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ORIGINAL ARTICLE – ADULT CARDIOLOGY

The effect of elevated glycated hemoglobin on in-hospital and short-term outcome of patients with acute anterior myocardial infarction

Efecto de la hemoglobina glicosilada elevada sobre el desenlace hospitalario y a corto plazo en pacientes con infarto agudo de miocardio anterior

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Abstract

Introduction: *Hyperglycemia has a negative impact on morbidity and mortality among patients with acute myocardial infarction (AMI).* **Objective:** *The objective of the study was to evaluate the impact of chronic hyperglycemia on in-hospital and short-term outcome in patients with acute anterior MI treated with streptokinase as thrombolytic therapy.* **Materials and methods:** *A total of 100 patients with acute anterior myocardial infarction received streptokinase as thrombolytic therapy were enrolled. They were classified according to the admission glycated hemoglobin (HbA1c) level into two groups: Chronic hyperglycemic group (HbA1c ≥ 6.5%) (36 patients) and non-chronic hyperglycemic group (HbA1c <6.5%) (64 patients). Laboratory investigation, conventional echocardiography, and speckle tracking were performed.* **Results:** *Global longitudinal strain (GLS) was significantly lower in patients with chronic hyperglycemia group compared to non-chronic hyperglycemia group (−13.52 ± 4.83 vs. −15.27 ± 1.87%, p = 0.009). In-hospital outcome: Heart failure and reinfarction were significantly increased in patients with chronic hyperglycemia (45.5 vs. 16.7% and 18.2 vs. 3.3%, respectively, p < 0.05). Six months outcome: Heart failure, left ventricular (LV) remodeling, arrhythmias, and bleeding rates were significantly increased in patients with chronic hyperglycemia (41.9 vs. 12.1%, 51.6 vs. 13.8%, 6.5 vs. 1.7%, and 6.5 vs. 1.7%, respectively, p < 0.05). GLS cutoff value ≥ −13.5 has the best diagnostic accuracy in predicting LV remodeling (sensitivity: 100%, specificity: 93%, positive predictive value: 94%, negative predictive value: 100%, accuracy: 97%, and area under curve: 0.99).* **Conclusion:** *Chronic hyperglycemia had higher incidence of heart failure and LV remodeling following acute MI. GLS can be used as a predictor of LV remodeling.*

Keywords: *Glycated hemoglobin. Acute myocardial infarction. Left ventricular remodeling.*

Resumen

Introducción: *La hiperglucemia tiene un impacto negativo sobre la morbimortalidad en pacientes con infarto agudo de miocardio.* **Objetivo:** *Evaluar el impacto de la hiperglucemia crónica sobre el desenlace hospitalario y a corto plazo en pacientes*

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con infarto agudo de miocardio (IAM) anterior, tratados con estreptoquinasa como terapia trombolítica. **Materiales y métodos:** *Se incluyeron un total de 100 pacientes con IAM anterior, quienes recibieron estreptoquinasa como terapia trombolítica. Se clasificaron en dos grupos de acuerdo con el nivel de hemoglobina glicosilada (HbA1c) al ingreso: el grupo con hiperglucemia crónica (HbA1c ≥ 6.5%) (36 pacientes) y el grupo sin hiperglucemia crónica (HbA1c <6.5%) (64 pacientes). Se practicaron estudios de laboratorio, y ecocardiografía convencional y con rastreo de marcas.* **Resultados:** *El strain longitudinal global (SLG) fue significativamente menor en pacientes del grupo con hiperglucemia crónica comparados con los del grupo sin hiperglucemia crónica (−13.52 ± 4.83 vs. −15.27 ± 1.87%, p = 0.009). Desenlace hospitalario: La falla cardíaca y el reinfarto aumentaron significativamente en los pacientes con hiperglucemia crónica (45.5 vs. 16.7% y 18.2 vs. 3.3%, respectivamente, p < 0.05). Desenlace a los seis meses: Las tasas de falla cardíaca, remodelación del ventrículo izquierdo (VI), arritmia, y sangrado aumentaron significativamente en pacientes con hiperglucemia crónica (41.9 vs. 12.1%, 51.6 vs. 13.8%, 6.5 vs. 1.7% y 6.5 vs. 1.7%, respectivamente, p < 0.05). El punto de corte de SLG ≥ −13.5 tiene la mejor precisión diagnóstica para predecir la remodelación del VI (sensibilidad: 100%, especificidad: 93%, VPP: 94%, VPN: 100%, precisión: 97% y área bajo la curva –AUC–: 0.99).* **Conclusión:** *La hiperglucemia crónica tuvo una mayor frecuencia de falla cardíaca y remodelación del VI luego de un infarto agudo de miocardio. El SLG se puede utilizar como predictor de la remodelación del VI.*

