Impact of stress hyperglycemia on myocardial salvage in patients with ST-Elevation myocardial infarction: Cardiac magnetic resonance study

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ABSTRACT

Cardiovascular complications in ST-segment–elevation myocardial infarction survivors remain substantial despite advances in the management of STEMI. We aimed to determine effect of AH on the area at risk (AAR), final infarct size (FIS), and salvage index (SI) in STEMI patients using cardiac magnetic resonance (CMR). 43 successfully reperfused STEMI patients were recruited. CMR was utilized to estimate AAR and FIS. SI was calculated: SI = AAR- FIS/AAR. AH showed significant positive correlations to FIS (r-value = 0.538, P < 0.001), and AAR (r-value = 0.435, P = 0.002), and a negative correlation with SI (r-value = −0.378, P = 0.006).

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1. Introduction

Accounting for more than fifteen million deaths in 2016, cardiovascular diseases are the leading causes of death worldwide.1 In the last decade, the mortality rates after ST-elevation myocardial infarction (STEMI) showed an obvious decline but, in low and middle-income countries, it is still relatively high.1 Admission hyperglycemia (AH) has been determined to inversely affect short and long-term prognosis in patients with STEMI regardless of their diabetic state.2 That can be partially explained by larger final infarct size (FIS) in AH patients compared with euglycemic patients.3 Single-photon emission computed tomography (SPECT) is the traditional imaging tool utilized to measure FIS and area at risk (AAR) but, it has a limited spatial resolution and, carry the risk of radiation.4 Cardiac magnetic resonance (CMR) is a relatively new cardiac imaging modality with many advantages, it can detect changes in cardiac contractile function and membrane integrity. Furthermore, CMR has a high spatial and temporal resolution which facilitates accurate assessment of cardiovascular structures. By the addition of late gadolinium enhancement (LGE) with CMR, transmural extension and scar tissues can be estimated.5 A few data about the sequelae of AH on AAR and salvage index (SI) after acute STEMI patients are available.

2. Methods

Forty-three patients (21 with stress hyperglycemia and 22 without) were selected from the Critical care Unit, Internal Medicine Department from April 2017, and May 2019. They presented with first STEMI and underwent successful reperfusion by primary percutaneous coronary intervention (PCI). Patients ≥85 years old, with life-limiting non-cardiac disease, prior STEMI, left bundle branch block (LBBB), with any of the standard contraindications to magnetic resonance imaging (MRI), an estimated glomerular filtration rate < 30 mL/min/1.73 m2, who were hemodynamically unstable, or who are clinically unfit to be transferred to CMR laboratory were excluded. Acute STEMI is defined according to the European Society of Cardiology/ACCF/AHA.6

AH was defined as the presence of random plasma glucose >140 mg/dL in non-diabetic patients within 2 h of admission.7 In diabetic patients, 250 mg/dL is considered the cut-off level for AH.8 Demographic data and clinical history were recorded with electrocardiogram (ECG) data. Venous blood samples were taken to perform biochemical investigations.

CMR was performed 4–6 days after acute STEMI with a 1.5-Tesla scanner (Philips, Achieva). Short-axis slices (thickness of 5 mm with a slices gap of 10 mm) were defined from the base to the apex of the...
heart. Imaging of the heart at the end-systolic and end-diastolic times to estimate left ventricular end-systolic volume (LVESV) and left ventricular end-diastolic volume (LVEDV) respectively. A dark-blood T2-weighted short-tau-inversion-recovery turbo-spin echo sequence (STIR) was applied to determine AAR (with edema) and a segmented inversion-recovery steady-state free precession sequence (PSIR) was used for late enhancement imaging 10 min after intravenous injection of 0.15 mmol/kg of gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA) (Magnevist; Bayer Schering, Berlin, Germany). CMR studies were analyzed then offline (Philips Medical Systems, Nederland B.V.). Also, the classic wall motion score index (WMSI), the new segmental 65-40-15 EF score, and the EF calculated from WMSI were all calculated.10

Left ventricular endo- and epicardial borders had been delineated, then reference normal area was drawn. AAR was defined as the percentage of LV volume delineated by the hyper-intense zone on T2-STIR images with signal intensity was >2 standard deviations above the mean signal obtained in the non-infarcted myocardium and was expressed as a percentage of normal myocardium. FIS was above the mean signal obtained in the non-infarcted myocardium and echocardiographic data are illustrated in (Table 1).

