International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Hyperglycemia, Diabetes Mellitus and the Outcomes of STEMI Patients

Arkel Duka[1], Edmond Zaimi[2], Endri Hasimi[3], Artan Kristo[4], Joana Seiti[5], Elizana Petrela[6], Idriz Balla[7]

[1, 3, 4, 5, 7]Cardiac Intensive Care Unit, UHC "Mother Teresa" Tirana, Albania

[2]Emergency Department, UHC "Mother Teresa" Tirana, Albania

[6]Department of Statistics, UHC "Mother Teresa" Tirana, Albania

Abstract: ***Cardiovascular disease is the leading cause of death worldwide. The most important cardiac emergency is ST-Segment Elevation Myocardial Infarction due to its high mortality rates, and in which early reperfusion, by Primary PCI or thrombolysis, is critical for patients' outcomes. Patients with Diabetes Mellitus, one of the independent risk factors for cardiovascular disease, present specific characteristics compared to nondiabetic patients in relation to mortality and morbidity. In this trial we enrolled all patients presenting with STEMI in our Coronary Care Unit within six hours from the beginning of chest pain, dividing them into diabetic and non-diabetic patients and in subgroups depending on their admission glycemic level. We then studied their morbidity and mortality outcomes depending on the treatment strategy, i.e. conservative vs. Primary PCI vs. thrombolysis and depending on their admission glycemic level. We found that there is an important benefit from revascularization in decreasing in-hospital mortality in patients with STEMI, but such benefit is lower in diabetic patients compared to non-diabetics. At the same time, this trial showed that revascularization is associated with a lower reduction in mortality in glycemic levels > 180mg/dL, especially in non-diabetic patients.***

Keywords: admission glycemia, Diabetes Mellitus, revascularization, heart failure, in-hospital mortality

1. Introduction

Cardiovascular disease is the leading cause of death worldwide. The most important cardiac emergency is ST-Segment Elevation Myocardial Infarction due to its high mortality rates. Early provision of therapy, particularly emergency reperfusion therapy, is critical to patient benefit. The routine management of STEMI in modern cardiology is emergency reperfusion therapy through Primary PCI or thrombolysis, which result in both lower mortality and complication rates. One of the most important independent risk factor for Ischemic Heart Disease is Diabetes Mellitus (DM). Diabetic patients present specific characteristics compared to non-diabetic patients in relation to mortality and morbidity, due to their structural and metabolic alterations in the cardiovascular system related to insulin resistance (IR) and hyperglycemia. IR and hyperglycemia cause endothelial dysfunction, oxidative stress and vascular inflammation, pro-coagulant and pro-thrombotic states, and eventually diabetic cardiomyopathy. In the acute phase of STEMI, there is an increase in catecholamines in blood and in the ischemic myocardium. Insulin levels remain low, whereas cortisol, glucagon and free fatty acids levels increase. Increases in glycemia at admission have been associated with a worse outcome in STEMI patients, independent of the presence of Diabetes Mellitus.

2. Literature Survey

There are some trials which have studied the association between hyperglycemia and mortality in STEMI in diabetic patients compared to non-diabetic patients, but there is limited data on the impact of emergency reperfusion in diabetic patients compared to non-diabetics, which is what this trial studied, together with the impact of increasing admission glycemic levels in the mortality of STEMI patients according to treatment and presence of DM.

3. Methods

3.1 Patients

We enrolled in this trial all the patients hospitalized in the Cardiac Intensive Care Unit of UHC "Mother Teresa" Tirana from February 2012 to February 2016 who presented within six hours from the beginning of chest pain. We collected patients' baseline characteristics such as gender, age, ethnicity, smoking, familial history, hypertension, DM and admission glycemia, White Blood Cells and Myocardial Infarction Type **(Table 1)**. Glycemia levels at admission were categorized in three groups: >180 mg/dL, 125-180 mg/dL and <125 mg/dL. Patients underwent emergency reperfusion with Primary PCI or thrombolysis, or were managed conservatively **(Table 2)**. We then studied in-hospital outcomes, including heart failure and mortality **(Table 3)**.