Palabras clave: *Hemoglobina glicosilada. Infarto agudo de miocardio. Remodelación ventricular izquierda.*

Introduction

Hyperglycemia was reported to deteriorate myocardial function in the setting of ischemia as it causes oxidative stress, stimulates apoptosis, and activates coagulation pathway[1].

In clinical practice, glycated hemoglobin (HbA1c) is used as a measure of chronic hyperglycemia[2]. However, it remains unclear how chronic hyperglycemia affects short-term outcomes in patients with acute myocardial infarction (AMI)[2].

Despite the advances in the management of AMI, ST-segment elevation myocardial infarction (STEMI) continues to be a major health problem worldwide and its fatality is in the first initial hours[3].

The aim of this study was to evaluate the impact of chronic hyperglycemia on in-hospital and short-term outcome in patients with the first acute anterior myocardial infarction (MI) treated with streptokinase as reperfusion therapy.

Materials and methods

It was a single-center, prospective, cross-sectional study that was conducted at the coronary care unit of Benha University Hospital, Egypt, during the period from December 2017 to September 2018. A total of 100 patients with the first acute anterior STEMI treated with streptokinase were enrolled in the study. They were classified according to the level of admission HbA1c into two groups: chronic hyperglycemic group (HbA1c ≥ 6.5%) and non-chronic hyperglycemic group (Hb1Ac < 6.5%). An informed consent was signed from all patients after its approval from the local ethics committee.

Patients with cardiogenic shock at presentation, contraindications to thrombolytic therapy, prior ischemic heart disease, rhythm other than sinus rhythm, and poor echogenicity were excluded from the study.

Laboratory investigation

Random blood sugar, HbA1c, cardiac enzymes (troponin and CKMB), and creatinine were done to all patients.

Echocardiography

All echocardiographic parameters were done during hospital admission by two experienced cardiologists blinded to patient clinical data. All examinations were done using the commercially available system (Vivid 7, GE Ultrasound, Horten, Norway). The left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and left ventricular ejection fraction (LVEF) were assessed using modified biplane Simpson's method[4]. After 6-month follow-up, the left ventricular (LV) volumes were reassessed and compared to baseline data to detect LV remodeling; defined by significant LV volume dilatation (> 20%) compared to baseline measurements[5]. Tissue Doppler imaging was used to assess systolic (S) wave and diastolic waves (é and a`)[6]. Speckle tracking echocardiography (STE) and three consecutive cardiac cycles with frame rate of 60-90 frames/s in the apical three, four, and two chamber views were used. The LV endocardial border was traced at end systole after identification of 3 points (basal septal, basal lateral, and apical), and the automatically created region of interest was manually

adjusted to the thickness of the myocardium. Segments were discarded if tracking was of persistent poor quality following readjustment of the region of interest. Subsequently, numeric and graphical bull's eye displays of deformation parameters were automatically generated for all LV segments to obtain global longitudinal strain (GLS). Aortic valve closure was defined in the apical long-axis view, and the interval between the R wave and this time point was then automatically measured to serve as a reference for identification of end systole[7].

