Introduction
The presence of high glucose levels, Diabetes Mellitus or both contributes to more than three million deaths by cardiovascular pathology each year.

With the increased incidence of obesity, insulin resistance and metabolic syndrome, it is estimated that the prevalence of diabetes will double by the year 2030. This “diabetes epidemic” will, obviously, be responsible for the increase in cardiovascular pathology attributed to diabetes.1

The first step, for an adequate approach to this pathology, will be the correct and timely establishment of the diagnosis of Diabetes Mellitus, based on the reference diagnostic criteria, which will enable the need for action to be defined, in the scope of hyperglycemia (Table I).

Coronary arterial disease is the main cause of morbidity and mortality in patients with Diabetes Mellitus. These patients are at higher risk of acute myocardial infarction or heart failure, presenting a high risk in relation to non-diabetics, of dying after an attack of acute coronary syndrome. These differences may be related to the severity and extent of the coronary disease in diabetics, as well as left ventricular remodeling and the presence of significant ventricular dysrhythmias.2

The problem of hyperglycemia in Acute Coronary Syndrome
The denomination acute coronary syndrome (ACS) includes unstable angina, acute myocardial infarction without ST elevation and acute myocardial infarction with ST elevation.

The evolution of the treatment and early healthcare significantly decreased the mortality rate in these patients, enabling the definition of objectives for stabilizing the residual cardiac function, with a possible improvement in the quality of life.

As the mortality and morbidity rates are being stabilized in patients with ACS, predictive factors of prognosis are sought that can be controlled, in order to positively influence the patient’s evolution.

The association between hyperglycemia/diabetes and cardiovascular disease, as well as the growing evidence in relation to lack of glycemic control in ACS and significant morbidity, have led to intense investigation in this area.

Various studies demonstrate that the presence of hyperglycemia is common in the admission of patients with Acute Coronary Syndrome. It is also demonstrated that hyperglycemia in these patients is a strong predictor of mortality and of increased...
risk of hospital complications, whether in diabetic or non-diabetic patients. However, there are many gaps in the knowledge of the mechanisms involved in the association between the high glucose levels and the unfavorable evolution in patients with acute coronary syndrome.

Some questions are of particular interest in the approach to this theme, for example: there is no current consensus on the glucose levels considered abnormal in the admission of these patients, and the best method for measuring and monitoring glucose levels. Also, the physiopathological process involved in the unfavorable association between hyperglycemia and the evolution of the ACS patient has not been fully defined.

**Hyperglycemia: marker of high risk or mediator of adverse effects?**

Various physiological studies demonstrate that hyperglycemia may have a direct harmful effect on the myocardium, through a variety of mechanisms; some of these studies reveal a decrease in collateral circulation and increased infarction in the presence of severe hyperglycemia.

In diabetic patients, postprandial hyperglycemia is associated with defects of myocardial perfusion, due to the microvascular dysfunction, a condition that improves with glycemic control.

It is also demonstrated that high levels of glucose are associated with a prothrombotic condition, as well as an increase in markers of vascular inflammation and products of oxidation, which could induce tissue damage.

In the particular case of ACS, hyperglycemia is associated with an increased concentration of free fatty acids, insulin resistance, and dysfunction of the use of glucose by the myocardium; thus, oxygen consumption increases, potentiation of ischemia, as well as the incidence of ventricular dysrhythmias. Finally, hyperglycemia proved to be associated with immune response dysfunction (Figure 1).

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**TABLE I**

Diagnosis criteria for Diabetes Mellitus (A.D.A. 2007)

<table>
<thead>
<tr>
<th>Glycemia, mg/dL</th>
<th>Clinical Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting &lt; 100</td>
<td>Normal</td>
</tr>
<tr>
<td>100-125</td>
<td>Abnormal fasting glycemia /pre-diabetes</td>
</tr>
<tr>
<td>≥ 126</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Glucose tolerance test (2 hours after oral intake of 75 g glucose)</td>
<td></td>
</tr>
<tr>
<td>&lt; 140</td>
<td>Normal</td>
</tr>
<tr>
<td>140-199</td>
<td>Reduced tolerance to glucose/ pre diabetes</td>
</tr>
<tr>
<td>≥ 200</td>
<td>Diabetes Mellitus</td>
</tr>
</tbody>
</table>

