Influence of Leukocytes and Glycemia on the Prognosis of Patients with Acute Myocardial Infarction

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Summary

Background: Previous studies have demonstrated that leukocytosis and hyperglycemia verified at the admission of patients with acute myocardial infarction (AMI) are associated with intrahospital mortality. However, little is known on the long-term impact of these markers.

Objective: To evaluate the short-and long-term influence of the levels of glucose and leukocytes on the prognosis of patients with AMI.

Methods: A total of 809 patients with AMI were retrospectively assessed (mean age: 63.2 ± 12.87 yrs) and prospectively and consecutively included in a specific database.

Results: a) At the intrahospital phase, the mean values were compared between patients that died and those who survived: Leukocytosis: 12156±5977 vs 10337±3528 (p=0.004, 95%CI = 976-2663); Glucose 176±105 mg/dl vs 140±72 mg/dl (p<0.001, 95%CI = 19.4 – 52.6), respectively. b) With the adjusted mode, the same pattern was observed [p values: 0.002 (t-ratio 3.05), 0.04 (t-ratio 2.06), respectively]. c) Long-term follow-up: the univariate analysis showed P values of 0.001 (t-ratio 3.3), <0.001 (t-ratio 4.16), respectively. The multivariate analysis showed P=0.001 (t-ratio 3.35), 0.08 (t-ratio 1.75), respectively. d) After the exclusion of the intrahospital deaths, the leukocyte (P=0.989) and glucose levels (P=0.144) did not remain significantly correlated with mortality. The same result was observed at the multivariate analysis.

Conclusion: The levels of glucose and leukocytes at the hospital admission of patients with AMI are excellent predictors of intrahospital mortality and poor predictors of long-term death. (Arq Bras Cardiol 2009;92(2):84-88)

Key words: Leukocytosis; glucose; myocardial infarction.

Introduction

Patients with unstable myocardial ischemic syndromes (UMIS) must be routinely submitted to risk stratification when admitted at the hospital. The objective of this early stratification is to determine the risk and prognosis of these patients, which allows establishing a more adequate therapeutic management and clinical follow-up of the patients. In this sense, the classification by Braunwald\(^\text{a}\) and the risk scores published by the TIMI group (Thrombolysis In Myocardial Infarction)\(^\text{b,c}\), for UMIS without ST-elevation as well as for acute myocardial infarction (AMI) with ST-elevation, have been largely used for early stratification. However, other risk markers have been investigated in an attempt to make the short- and long-term prognostic assessments more accurate. Previous studies demonstrated that leukocytosis and hyperglycemia verified at the hospital admission of patients with AMI are correlated with intrahospital mortality\(^\text{d,2}\). However, little is known about the long-term impact of these markers.

Thus, the main purpose of this study was to evaluate the short- and long-term influence of the levels of glucose and leukocytes on the prognosis of patients with AMI and compare the impact of these “new” markers with that of the “traditional” ones, such as left ventricular (LV) ejection fraction (EF) and age.

Methods

This is a unicentric study, in which all patients were selected from an Intensive Care Coronary Unit. A total of 809 patients with AMI were retrospectively assessed (mean age: 63.2 ± 12.87 yrs) and prospectively and consecutively included in a specific database, between February 1998 and July 2005. The criteria used for the AMI diagnosis were: troponin curve or fraction of creatine kinase (CK-MB) associated to at least of the following: ischemic symptoms, development of pathological Q waves at the electrocardiogram (ECG), electrocardiographic alterations indicative of ischemia (ST elevation or depression) or post-coronary intervention.
The patients were followed for up to 6.4 years (mean survival time of 5.15 years), with annual prospective assessments in relation to mortality. The follow-up of the study population was carried out annually by phone or personal interview. The patients (or their family members) were contacted by phone, visits to the office or active personal search (personal search at the workplace, residence, neighbors’ houses, etc).

The values of the first leukocyte and glycemia measurements were analyzed in relation to the intrahospital and long-term prognosis. The blood collection for glycemia and leukocytosis measurement was carried out at the moment of the hospital admission.

In the adjusted models, the following variables were considered: history of angioplasty, myocardial revascularization surgery, myocardial infarction, diabetes, smoking, history of heart failure (HF), age, sex, heart rate (HR), systolic arterial pressure (SAP), ST-segment elevation, glycemia, leukocytosis, EF (first echocardiogram; Simpson’s method), presence of fibrinolysis and primary angioplasty.

For the intrahospital phase, the Student’s t test or Kruskal-Wallis test (univariate analysis) and logistic regression (multivariate analysis) were used. For the long-term analysis, Cox proportional hazards estimation was used. The stepwise method with an entry of 0.10 and removal of 0.10, was used for the logistic regression analysis.

Results
A. Study population
The data regarding the studied population are shown in Table 1.