Outcome

Patients were followed up in-hospital and for 6 months post-discharge, for the development of any major adverse cardiac events (MACEs) including; death, heart failure, reinfarction, arrhythmias, stroke, bleeding, and LV remodeling.

Statistical analysis

Data management was performed using Statistical Package for the Social Sciences (SPSS) program version 20 (SPSS, Chicago, IL, USA). Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as numbers and percentages. Comparison of continuous variables among groups was made using the Student's t-test. Associations between two categorical variables were tested using the Likelihood ratio χ^2 test, as appropriate. All tests of significance were two-tailed and $p < 0.05$ was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cutoff value for GLS with maximum sensitivity and specificity for prediction of LV remodeling.

Results

A total of 100 patients with anterior STEMI were included in the study. They were classified according to admission plasma HbA1c level into two groups, chronic hyperglycemic group (patients with HbA1c ≥ 6.5%) (36 patients) and non-chronic hyperglycemic group (patients with HbA1c < 6.5%) (64 patients). Baseline demographics and clinical characteristics of study groups are shown in table 1.

Table 1. Baseline demographics and clinical characteristics of study groups

Variables	Chronic hyperglycemia, (n = 36)	Non-chronic hyperglycemia, (n = 64)	p value
Age (mean ± SD)	57.86 ± 8.05	53.82 ± 6.41	0.007
Gender Male Female	 32 (88.9%) 4 (11.1%)	 40 (62.5%) 24 (37.5%)	 0.03
Hypertension	32 (88.9%)	36 (56.2%)	< 0.001
Diabetes	32 (88.9%)	2 (3.1%)	< 0.001
Dyslipidemia	30 (83.3%)	26 (40.6%)	< 0.001
Smoking	25 (69.4%)	8 (12.5%)	< 0.001
BMI (mean ± SD)	29.08 ± 2.43	29.43 ± 2.93	0.12
SBP (mmHg)	147.58 ± 14.3	118.68 ± 17.9	< 0.001
DBP (mmHg)	93.08 ± 10.21	75.82 ± 9.51	< 0.001
Heart rate	85.16 ± 6.94	89.12 ± 11.93	0.07
Killip class I II III	 23 (63.8%) 10 (27.7%) 3 (8%)	 42 (65.6%) 16 (25%) 6 (9%)	 0.17 0.16 0.11

All values are in mean ± SD, number, and percent %. BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure.

Laboratory investigation

Patients with chronic hyperglycemia had significantly higher levels of serum creatinine level (1.38 ± 0.37 vs. 0.83 ± 0.19 mg/dl, $p < 0.001$), random blood sugar (298.5 ± 82.5 vs. 138.5 ± 65.5 mg/dl, $p < 0.001$), and HbA1c (10.61 ± 1.89 vs. 5.58 ± 0.24%, $p < 0.001$). There was no significant difference between both groups as regard CKMB (157.36 ± 53.15 vs. 150.48 ± 33.69 u/l, $p = 0.21$) and troponin levels (6.19 ± 1.46 vs. 6.10 ± 1.62 ng/ml, $p = 0.91$).

Management of hyperglycemia

During hospital stay, all patients received rapid acting insulin subcutaneous injection. After discharge, patients with HbA1c ≤ 7.5% continue on oral hypoglycemic drugs and patients with HbA1c > 7.5% continue on long-acting insulin.

Echocardiographic parameters

There was no significant statistical difference between the two groups regarding baseline LVEDV (105.69 ± 9.16 vs. 99.92 ± 9.35 ml, $p = 0.09$), LVESV (56.31 ± 7.83 vs. 53.67 ± 6.59 ml, $p = 0.07$), and LVEF

Table 2. Baseline and 6 months follow-up echocardiographic parameters of study groups

