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Clinical paper

The association between long-term glycaemic control, glycaemic gap and neurological outcome of in-hospital cardiac arrest in diabetics: A retrospective cohort study☆

Chih-Hung Wang[a,b,1], Jin-Lin Chang[c,1], Chien-Hua Huang[a,b], Wei-Tien Chang[a,b], Min-Shan Tsai[a,b], Ping-Hsun Yu[d], Yen-Wen Wu[e,f,g], Wen-Jone Chen[a,b,h,*,2,3], Wei-Kung Tseng[i,**,2,3]

[a] Department of Emergency Medicine, National Taiwan University Hospital, Taipei, Taiwan
[b] Department of Emergency Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan
[c] Emergency Department, Department of Emergency and Critical Medicine, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan
[d] Department of Emergency Medicine, Taipei Hospital, Ministry of Health and Welfare, New Taipei City, Taiwan
[e] Departments of Internal Medicine and Nuclear Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan
[f] Department of Nuclear Medicine and Cardiology Division of Cardiovascular Medical Center, Far Eastern Memorial Hospital, New Taipei City, Taiwan
[g] National Yang-Ming University School of Medicine, Taipei, Taiwan
[h] Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan
[i] Division of Cardiology, E-DA Hospital, Kaohsiung, Taiwan

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ABSTRACT

Aim: Resuscitation guidelines do not recommend a target blood glucose (BG) level specifically tailored for diabetics experiencing an in-hospital cardiac arrest (IHCA). The glycosylated haemoglobin (HbA1c) level may be associated with neurological prognosis and used to identify the optimal BG level for diabetic IHCA patients.
Methods: This study was a retrospective study in a single medical centre. Patients with an IHCA between 2006 and 2015 were screened. The estimated average glucose (eAG) level was converted from the HbA1c level measured within three months prior to the IHCA. The minimum glycaemic gap was calculated from the post-resuscitation minimum BG level minus the eAG level.
Results: A total of 141 patients were included in this study. The mean HbA1c was 7.2% (corresponding eAG: 160.2 mg/dL [8.9 mmol/L]). Multivariable logistic regression analysis indicated an eAG level of less than 196 mg/dL (10.9 mmol/L; corresponding HbA1c: 8.5%) was positively associated with a favourable neurological outcome at hospital discharge (odds ratio [OR]: 5.12, 95% confidence interval [CI]: 1.11–23.70; p-value = 0.04). An absolute minimum glycaemic gap of less than 70 mg/dL (3.9 mmol/L) was also positively associated with a favourable neurological outcome (OR: 5.41, 95% CI: 1.41–20.78; p-value = 0.01).
Conclusion: For diabetic patients, poor long-term glycaemic control correlated with worse neurological recovery following an IHCA. The HbA1c-derived average BG level could be used as a reference point for glycaemic management during the early stage of post-cardiac arrest syndrome. The glycaemic gap could be used to identify the optimal glycaemic range around the reference point.

Introduction

In the United States, approximately 209,000 patients experience an in-hospital cardiac arrest (IHCA) each year [1]. Only 20% of IHCA patients survive to hospital discharge. Among these survivors, as high as 28% suffer from significant neurological disability [2]. About 30% of

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* Corresponding author at: No. 7, Zhongshan S. Rd., Zhongzheng Dist., Taipei City 100, Taiwan.
** Corresponding author at: No. 1, Yi-Da Road, Jiau-Shu Village, Yan-Chau District, Kaohsiung City, 824, Taiwan.
E-mail addresses: wjchen1955@ntu.edu.tw (W.-J. Chen), tsengarthur@gmail.com (W.-K. Tseng).
[1] The first two authors contributed equally to this work.
[2] The two corresponding authors contributed equally to this work.
[3] The corresponding authors had full access to all data and final responsibility to submit the results for publication.

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Table 1
Baseline characteristics of study patients stratified by neurological outcome.

Variables	All patients (n = 141)	Patients with favourable neurological outcome at hospital discharge (n = 30)	Patients without favourable neurological outcome at hospital discharge (n = 111)	*p*-value
Age, y (SD[a])	68.5 (12.8)	65.8 (11.0)	69.3 (13.2)	0.10
Male, n (%)	88 (62.4)	20 (66.7)	68 (61.3)	0.67
Comorbidities, n (%)				
Heart failure, this admission	50 (35.5)	14 (46.7)	36 (32.4)	0.20
Heart failure, prior admission	43 (30.5)	7 (23.3)	36 (32.4)	0.38
Myocardial infarction, this admission	30 (21.3)	7 (23.3)	23 (20.7)	0.80
Myocardial infarction, prior admission	12 (8.5)	2 (6.7)	10 (9.0)	1
Arrhythmia	43 (30.5)	8 (26.7)	35 (31.5)	0.66
Hypotension	43 (30.5)	7 (23.3)	36 (32.4)	0.38
Respiratory insufficiency	92 (65.2)	18 (60.0)	74 (66.7)	0.52
Renal insufficiency	76 (53.9)	12 (40.0)	64 (57.7)	0.10
Hepatic insufficiency	21 (14.9)	2 (6.7)	19 (17.1)	0.25
Metabolic or electrolyte abnormality	30 (21.3)	4 (13.3)	26 (23.4)	0.32
Baseline evidence of motor, cognitive, or functional deficits	78 (55.3)	14 (46.7)	64 (57.7)	0.31
Acute stroke	11 (7.8)	2 (6.7)	9 (8.1)	1
Favourable neurological status 24 h before cardiac arrest[b]	83 (58.9)	21 (70.0)	62 (55.9)	0.21
Bacteraemia	9 (6.4)	1 (3.3)	8 (7.2)	0.68
Metastatic cancer or any blood borne malignancy	9 (6.4)	0 (0)	9 (8.1)	0.20
Charlson comorbidity index (SD)	3.4 (2.4)	2.4 (1.9)	3.7 (2.4)	0.003