### 4. Discussion

The main finding of our study is that both CMR detected AAR and FIS in acute STEMI patients were positively correlated with admission plasma glucose while SI negatively correlated with it.

Low-income nations have special demographic and social characteristics which in turn, increase the possibility of the stress-induced conditions and its health-associated problems. Previous studies confirmed that elevated admission glucose level is a strong predictor of short-term adverse outcomes in patients with AMI but, no previous studies in our country regarding the impact of AH on AAR, FIS, or SI which is the major concept of our research.11

An Indian study had addressed the association of AHG and increased myocardial damage evidenced by cardiac biomarkers and echocardiographic derived data but without using CMR.12 In that study increased admission plasma glucose was associated with lower LVEF, higher WMSI, higher CKMB in STEMI patients, all in line with our results except for LVEF which had an insignificant association with APG in our studied population.12

APG was found to positively correlate with AAR in very few studies.13 This could be explained by the augmented inflammatory response and expression of pro-inflammatory cytokines in phase of acute inflammation in acute AH group, had significantly larger FIS and smaller SI than the euglycemic group (Table 2). There was a positive correlation between glucose level at admission and FIS (r value = 0.538) and AAR (r value = 0.435) and negative correlation with SI (r value = −0.378).

Multivariate linear regression analysis showed that male sex, smoking, APG, anterior infarction, and classic WMSI estimated by CMR might be independent predictors of SI (Table 3).

### 3. Results

The data showed that male is the predominate gender. Clinical and echocardiographic data are illustrated in (Table 1).

### Table 1

| Patients clinical and echocardiographic characteristics | Euglycemic n = 22 | Admission hyperglycemia n = 21 | p-value |
|--------------------------------------------------------|--------------------|-------------------------------|---------|
| Age/year (mean ± SD)                                    | 56.49 ± 11.4       | 58.95 ± 11.3                  | 0.487   |
| Sex (males%)                                            | 19 (86.4%)         | 17 (81%)                      | 0.473   |
| Hypertension n (%)                                      | 12 (54.5%)         | 9 (42.9%)                     | 0.443   |
| Diabetes n (%)                                          | 3 (13.6%)          | 6 (28.6%)                     | 0.538   |
| Smoking n (%)                                           | 15 (68.2%)         | 11 (52.4%)                    | 0.289   |
| Chest Pain Duration/hours (mean ± SD)                  | 6.36 ± 3.2         | 9.81 ± 5.2                    | 0.019   |
| BMI (kg/m2)                                             | 26.64 ± 4.8        | 25.52 ± 4.7                   | 0.448   |
| Heart Rate (beat/min)                                   | 84.09 ± 14.9       | 92.05 ± 11.2                  | 0.050   |
| SBP (mm/Hg)                                             | 118.46 ± 21.7      | 122.38 ± 23.2                 | 0.587   |
| DBP (mm/Hg)                                             | 75.91 ± 11.2       | 77.14 ± 15.1                  | 0.767   |
| Killip Score                                            |                     |                               |         |
| Class I                                                | 19 (86.4%)         | 18 (85.7%)                    | 0.951   |
| Class II                                               | 3 (13.6%)          | 3 (14.3%)                     |         |
| Anterior n (%)                                          | 7 (31.8%)          | 13 (61.9%)                    | 0.049   |
| Admission Sum of STE/mm (mean ± SD)                    | 11.09 ± 9.8        | 18.14 ± 7.9                   | 0.002   |
| Admission Max. STE/mm (mean ± SD)                      | 3.59 ± 2.3         | 5.10 ± 1.8                    | 0.003   |
| Resolution of STE n (%)                                 |                     |                               |         |
| ≤50–70                                                 | 10 (45.5%)         | 8 (38.1%)                     | 0.625   |
| >70                                                    | 12 (54.5%)         | 13 (61.9%)                    |         |
| LDL (mg/dl) (mean ± SD)                                 | 108.41 ± 35.5      | 106.38 ± 28.6                 | 0.874   |
| S. Creatinine (mg/dl) (mean ± SD)                       | 0.95 ± 0.2         | 1.01 ± 0.2                    | 0.259   |
| Initial CK-MB (ng/ml) (mean ± SD)                      | 57.14 ± 36.9       | 64.76 ± 42.5                  | 0.381   |
| Peak CK-MB (ng/ml) (mean ± SD)                          | 245.23 ± 184.3     | 306.38 ± 174.2                | 0.162   |
| HBA1c                                                  | 5.11 ± 0.9         | 5.59 ± 0.9                    | 0.087   |
| Classic WMSI (mean ± SD)                                | 1.38 ± 0.3         | 1.52 ± 0.2                    | 0.042   |
| LVEF (ml) (mean ± SD)                                   | 41.71 ± 13.7       | 40.96 ± 12.7                  | 0.356   |
| LVEDV (ml) (mean ± SD)                                  | 81.95 ± 18.5       | 75.60 ± 15.9                  | 0.789   |
| EF % (mean ± SD)                                        | 54.05 ± 11.5       | 50.81 ± 12.0                  | 0.462   |