Variables		Chronic hyperglycemia (n = 36)	Non-chronic hyperglycemia (n = 64)	p-value
EDV (ml) (baseline)	Mean ± SD	105.69 ± 9.16	99.92 ± 9.35	0.09
EDV (ml) (follow-up)	Mean ± SD	119.63 ± 14.24	105.14 ± 9.19	0.02
ESV (ml) (baseline)	Mean ± SD	56.31 ± 7.83	53.67 ± 6.59	0.07
ESV (ml) (follow-up)	Mean ± SD	68.91 ± 13.59	56.42 ± 6.95	0.003
EF (%) (baseline)	Mean ± SD	43.47 ± 3.14	46.93 ± 4.62	0.08
EF (%) (follow-up)	Mean ± SD	38.16 ± 4.94	47.18 ± 4.28	< 0.001
E wave (cm/s)	Mean ± SD	67.96 ± 21.45	43.20 ± 6.83	< 0.001
A wave (cm/s)	Mean ± SD	65.99 ± 29.44	95.15 ± 14.82	< 0.001
E/A ratio	Mean ± SD	1.31 ± 0.72	0.52 ± 0.21	< 0.001
WMSI	Mean ± SD	1.92 ± 0.56	1.29 ± 0.42	0.03
é wave (cm/s)	Mean ± SD	5.85 ± 0.57	6.45 ± 0.75	< 0.001
a` wave (cm/s)	Mean ± SD	3.25 ± 0.57	3.85 ± 0.57	< 0.001
E/é ratio	Mean ± SD	11.66 ± 4.22	6.76 ± 1.61	< 0.001
S wave (cm/s)	Mean ± SD	7.29 ± 0.6	8.4 ± 0.91	< 0.001
GLS (%)	Mean ± SD	–13.52 ± 4.83	–15.27 ± 1.87	0.009

EDV: end-diastolic volume, ESV: end-systolic volume, EF: ejection fraction, WMSI: wall motion score index, GLS: global longitudinal strain.

(43.47 ± 3.14 vs. 46.93 ± 4.62%, p = 0.08). GLS was significantly lower in patients with the chronic hyperglycemic group compared to the non-chronic hyperglycemic group (–13.52 ± 4.83 vs. –15.27 ± 1.87%, p = 0.009).

After 6 months, EDV and ESV were significantly increased in patients with chronic hyperglycemia (119.63 ± 14.24 vs. 105.69 ± 9.16 ml and 68.91 ± 13.59 vs. 56.31 ± 7.83 ml, p = 0.04 and 0.003, respectively). EF was significantly decreased in patients with chronic hyperglycemia (38.16 ± 4.94 vs. 43.47 ± 3.14%, p = 0.004). All echocardiographic parameters illustrated in table 2.

In-hospital outcome

Heart failure and reinfarction were significantly higher in patients with chronic hyperglycemia (15 patients "45.5%" vs. 10 patients "16.7%" and six patients "18.2%" vs. two patients "3.3%," respectively, p < 0.05). There was no statistical difference regarding arrhythmia, bleeding, and mortality (Table 3).

Table 3. In-hospital outcome of study groups

Variables	Chronic hyperglycemia (n = 36)	Non-chronic hyperglycemia (n = 64)	p-value
Mortality	3 (8.3%)	4 (6.3%)	0.14
Heart failure	15 (45.5%)	10 (16.7%)	0.005
Reinfarction	6 (18.2%)	2 (3.3%)	0.003
Arrhythmias	1 (3%)	2 (3.3%)	0.73
Stroke	0 (0%)	0 (0%)	-
Bleeding	1 (3%)	0 (0%)	0.07

Six months outcome

Patients with chronic hyperglycemia had higher incidence of complications. Heart failure, LV remodeling, arrhythmias, and bleeding rates were significantly increased in patients with chronic hyperglycemia (13 patients "41.9%" vs. seven patients "12.1%", 16 patients "51.6%" vs. eight patients "13.8%," two patients "6.5%" vs. one patient "1.7%," and two patients "6.5%" vs. one patient "1.7%," respectively, p < 0.05) (Table 4).