Table 1: Baseline characteristics

Variable	*Diabetic Patients (n=299)*	*Non-Diabetic Patients (n=725)*	*Total (n=1024)*	*p value*
Gender (Males)	210 (70.20%)	575 (79.30%)	785 (76.70%)	0.002
Age	66.2±9.7	64.1±12.6	63.64±11.61	0.01
Ethnicity (Caucasian)	284 (94.50%)	682 (94.00%)	953 (94.30%)	0.217

Smoking	73 (24.40%)	310 (42.80%)	383 (37.40%)	<0.001
Familial History	28 (9.40%)	94 (13.00%)	122 (11.90%)	0.106
Hypertension	201 (67.20%)	348 (48.0%)	549 (53.70%)	<0.001
Glycemia at admission	283.5±120.1	144.6±48.1	184.35±94.13	<0.001
White Blood Cells	11677±4034	11051±3412	11037±3573	0.012
Inferior STEMI	114 (38.20%)	318 (43.80%)	432 (42.20%)	0.535
Inferior and RV STEMI	24 (8.00%)	46 (6.30%)	70 (6.80%)	0.135
Anterior STEMI	149 (49.80%)	338 (46.60%)	487 (47.60%)	0.121
Postero-Lateral STEMI	11 (3.70%)	26 (3.60%)	37 (3.60%)	0.347

Table 2: Types of Treatment

Variable	*Diabetic Patients (n=299)*	*Non-Diabetic Patients (n=725)*	*Total (n=1024)*	*p value*
Conservative	144 (48.20%)	314 (43.30%)	458 (44.70%)	0.355
Thrombolysis	27 (9.00%)	68 (9.40%)	95 (9.30%)	
Primary PCI	128 (42.80%)	343 (47.30%)	471 (46.00%)	

Table 3: In-hospital outcomes

Variable	*Diabetic Patients (n=299)*	*Non-Diabetic Patients (n=725)*	*Total (n=1024)*	*p value*
Heart Failure	114 (38.10%)	148 (20.40%)	262 (25.60%)	<0.001
Death	45 (19.60%)	60 (8.20%)	105 (10.30%)	0.001

3.2 Definitions

ST-Segment Elevation Myocardial Infarction (STEMI) was defined according to the following criteria: 1) typical anginal chest pain > 20 min; 2) ST elevation at the J point in at least 2 contiguous leads of ≥2 mm (0.2 mV) in men or ≥1.5 mm (0.15 mV) in women in leads V2–V3 and/or of ≥1 mm (0.1 mV) in other contiguous chest leads or the limb leads; 3) detection of a rise and/or fall of cardiac biomarkers values.

Diabetes Mellitus diagnosis was based on anamnestic data from the patient or family members in cases of known DM, and ADA/WHO diagnostic critera. Treatment of DM with high glycemic levels depended on patients conditions. Complicated patients with acute heart failure, cardiogenic shock or extremely high glycemia were treated with infusion insulin, and uncomplicated patients were treated with subcutaneous insulin injections several times a day aiming at glycemic levels < 200 mg/dL.

3.3 Statistical analysis

- Continuous data was presented as the mean value and standard deviation
- Discrete data was presented in absolute value and percentage
- Differences between the two groups for continuous quantitative variables were performed by t test
- Differences between groups for discrete variables were performed by Chi-Square test
- Binary logistic regression and Kendall's Tau correlation coefficient were used to analyze the correlation between variables. Odds ratio and confidence interval (CI95%) was calculated for each variable in the regression equation.
- Data analysis was performed with SPSS statistical package, version 20, (Statistical Package for Social Sciences)
- It was considered a significant value of p ≤0.05

4. Results

1024 patients were followed in total. The average glycemia in non-diabetic and diabetic patients was 144.6±48.1 mg/dL and 283.5±120.1 mg/dL, respectively. Mortality in non-diabetic patients was 8.2% whereas in diabetic patients it was 19.6%. The average mortality in the total population was 10.3%, being 4.8% in the revascularized group vs. 16.4% in the conservative treatment group. In diabetic patients, mortality rates were 21.5% in the conservatively treated/non-revascularized group and 9% in the revascularized group. In non-diabetic patients, mortality rates were 14.6% in the conservatively treated/non-revascularized group and 3.4% in the revascularized group. You can clearly notice that revascularization decreases mortality risk 2.65 fold in diabetic patients and 4.3 fold in non-diabetic patients **(Fig. 1).**