B. Intra-hospital phase
At the intrahospital phase, 92 patients (11.37%) died. The mean time until death was 94 hours (95%CI; 60.90-127.0). The mean values measured for the variables were compared between patients that died and those who survived: Leukocytosis 12156±5977 vs 10337±3528 (p=0.004, 95% CI = 976-2663); Glucose 176±105 mg/dl vs 140±72 mg/dl (p<0.001, 95% CI = 19.40-52.60), respectively. As it can be observed, the two analyzed variables significantly correlated with the worst prognosis.

Table 2 demonstrates the results of the multivariate model. After the logistic regression analysis of 16 variables, through the stepwise model (with an entry of 0.10 and removal of 0.10), it was observed that only 5 variables significantly and independently correlated with the intrahospital mortality: glycemia, leukocytes, age, EF and SAP.

C. Late follow-up
C.1. General population
During the extra-hospital phase, there were 94 additional deaths. The probability of global survival was 77% (Kaplan-Meyer). Regarding the long-term follow-up, considering the totality of patients, significant correlations were observed between glycemia/leukocytes and mortality, as shown in Table 3. Table 4 shows that, in the multivariate model, six analyzed variables remained as prognostic factors for the long-term evolution in the global population. However, glycemia showed only a tendency to correlate with mortality.

C.2. Patients that survived the intrahospital phase
As shown in Table 5, when the intrahospital deaths were excluded, leukocytes and glycemia levels no longer correlated
with the long-term evolution. In other words, the prognostic value of leucocytes and glycemia levels is restricted to the intrahospital phase, presenting no impact after hospital discharge. This behavior does not present alterations in the adjusted models, as shown in Table 6, where only the history of HF, age and EF correlate with mortality.

**Discussion**

In the last three decades, the treatment of AMI showed significant advancement, which resulted in the decrease of the morbimortality related to the disease. That occurred mainly due to new pharmacological and mechanical primary reperfusion strategies, multiple anti-aggregation, in addition to the broad use of invasive stratification and the possibility of revascularization with angioplasty and stents.

However, patients with UMIS have different characteristics, which determine their risk and prognosis variability. Some of these patients benefit from aggressive therapeutic measures, such as percutaneous invasive approach and strict glycemia control.

In this sense, to identify patients at higher risk has been a constant concern in literature. In addition to the studies to validate risk scores and the variables that are traditionally associated with a poor prognosis, such as age and left ventricular dysfunction, investigators have recently worked on the identification of new prognostic variables, such as inflammatory markers, natriuretic peptide, leucocytosis and hyperglycemia, among others.

Diabetic patients are recognized as being high-risk patients and having worse short- and long-term prognosis after AMI. The MONICA report showed that the mortality for diabetic and non-diabetic infarcted patients, after 28 days of evolution, was 12.6% and 7.3%, respectively. Therefore, the inclusion of diabetes mellitus in the early risk stratification is justified.

However, the presence of hyperglycemia was also identified as a poor prognosis factor in non-diabetic infarcted patients. It was recently demonstrated that hyperglycemia is still a poor prognosis factor also in patients submitted to percutaneous coronary intervention, regardless of the presence of diabetes. It was also verified in this and in other studies that there is an association between hyperglycemia, no-reflow phenomena and ventricular remodeling, which are known factors of severity and worse prognosis in the evolution of patients with AMI.

Similarly, another study demonstrated that hyperglycemia, but not diabetes, was a poor intrahospital prognostic factor. Regarding the long-term follow-up, previous studies demonstrated that hyperglycemia, regardless of the presence of diabetes, was also a risk factor for mortality in patients with AMI.

The data obtained in our study were similar to those found by other authors regarding the influence of glycemia on mortality. Glycemia levels at the hospital admission were significantly higher in patients that died during the hospital stay. During the follow-up of more than 6 years, hyperglycemia remained as a bad prognosis factor, although the adjusted model showed only a tendency to worse mortality. However, after the exclusion of the intrahospital deaths, the variables age, ejection fraction (EF) and history of HF remained significantly correlated with mortality, but not the levels of leucocytes or glycemia. This fact might be related to the hypotheses that hyperglycemia is not only a prognostic marker, but a direct cardiovascular system aggressor in the acute phase of AMI.

Experimental studies demonstrated that hyperglycemia is capable of causing platelet thrombosis, increasing the circulation of leucocyte adhesion molecules and decreasing the endothelium-dependent vasodilation, nitric oxide availability and the collateral coronary circulation. The decrease in nitric oxide and prostacyclin levels, or even the increase in vasoconstrictors such as endothelin, are enhanced by hyperglycemia through protein kinase C activation, hexosamine increase and the activation of the pro-inflammatory nuclear factor Kappa B, with the consequent formation of superoxide radicals. A study that induced diabetes in swine demonstrated an increase in IL-6, tumor necrosis factor (TNF), macrophage chemotactic proteins and adhesion molecules in fibroblasts of the coronary adventitia.

Regarding the leucocytosis, some studies explored its prognostic value in AMI. One of the most relevant ones included leucocytosis as part of a risk score for infarcted patients. In this study, men with leucocyte levels > 9,000/
Leucocytes and glycemia in the prognosis of AMI

References