ROC curve was used to assess the overall accuracy of GLS in predicting LV remodeling. Optimal cutoff value of GLS that predicts LV remodeling was ≥–13.5 – sensitivity: 100%, specificity: 93%, positive

Table 4. Six months outcome of studied groups

Variables	Chronic hyperglycemia (n = 36)	Non-chronic hyperglycemia (n = 64)	p-value
Mortality	2 (6.1%)	2 (3.3%)	0.09
Heart failure	13 (41.9%)	7 (12.1%)	0.006
Reinfarction	2 (6.5%)	3 (5.2%)	0.26
Arrhythmias	2 (6.5%)	1 (1.7%)	0.02
Stroke	1 (3.2%)	0 (0%)	0.08
Bleeding	2 (6.5%0	1 (1.7%)	0.02
LV remodeling	16 (51.6%)	8 (13.8%)	0.005

predictive value: 94%, negative predictive value: 100%, accuracy: 97%, and area under curve: 0.99.

Discussion

Hyperglycemia is associated with increased morbidity and mortality in patients with AMI. In the thrombolysis era, it has been reported that diabetes and chronic hyperglycemia as assessed by HbA1c level are prognostic factors for in-hospital mortality in patients with AMI[8].

The purpose of the study was to evaluate the impact of chronic hyperglycemia on in-hospital and short-term outcome in patients with the first acute anterior MI treated with streptokinase as thrombolytic therapy.

The present study showed that hypertension, diabetes mellitus, smoking, and dyslipidemia were significantly more prevalent in the chronic hyperglycemic group.

These results are discordant with those reported by Fujino et al.[9] who reported that there was no significant difference between patients with chronic hyperglycemia and patients without as regard hypertension and history of smoking (p = 0.065 and 0.736, respectively), while there was a significant difference between both patient's groups as regard dyslipidemia (p = 0.031). This discrepancy might be attributed to larger sample volume included in their study.

The present study showed that serum creatinine was higher in patients with chronic hyperglycemia. This could be explained by the fact that diabetes mellitus is recognized as a leading cause of chronic kidney disease and end-stage renal failure.

In the present study, there was no significant difference regarding in-hospital mortality between the two groups (p = 0.14). Furthermore, Fujino et al.[9] found no significant difference between chronic hyperglycemia and non-chronic hyperglycemia patients regarding in-hospital mortality (p = 0.79). Similarly, Chan et al.[10] reported that elevated HbA1c levels were not associated with short-term cardiovascular outcome (all-cause mortality, cardiovascular mortality, rehospitalization for angina, and hospitalization for heart failure).

On the other hand, Timmer et al.[11] observed that increasing levels of HbA1c were associated with increased mortality rates over an average 3.3 years of follow-up in 4176 consecutive STEMI patients submitted to PCI. This finding was partially related to the fact that increasing HbA1c levels were associated with adverse baseline characteristics such as a high cardiovascular risk profile.

After 6 months, there was no significant difference in mortality between both groups (p = 0.09). This was in agreement with Zaghla et al.[12] who reported that HbA1c level was not found to be correlated with 6 months mortality.

Heart failure and LV remodeling were significantly increased in patients with chronic hyperglycemia. LV remodeling occurred in 51.6% versus 13.8% in the non-chronic hyperglycemia group, which was statistically significant. In the present study, patients with chronic hyperglycemia had lower level of GLS which can be used as a predictor of adverse myocardial changes, especially LV remodeling.

These findings consistent with the results by Mele et al.[13] who found that patients with LV remodeling following AMI had lower GLS (–11.2 ± 2.5 vs. –14.8 ± 3.2, p = 0.003).

Conclusion

Chronic hyperglycemia patients had higher incidence of heart failure and LV remodeling following AMI. Speckle tracking can be used as a predictor of LV remodeling in this group of patients.

Study limitation

It was a single center study with relatively small number of patients and limited follow up period. Our study was applied on the first acute anterior MI patients only, excluding those with other types of acute coronary syndrome and previous MI. The reperfusion strategy was fibrinolytic therapy (streptokinase) and percutaneous coronary intervention (PCI) was not included.

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Conflicts of interest

The authors declare have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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