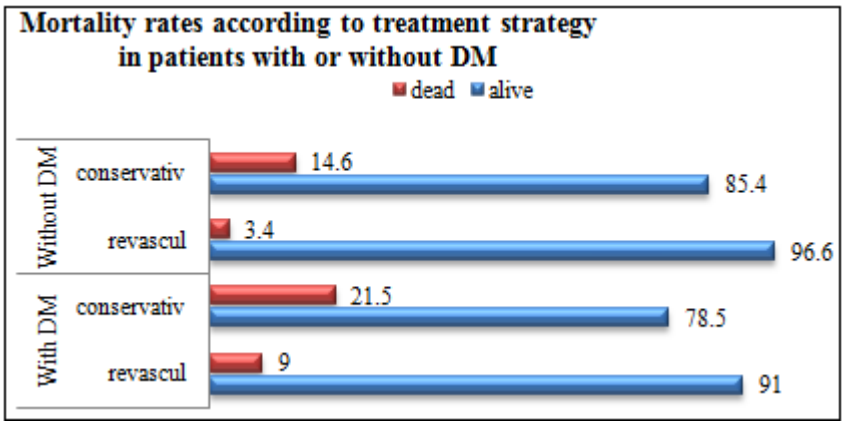

Figure 1: Mortality rates according to treatment methods in patients with or without DM.

From the binary logistic regression analysis it resulted that an increase in glycemia by 1 mg/dL leads to an increase in mortality odds by 1% (OD=1.01, CI 95%, 1.001-1.13). We observed that there was a statistically significant correlation between glycemia and mortality ($p<0.001$) (Table 1) and that the impact of different treatment strategies in mortality is statistically significant ($p<0.001$) Despite higher mortality in conservative patients compared to those undergoing revascularization, it was noted that mortality in glycemias >180 mg/dL compared to mortality in glycemias 125 mg/dl and 125-180 mg/dl is increased several times more in revascularized patients (11.8% vs. 0.7% and 1.5% respectively) compared to those managed conservatively (28.6% vs. 3.4 % and 11.8% respectively) **(Fig. 2)**.

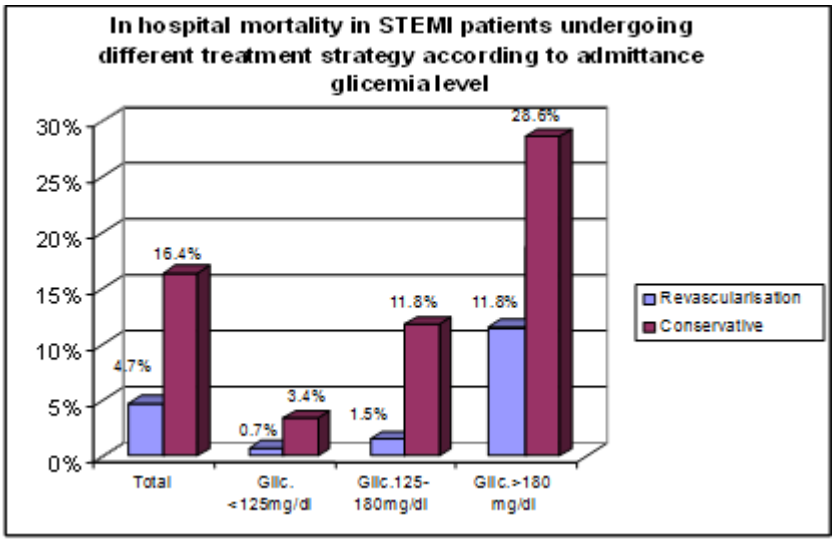

Figure 2: In-hospital mortality rates in STEMI patients according to treatment strategy and admission glycemia

Increasing glycemia was associated with increasing mortality in both groups (diabetic and non-diabetic patients), and the increase in mortality due to increasing glycemia was higher in non-diabetic patients (0%, 5.7%, 18.2% vs. 1.9%, 6.9%, 28.8% in diabetic and non-diabetic patients and according to three glycemic groups mentioned above, respectively). **(Fig. 3)**

