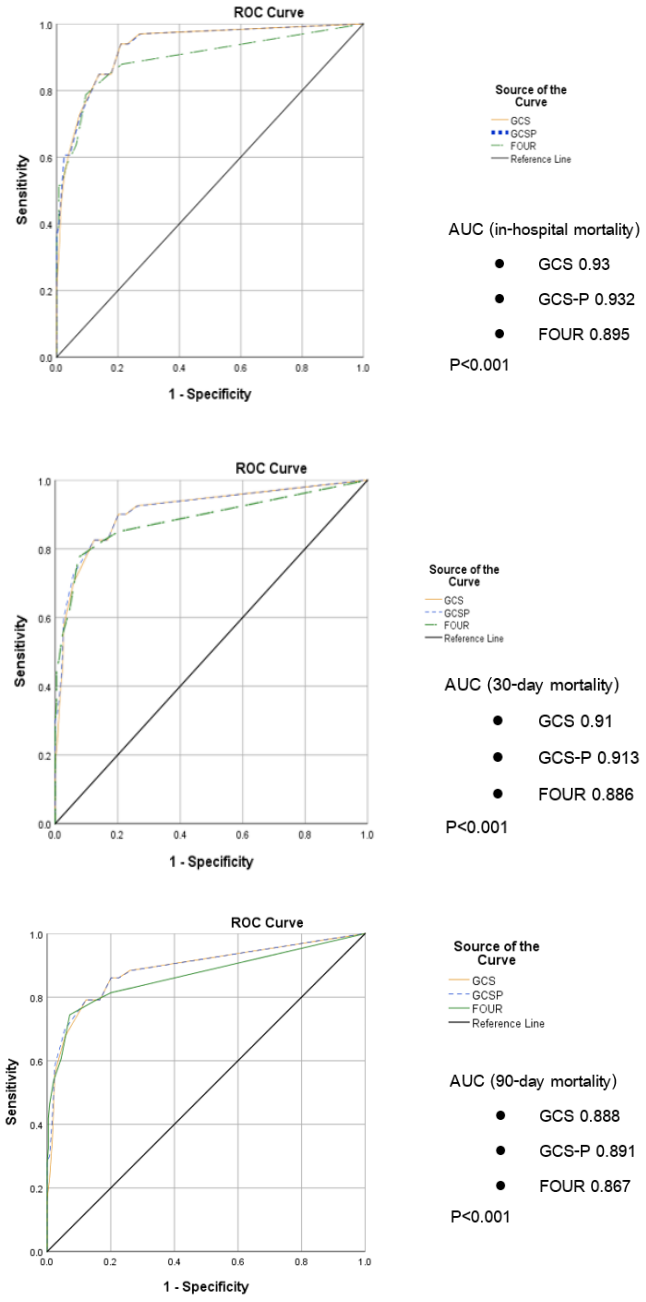
PPV, positive predictive value; NPV, negative predictive value; GCS, Glasgow Coma Scale; GCS-P, Glasgow Coma Scale-Pupil; FOUR, Full Outline of UnResponsiveness.

scores (Spearman's rank correlation coefficient (rs) -0.510 to -0.563, demonstrated in the supplemental material). For predicting the permanent disability at 30 and 90 days, the GCS-P score showed acceptable performance with the AUC of 0.717 and 0.746. (Table 4)

Table 4 Area under the curve of Glasgow Coma Scale, Glasgow Coma Scale-Pupil, and Full Outline of UnResponsiveness score for the prognostication of 30-day and 90-day permanent disability.

Coma score	30 days		90 days	
	AUC (95% CI)	p-value	AUC (95% CI)	p-value
GCS score	0.712 (0.652-0.773)	<0.001	0.741 (0.678-0.804)	<0.001
GCS-P score	0.717 (0.657-0.777)	<0.001	0.746 (0.684-0.809)	<0.001
FOUR score	0.673 (0.610-0.736)	<0.001	0.721 (0.656-0.786)	<0.001

CI, confidence interval; AUC, the area under the curve; GCS, Glasgow Coma Scale; GCS-P, Glasgow Coma Scale-Pupil; FOUR, Full Outline of UnResponsiveness.



ROC, receive operating characteristics curve; AUC, an area under the curve; GCS, Glasgow Coma Scale; GCS-P, Glasgow Coma Scale-Pupil; FOUR, Full Outline of UnResponsiveness.

Figure 1 Receive operating characteristics curve and area under the curve of Glasgow Coma Scale, Glasgow Coma Scale-Pupil, and Full Outline of UnResponsiveness score for the prognostication of in-hospital, 30-day, and 90-day mortality.

Discussion

The GCS, GCS-P, and FOUR scores have an excellent relationship with the mortality rate of stroke patients. Median coma scores of the survival are statistically significantly higher. If the stroke patient has GCS>8, GCS-P>8, and FOUR>9 at the ED arrival, the in-hospital mortality rate would be very low (negative predictive value of 95.42, 95.41, and 94.59, respectively). Among the coma scoring systems in the study, the GCS-P score has the greatest predictive ability for predicting the in-hospital, 30, and 90-day mortality rate. This result is similar to Mader MM's study[17], which reported that in aneurysmal subarachnoid hemorrhage patients, the GCS-P score is better than the GCS score for identifying the in-hospital mortality (AUC 0.813 (95% CI 0.760-0.865) vs AUC 0.803 (95% CI 0.751-0.855)).

To date, this is the first study that attempts to compare the GCS-P and FOUR scores. The GCS-P score showed a higher performance than the FOUR score. Although the FOUR score had the least prognostication in this study, the FOUR score has been proven to be an effective prognostic tool in variable neurological diseases [9]. The remarkable utilization of the FOUR score for prognostication is the patients with limitations in scoring the verbal response parameter, such as those with language center lesions or intubation.

The moderate relationship between the coma scoring systems and the neurological outcome could result from the better definite treatment modality for stroke patients in the present. If the patients with low consciousness received thrombolytic therapy, mechanical thrombectomy, or surgery, they could have good neurological outcomes in the long term, as described in the previous studies[18, 19]. Although the prediction for permanent disability is acceptable, the study's findings could be used to discuss the outcome with the patient and relatives. Stroke patients with lower coma scores, especially those who do not get definite treatment or arrive at the ED late, are more likely to have a permanent disability when compared to those with higher scores.

Limitation

The study was conducted in a single center focused on acute stroke patients in the emergency department. Therefore, the generalization of the result is limited. Moreover, the data at 30 and 90 days are from the telephone follow-up. The accuracy is lower than the in-person follow-up. And the cause of the mortality couldn't be identified.

Conclusion

The GCS-P score is better than the GCS and FOUR scores for predicting acute stroke patients' in-hospital, 30, and 90-day mortality. The application of the GCS-P score for the mortality prognostication is highly reliable, while the forecasting of the neurological outcome is acceptable.

Conflict of interest

Nothing to declare

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