BMI, body mass index; CK, creatinine kinase; DBP, diastolic blood pressure; EF, ejection fraction; HBA1c, glycated hemoglobin; LDL, low density lipoprotein; LVEDV, left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; Max of STE, maximum ST-segment elevation; WMSI, wall motion score index.

p-value ≤0.05 is significant.

a Independent t-test was used to compare the mean difference between groups.
b Chi-square test was used to compare the proportion differences.
c Mann-Whitney U test was used to compare the median difference between groups.
response during STEMI induced by hyperglycemia which in turn increases the microvascular permeability and tissue edema.\(^1\)

Ekmekci et al was the first to study SI in STEMI patients and have demonstrated that admission hyperglycemia independently predicted the extent of SI in non-diabetic patients.\(^2\) On the contrary, Lanborg et al found that admission hyperglycemia was associated with larger AAR and AAR without affecting SI.\(^3\) In ours, admission hyperglycemia inversely affected the SI. The rapid rise in plasma glucose levels acutely exaggerates inflammation by increasing the levels of circulating cytokines, which increase intracellular Ca \(^2\) overload and subsequent progression into irreversible cell death which in turn increases FIS and reduces salvageable myocardium.\(^4\)

To determine the independent predictors of SI, the current study showed that smoking and male gender were independent predictors of impaired SI. Male predominance in our study population and high smoking percent can explain these results. In agreement with a previous study, WMSI was an independent predictor of salvageable myocardium.\(^5\)

In another study, the anterior location was an independent predictor of myocardial salvage,\(^6\) agreeing with our results, this is mostly explained by larger AAR in anterior infarctions.

APG was the strong independent predictor of SI detected in our study in concordance with a previous study which addressed the benefits of glycemic control on admission.\(^7\)

The majority of the mentioned studies entailed AHG in non-diabetics only, and if diabetics were included, they utilized lower cut-off values for diagnosis of AHG which thus may include many falsely diagnosed candidates.

The current study is limited by the absence of follow-up data which could better determine the actual scar size. Moreover, interpretation should be applied to low- and moderate-risk STEMI patients as high-risk STEMI patients were excluded.

Key message

Admission hyperglycemia is an independent predictor of CMR assessed AAR, FIS, and SI in successfully reperfused STEMI. These results favor the importance of strict glucose control at the acute phase of STEMI.

Declaration of competing interest

All authors have none to declare.

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