OCT 30, 2023

OPEN ACCESS

DOI:
dx.doi.org/10.17504/protocols.io.bp2l6xr8klqe/v1

External link:
https://orcid.org/0000-0003-4563-9222

Protocol Citation: Sarawut Krongsut, Chatchon Kaewkrasaesin 2023. Performance comparison of stress hyperglycemia ratio for predicting fatal outcomes in patients with thrombolyzed acute ischemic stroke. **protocols.io** https://dx.doi.org/10.17504/protocols.io.bp2l6xr8klqe/v1

Performance comparison of stress hyperglycemia ratio for predicting fatal outcomes in patients with thrombolyzed acute ischemic stroke

Sarawut Krongsut[1], Chatchon Kaewkrasaesin[2]

[1]Division of Neurology, Department of Internal Medicine, Faculty of Medicine, Saraburi Hospital;
[2]Division of Endocrinology, Diabetes and Metabolism, Faculty of Medicine Taksin hospital, Medical Service Department, Bangkok Metropolitan Administration, Bangkok, Thailand

Sarawut Krongsut

 [redacted]

DISCLAIMER

The authors have no conflicts of interest directly relevant to the content of this article.

ABSTRACT

Stroke is a prevalent neurological condition and a primary global cause of death, resulting in
approximately 6 million annual fatalities [1].Stroke is the leading cause of death in Thailand, accounting for over 250,000 new cases and 50,000 annual fatalities [2]. Recombinant tissue plasminogen activator (rt-PA) is recommended as a safe and effective treatment [3]. Elevated blood sugar in 40-50%of acute stroke patients may exacerbate ischemic injury through heightened oxidative stress, endothelial dysfunction, and impaired fibrinolysis, resulting in larger infarctions, worse clinical outcomes, and increased mortality rates.[4-5]. Stress hyperglycemia (SH) refers to transient hyperglycemia in the context of illness accompanied by diabetes mellitus (DM) or non-DM. Recently, Roberts et al. [6] introduced the
stress hyperglycemia ratio (SHR) to evaluate SH. Hemoglobin A1c (HbA1c), a stable indicator, was used to assess glycemic management in DM patients over three months. SHR is calculated by dividing the admission glucose concentration by the estimated average glucose concentration derived from HbA1c [7]. Different studies employed the glucose/HbA1c ratio to define SHR, aiming for its practical use in

Protocol status: Working
We use this protocol and it's working

Created: Oct 29, 2023

Last Modified: Oct 30, 2023

PROTOCOL integer ID: 90072

Funders Acknowledgement:
Medical Education Center, Saraburi Hospital
Grant ID: MC012-2566, 2023

clinical settings [8-10].

Poor outcomes and symptomatic intracerebral hemorrhage (sICH) in acute ischemic stroke (AIS) patients treated with rt-PA were associated with hyperglycemia. According to the American Diabetes Association, patients were classified as DM, newly diagnosed DM, or experiencing transient hyperglycemia during hospitalization. The definition of SH remains unclear, but an abrupt increase in plasma glucose levels above the average blood glucose level serves as a reliable indicator [6,11]. Two types of biological markers for SH, SHR and glycemic gap (GG), have been developed to represent SH [11]. Recently, the SHR, a ratio of plasma glucose level to HbA1c, has emerged as a prognostic biomarker for poor outcomes in AIS patients receiving rt-PA treatment.

Although different SHR equations effectively predicted unfavorable outcomes or critical illness in AIS patients [12], the optimal threshold of SHR for assessing SH and predicting fatal outcomes (in-hospital mortality [IHM], malignant cerebral edema [MCE], and sICH) has not been definitively confirmed. Limited data currently exists regarding the comparative predictive value of various types of SHR, GG, absolute plasma glucose, and HbA1c in predicting fatal outcomes in AIS patients treated with rt-PA. Hence, this study aims to explore the predictive performance, optimal thresholds, and association between these variables in predicting fatal outcomes.