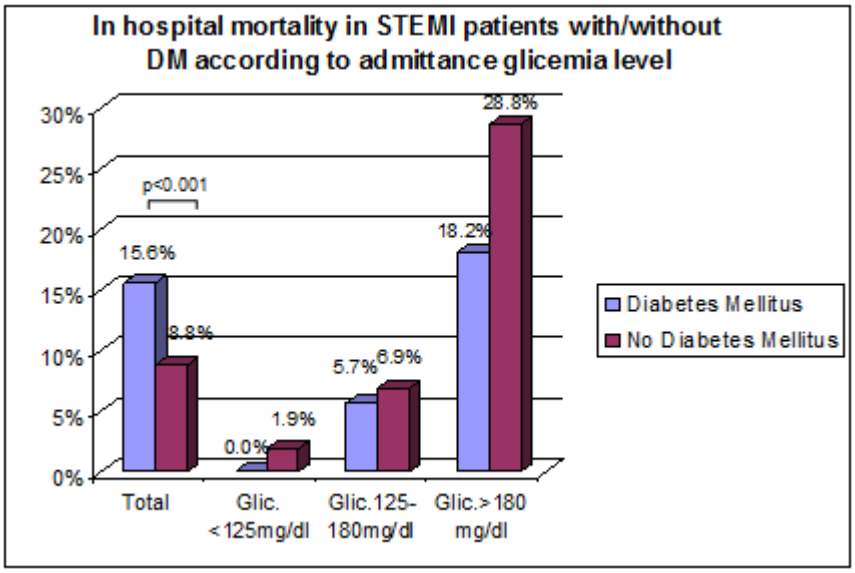

Figure 3: In-hospital mortality rates in STEMI patients according to the presence of DM and admission glycemia levels.

5. Discussion

This trial was based on patients presenting with STEMI and showed that hyperglycemia is a predictor of mortality independently of treatment strategy and presence of diabetes mellitus, in accordance with the results of other similar trials [1]-[3]. In similar trials with patients presenting with STEMI treated mainly with Primary PCI, hyperglycemia at admission was associated with increased in-hospital mortality [4], [5]. Another study with patients older than 75 years in the CCU with STEMI showed that hyperglycemia is an independent predictor of increased mortality [6]. Myocardial infarction size and coronary flow dysfunction is greater in patients with hyperglycemia compared to normoglycemic patients [7].

Our trial also concluded that, in spite of the decrease in mortality thanks to revascularization, such decrease is lower in diabetic patients compared to non-diabetics. (2.65 fold vs. 4.3 folds, respectively). This can be explained with the chronic damages caused by insulin resistance and hyperglycemia, such as endothelial dysfunction, oxidative stress and vascular inflammation [8], [9], pro-coagulant and pro-thrombotic states [10], [11], diabetic cardiomyopathy [12], diabetic nephropathy, diabetic neuropathy and polyarteriopathy. Such finding shows that the treatment of diabetic patients with STEMI should probably be more aggressive than in non-diabetics and, since the cardiovascular risk continues to be present despite intensive glycemic control, new strategies based in new mechanisms are needed, along with an optimal multidimensional treatment.

Among non-diabetic patients, hyperglycemia might reflect Diabetes Mellitus not yet diagnosed, stress hyperglycemia or both. In this trial, hyperglycemia > 180 mg/dL in both diabetic and non-diabetic patients was associated with an increase in mortality compared to the other two glycemic groups in relation to the benefit from revascularization compared to conservative treatment. This might be explained with the fact that hyperglycemia is associated with coronary flow dysfunction before reperfusion and is associated with an increase in thrombin formation, platelet activation and increased thrombus resistance to lysis and this phenomenon has been found as well in other trials where non-diabetic patients with hyperglycemia at admission and diabetic patients with increased hyperglycemia at admission represent a group of patients with increased mortality in cases of STEMI treated with Primary PCI [13]. At the same time, the presence of hyperglycemia has been found to be associated with an increase in reperfusion lesions [14], [15].

This trial has of course some limitations, including the inability to study long-term mortality. On the other hand, the systolic function was not routinely evaluated to study an association between hyperglycemia and a decrease in systolic function.

6. Conclusions

In spite of the important benefit of revascularization in decreasing in-hospital mortality in patients with STEMI, this benefit in diabetic patients is lower than in non-diabetic patients. This shows that multidimensional treatment in these patients should be more aggressive. At the same time, this trial showed that revascularization is associated a lower reduction in mortality in glycemic levels > 180 mg/dL, especially in non-diabetic patients.