[a] SD, standard deviation.
[b] A favourable neurological status was defined as a score of 1 or 2 on the Cerebral Performance Category scale.

IHCA patients have diabetes mellitus (DM) [2,3]. One study [3] has shown that diabetic patients have worse IHCA outcomes than non-diabetic patients. Thus, optimizing the post-resuscitation care of diabetic IHCA patients may have a significant impact on the overall IHCA prognosis.

Dysregulated glucose homeostasis following cardiopulmonary resuscitation (CPR) is common [4]. Elevated blood glucose (BG) levels after the return of spontaneous circulation (ROSC) were shown to correlate with worse outcomes following out-of-hospital cardiac arrest (OHCA) [5,6]. Beiser et al. [7] suggested that DM may modify the physiologic responses to hyperglycaemia following IHCA. The survival odds in diabetics are relatively insensitive to elevated BG levels with decreased survival only associated with extreme hyperglycaemia (240 mg/dL, 13.3 mmol/L) [7]. Nevertheless, the resuscitation guidelines [8,9] do not recommend a target BG level specifically tailored to diabetics. The European Resuscitation Council [8] suggests that following ROSC, the BG level should be maintained below 180 mg/dL (10 mmol/L). The American Heart Association [9] does not recommend any target BG level.

Glycosylated haemoglobin (HbA1c) may be used to estimate the optimal BG level for diabetic IHCA patients. Patients with elevated HbA1c tend to suffer from early neurological deterioration [10] or new ischemic lesions [11] after acute ischemic stroke (AIS). HbA1c can be expressed as the estimated average glucose (eAG) [12] level for the preceding three months. The glycaemic gap is calculated from a certain BG level minus the eAG level. A higher glycaemic gap at admission has been shown to predict worse outcomes for patients with acute myocardial infarction [13] or those admitted to an intensive care unit (ICU) [14].

In the current study, we analysed the association between the eAG and neurological outcome among diabetic patients following an IHCA. In addition, we attempted to identify the optimal BG level during the acute phase of post-cardiac arrest syndrome by using the glycaemic gap.

Materials and methods

Setting

This retrospective cohort study was performed in a tertiary medical centre, National Taiwan University Hospital (NTUH). NTUH has 2600 beds, including 220 beds in the ICUs. This study was conducted in accordance with the Declaration of Helsinki. Before data collection, the Research Ethics Committee of the NTUH approved this study and waived the requirement for informed consent (Reference number: 201805098RINC). According to hospital policy, a code team is activated when cardiac arrest events occur on the general wards. A code team consists of a senior resident, four junior residents, a respiratory therapist, a head nurse, and two ICU nurses. Each code team member is certified to provide advanced cardiac life support and capable of offering CPR according to current resuscitation guidelines. For cardiac arrest events in the ICUs, a code team is not mobilised since a sufficient number of experienced staff is always present in the ICUs. In this case, resuscitation is performed by the staff of the ICU where the cardiac arrest event occurred and by staff from neighbouring ICUs.

Participants

Patients who suffered an IHCA at the NTUH between 2006 and 2015 were screened. The included patients met the following criteria: (1) age 18 years or older, (2) documented absence of pulse with performance of chest compressions for at least 2 min, (3) no documentation of a do-not-resuscitate order, (4) presence of DM, and (5) a sustained ROSC (i.e., ROSC $\geq$ 20 min without resumption of chest compressions). If multiple cardiac arrest events occurred in a single patient, only the first event of the same hospitalisation was recorded. We excluded patients with missing HbA1c or post-ROSC BG values. We also excluded patients who had suffered a cardiac arrest related to major trauma.

Data collection and outcome measures

As shown in Tables 1 and 2, the following information was recorded for each patient: age, gender, comorbidities, variables derived from the Utstein template [15], critical interventions implemented at the time of cardiac arrest or after sustained ROSC, and the first/maximum/minimum BG levels measured during the initial 24 h after sustained ROSC. HbA1c values measured within three months prior to the IHCA were recorded. The eAG level for the preceding three months was calculated from the equation: eAG = 28.7 × HbA1c – 46.7 (mg/dL) [12].