ATTACHMENTS

Lab Protocol Article Template Stress hyperglycemia ratio.pdf

MATERIALS

Study population

We conducted a retrospective observational cohort study by collecting data on 345 AIS patients who were treated with intravenous rt-PA at Saraburi Hospital, a stroke referral center of a provincial hospital in Thailand, between January 1, 2015 and July

31, 2022. Treatment involved administering intravenous rt-PA following the 2019 AIS management guideline
[13]. Inclusion criteria: (1) age ≥ 18 years; (2) AIS within 4.5 hours of the last known normal; (3) acute anterior circulation ischemic stroke; and (4) rt-PA treatment only. Exclusion criteria: (1) minor stroke; (2) pregnancy; (3) ICH or infarction > 1/3 the middle cerebral artery (MCA) territory; (4) referred patients with unattainable follow-up; (5) missing data: National Institutes of Health Stroke Scale (NIHSS), non-contrast computed tomography (NCCT) imaging, and laboratory results. Our study did not include AIS patients undergoing EVT due to the study period not being fully reimbursed by Thailand's public health coverage, resulting in difficulty accessing EVT treatment. Data comprising clinical and imaging information were retrieved from our electronic medical records, with diagnoses established using the International Classification of Diseases, 10th Revision codes (I63). The data were fully anonymized before we accessed them, and the ethics committee waived the requirement for informed consent. We don't collect patient-identifying information, including hospital numbers, admission numbers, identity card numbers, or birthdates. The study received ethical approval from the human research ethics committee of Saraburi Hospital on January 30, 2023 (Certificate No. EC004/2566). We accessed the data for research purposes on February 5, 2023.

Data collection

Demographic data, encompassing age, gender, initial clinical presentation, medical history, laboratory investigations, time from symptom onset to treatment, admission blood pressure, Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, and neuroimaging results, were collected. The extent of early ischemic changes was evaluated using the Alberta Stroke Program Early Computed Tomography Score (ASPECTS). Certified neurologists utilized NIHSS to evaluate stroke severity upon admission. Functional outcome was assessed at the time of hospital discharge using the modified
Rankin Scale (mRS), with stroke-certified registered nurses responsible for conducting the assessment. The plasma
glucose level on admission was measured before thrombolytic treatment. The history of DM was established by reviewing the patient's medical diagnosis and their antidiabetic drug usage record.

Collection and processing of blood samples and laboratory tests

- **Patient preparation**

We collected fasting plasma glucose (FPG) and HbA1c after an 8-14 hour fasting but not exceeding 16 hours, to avoid starvation, with a morning collection between 6:00 a.m. and 10:00 a.m. Random plasma glucose (RPG) was measured upon hospital arrival regardless of the time since the last meal.

Methods for collecting and submitting specimens

Blood collection tubes with anticoagulants like sodium fluoride/potassium oxalate were used to collect 2 cc of blood for plasma glucose testing, and tubes with ethylene diamine tetra acetate were used for HbA1c testing. The samples were analyzed within 45 minutes of collection, with results reported within 1 hour. Blood samples for plasma glucose were analyzed using an automated analyzer (Beckman Coulter DxC 700 AU) with the Beckman Coulter glucose reagent. Blood samples for HbA1c were analyzed using an automated analyzer (Mindray BS-820M) with the HbA1c reagent.

We collected data on various glucose metrics, including different types of SHR, GG, absolute blood glucose (RPG and FPG), and HbA1c. SHR and GG were calculated using the following equations: SHR1 [14], [FPG (mmol/L)]/[HbA1c (%)]; SHR2 [15], [admission RPG (mmol/L)]/[HbA1c (%)]; SHR3 [12], FPG (mmol/L)/[(1.59 × HbA1c)−2.59]; SHR4 [16], [admission RPG (mmol/L)]/[(1.59 × HbA1c)−2.59]; and GG [17], admission RPG − [(1.59 × HbA1c)−2.59]. In this study, both the treating physicians and nurses were not involved in measurement the SHR and GG values.

Outcomes assessment

The primary outcome of the study was IHM defined as patients with thrombolyzed AIS who died in the hospital. The secondary outcomes were MCE and sICH. The diagnostic criteria for malignant cerebral edema (MCE) were as follows: (i) acute complete MCA infarction with parenchymal hypodensity covering at least 50% of the MCA territory, along with sulcal effacement and lateral ventricle compression; (ii) excessive midline shift exceeding 5 mm and obliteration of basal cisterns; and (iii) neurological deterioration was characterized by an increase in NIHSS score (more than 2 points) and a decline in consciousness level (at least 1 point in item 1A of the NIHSS assessment) [18]. Based on the National Institute of Neurological Disorders and Stroke criteria, sICH was defined as any deterioration in NIHSS score or mortality within 7 days of thrombolysis initiation, along with the presence of any type of intracerebral hemorrhage on posttreatment imaging. [19]. NCCT scans were done within 4.5 hours of symptom onset and repeated at 24 hours post-thrombolysis. An emergency NCCT would be performed for deteriorating neurological deficits.

1 **Performance comparison of stress hyperglycemia ratio for predicting fatal outcomes in patients with thrombolyzed acute ischemic stroke**