7. Future Scope

Other trials are needed to better clarify the association between admission hyperglycemia and outcomes in STEMI patients, comparing diabetics to non-diabetics, and also comparing different treatment strategies. Future results with longer follow-up will assist in studying long-term differences in heart failure and mortality between different groups, and a routine measurement of Left Ventricle systolic function would help to study an association between hyperglycemia and a decrease in systolic function.

References

[1] Wahab NN, Cowden EA, Pearce NJ, *et al* Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am Coll Cardiol 2002; 40: 1748–1754
[2] Stranders I, Diamant M, van Gelder RE, *et al* Admission blood glucose level as risk indicator of death after myocardial infarction in patients with and without diabetes mellitus. Arch Intern Med 2004; 164: 982–988
[3] Squire IB, Nelson CP, Ng LL, *et al* Prognostic value of admission blood glucose concentration and diabetes diagnosis on survival after acute myocardial infarction; Results from 4702 index cases in routine practice. Clin Sci 2010; 118: 527–5357
[4] Pinto DS, Kirtane AJ, Pride YB, *et al* Association of blood glucose with angiographic and clinical outcomes among patients with ST-segment elevation myocardial infarction (from the CLARITY-TIMI-28 study). Am J Cardiol 2008; 101: 303–307
[5] Pres D, Gasior M, Strojek K, *et al* Blood glucose level on admission determines in-hospital and long-term mortality in patients with ST-segment elevation myocardial infarction complicated by cardiogenic shock treated with percutaneous coronary intervention. Kardiol Pol 2010; 68: 743–751
[6] Kosiborod M, Rathore SS, Inzucchi SE, *et al* Admission glucose and mortality in elderly patients hospitalized with acute myocardial infarction: implications for patients with and without recognized diabetes. Circulation 2005; 111: 3078–3086
[7] Cruz-Gonzalez I, Chia S, Raffel OC, *et al* Hyperglycemia on admission predicts larger infarct size in patients undergoing percutaneous coronary intervention for acute ST-segment elevation myocardial infarction. Diabetes Res Clin Pract 2010; 88: 97–102
[8] Kim JA, Montagnani M, Koh KK, Quon MJ. Reciprocal relationships between insulin resistance and endothelial dysfunction: molecular and pathophysiological mechanisms. *Circulation* 2006*;* **113***:*1888-1904.
[9] Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *J Am Coll Cardiol* 2010*;* **55***:*1318-1327.
[10] Grant PJ. Diabetes mellitus as a prothrombotic condition. *J Intern Med* 2007*;* **2 62***:*157-172.
[11] Ferreiro JL, Angiolillo DJ. Diabetes and antiplatelet therapy in acute coronary syndrome. *Circulation*2011*;* **123***:*798-813.
[12] Poornima IG, Parikh P, Shannon RP. Diabetic cardiomyopathy: the search for a unifying hypothesis. *Circ Res* 2006*;* **98***:*596-605.
[13] Ergelen M, Uyarel H, Cicek G, *et al* Which is worst in patients undergoing primary angioplasty for acute myocardial infarction? Hyperglycaemia? Diabetes mellitus? Or both? Acta Cardiol 2010; 65: 415–423
[14] Timmer JR, Ottervanger JP, de Boer MJ, et al. Zwolle Myocardial Infarction Study Group. Hyperglycemia is an important predictor of impaired coronary flow before reperfusion therapy in ST-segment elevation myocardial infarction. *J Am Coll Cardiol*2005*;* **45***:*999–1002pmid:15808754
[15] Undas A,Wiek I, Stêpien E, Zmudka K, Tracz W. Hyperglycemia is associated with enhanced thrombin formation, platelet activation, and fibrin clot resistance to lysis in patients with acute coronary syndrome. *Diabetes Care* 2008*;* **31***:*1590–1595pmid:18487475

Author Profile

Arkel Duka received his M.D. degree from the Faculty of Medicine, University of Tirana, Albania in 2000. During 2000-2002 he worked as a General Practitioner (GP) in the Emergency Department of the Hospital of Saranda, Albania. He did his specialization in Cardiology during 2002-2006 in the Faculty of Medicine, University of Tirana. During 2007-2009 he worked as a cardiologist at the Prisons Hospital and from 2009 he works as a cardiologist at the Cardiac Intensive Care Unit in the University Hospital Center “Mother Teresa”, Albania.