Diagnosis criteria for Diabetes Mellitus

Diabetes symptoms (polyuria, polydipsia, non explained weight loss, + occasional plasmatic glycemia > 200 mg/dL)

or

Fasting Glycemia > 126 mg/dL

or

Glycemia >200 mg/dL 2 hours after the glucose tolerance test with 75g of oral glucose

a) One of these three criteria is enough to establish a diagnosis of Diabetes Mellitus. These parameters must be confirmed repeating the test on a subsequent day, in the absence of unequivocal hyperglycemia.
**Monitoring of glycemic control during hospitalization of the ACS patient**

Despite the usefulness of Hemoglobin A1c (HbA1c) in the outpatient, this parameter has limited usefulness as a predictive factor of morbidity and mortality in ACS. In reality, there is a simple laboratory test (like HbA1c) that permits adequate monitoring of glycemic control during hospitalization. The best form of verifying glycemic control is regular medication with capillary glucose, in different times of the day, and linking it to the patient's nutritional state at a given time.

New technologies, such as continual glucose monitors, are currently being developed, and could simplify the function of monitoring glycemic control in the patient.

**Treatment of hyperglycemia: Relationship between glycemic control and evolution of the ACS patient**

Although there is little doubt as to the benefits of aggressive and intensive control of hyperglycemia in the clinical evolution of the ACS patient, there remains, among health professionals, an underlying fear of using insulin therapy when indicated. Effectively, the adequate and timely use of insulin, with the most rigorous control possible of glucose levels, is the best treatment option for these patients.

The most relevant studies in this area demonstrate a significant association between hospitalization time, mortality and/or morbidity vs. glycemic control.17-22

Faced with this evidence, the use of insulin is recommended in the presence of hyperglycemia, from...
the time the patient is admitted, and with adequate use during the hospitalization, according to the glucose levels in the ACS. Intensive therapy appears to be the most appropriate, with its benefits largely outweighing the risk of side effects (hypoglycemia).

The maximum benefit was found for an average average glucose level <110mg/dL; hyperglycemia should be controlled in patients with or without a history of diabetes (a definition of hyperglycemia is suggested as being a plasma glucose level on admission >140mg/dL). The protocols for use of insulin should be adapted according to the evolution of the glycemic values.

**General recommendations for the approach of hyperglycemia in ACS (Adapted from the American Heart Association, March 2008)**

Glucose level should be a part of the initial laboratory evaluation in all patients with suspected or confirmed ACS.

In patients admitted to an Intensive Care Unit (ICU) with ACS, glucose levels should be monitored closely. Glucose levels > 180mg/dL, regardless of prior diabetes history, should be treated aggressively; although an optimum level of treatment has not yet been defined, a value of <110mg/dL is suggested, with an acceptable range of 90 to 140mg/dL.

Insulin, administered as an intravenous infusion, is currently the most effective method for controlling glucose among patients hospitalized in the ICU; care should be taken to avoid hypoglycemia.

Treatment should be instituted as soon as feasible, without compromising the administration of urgent and therapeutic measures appropriate for ACS.

In patients hospitalized in the non-ICU setting, efforts should be directed at maintaining plasma glucose levels <180mg/dL with subcutaneous insulin regimens.

ACS patients with hyperglycemia, but without prior history of diabetes, should have further evaluation (preferably before hospital discharge) to determine the severity of their metabolic derangements; this evaluation may include fasting glucose and HbA1c assessment and, in some cases, a postdischarge oral glucose tolerance test.

Before discharge, plans for optimal outpatient glucose control should be determined in those patients with established diabetes, newly diagnosed diabetes, or evidence of insulin resistance.

**CONCLUSION**

Hyperglycemia is very common in the context of ACS, and is often dealt with inappropriately, despite being clearly associated with unfavorable evolution in these patients. The concrete mechanism that measures this unfavorable association remains obscure, and doubts remain as to whether hyperglycemia is a marker or a mediator of high mortality, and the target value to be achieved in the treatment.

Future studies may answer these questions, enabling the care and evolution of ACS patients to be improved.

**References**