

## Comparison of Inflammatory Biomarkers between Diabetic and Non-Diabetic Patients with Unstable Angina

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### Summary

**Background:** Studies comparing inflammatory activity between diabetic and non-diabetic individuals with acute coronary syndrome are scarce, and none including only patients with unstable angina (UA) has been published to date.

**Objective:** We compared serum C-reactive protein (CRP), and interleukin-6 (IL-6) between diabetic and non-diabetic patients with unstable angina (UA) to determine if difference in inflammatory activity is responsible for a worse prognosis in diabetic patients. We also evaluated the correlation between inflammatory markers and the metabolic profile in diabetic patients and the correlation between inflammatory response and in-hospital outcomes: death, acute myocardial infarction, congestive heart failure, and length of stay in hospital.

**Methods:** A prospective cohort study of 90 consecutive patients admitted to a chest pain unit with UA and divided into two groups, diabetic and non-diabetic. Serum CRP, IL-6, metabolic profile and leukocyte count were measured at hospital arrival.

**Results:** Forty-two patients (47%) were diabetic (age  $62 \pm 9$ ) vs. 48 (53%) non-diabetic (age  $63 \pm 12$ ). No differences between median C-reactive protein (1.78 vs. 2.23 mg/l,  $p=0.74$ ) and interleukin-6 (0 vs. 0 pg/ml,  $p=0.31$ ) were found between the two groups. There was a positive correlation between CRP and total cholesterol ( $r_s = 0.21, p = 0.05$ ), CRP and LDL-cholesterol ( $r_s=0.22, p=0.04$ ) and between CRP and leukocyte count ( $r_s = 0.32, p = 0.02$ ) in both groups. No associations were found between inflammatory markers and in-hospital outcomes.

**Conclusion:** We found no difference in inflammatory activity between diabetic and non-diabetic patients with UA, suggesting that this clinical condition may result in balanced inflammatory activity between the two groups and increase acute-phase proteins independently of metabolic state. (Arq Bras Cardiol 2009;92(4):269-274)

**Key words:** Atherosclerosis / complications; diabetes mellitus; inflammation / complications; angina pectoris.

### Introduction

Atherosclerosis is responsible for 80% of all deaths in diabetic patients<sup>1</sup>. As the prevalence of diabetes is estimated to double by the year 2025, the burden of cardiovascular disease with this condition will dramatically increase<sup>2</sup>.

Compared with non-diabetic individuals, diabetic patients have a two- to four-fold increased risk of coronary heart disease<sup>3</sup>, two fold-higher risk of short-term mortality after acute myocardial infarction<sup>4</sup>, and poorer results when submitted to angioplasty with increased risk of restenosis<sup>5</sup>. Inflammatory activity is increased in individuals with type 1<sup>6</sup> and type 2 diabetes and strongly associated with risk of atherothrombosis<sup>7</sup>.

C-reactive protein (CRP) is the principal downstream mediator of acute phase response and is primarily derived

via IL-6 dependent hepatic biosynthesis and has long been recognized as a very stable protein<sup>8</sup>. Levels of CRP increase very rapidly in response to trauma, inflammation, and infection and decrease just as rapidly with the resolution of the condition<sup>9</sup>. Thus, measurement of CRP is widely used to monitor various inflammatory states. The synthesis of CRP is predominantly under the control of IL-6<sup>10</sup>, which in turn has been assumed to originate from activated leukocytes, adipocytes, and endothelial cells<sup>11</sup>.

Increased levels of C-reactive protein (CRP) and interleukin-6 (IL-6) are associated with higher incidence of adverse cardiac events in patients with acute coronary syndromes, as well as in patients undergoing coronary stenting<sup>12</sup>. Aggarwal et al<sup>13</sup> found increased CRP levels (two fold) in diabetic than in non-diabetic subjects with acute coronary syndrome before and after coronary stenting.

Studies comparing inflammatory activity between diabetic and non-diabetic individuals with acute coronary syndrome are scarce, and none including only patients with unstable angina (UA) has been published to date. The aim of this study was to compare high sensitivity C-reactive protein (hs-CRP), interleukin-

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6 and leukocyte count levels between diabetic and non-diabetic patients to determine if differences in inflammatory activity could explain the worsened clinical or procedure results in diabetic patients with acute coronary syndrome.

## Methods

### Study design

In this observational, cross-sectional study with a comparison group, performed at the chest pain unit of the Santa Isabel Hospital from February to October of 2005, 90 patients with unstable angina pectoris were consecutively included, irrespective of age and gender. Patients were classified into two groups: diabetic and non-diabetic subjects. At admission, all patients were immediately examined by a cardiologist who measured their heart rate, blood pressure and pulse oximetry. All patients received 200 mg of aspirin and underwent 12-lead electrocardiograms. Blood samples for laboratory evaluation were drawn within 15 minutes of admission.

Inclusion criteria were age > 30 years old, both sexes, unstable angina and time from onset of chest pain to admission not superior to 12 hours.

Unstable angina was defined according to Braunwald<sup>14</sup>, and only patients with class IIIB were included in the study.

Patients with recent myocardial infarction (less than four weeks), dilated cardiomyopathy or Chagas heart disease, atrial fibrillation, valvular heart disease, raised levels of myocardial necrosis markers within 12 hours of admission (troponin T > 0.1 µg/ml and creatine kinase-MB mass > 4.94 µg/ml with a characteristic rise and fall curve), thromboembolism, surgery, PTCA in the last four weeks, inflammatory or neoplastic disease, chronic renal failure and fever in the previous week were excluded.

Patients were classified according to: age, sex, precordial pain at admission, TIMI risk score, diabetes duration, hypertension, smoking, previous coronary artery disease, percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), previous myocardial infarction, dyslipidemia, chest pain duration, time from onset of chest pain to admission (delta T in minutes), alcohol intake, family history of premature coronary artery disease and body mass index calculated from self-reported height and weight. Previous treatment used before inclusion in this study and also in-hospital treatment according to the chest pain unit routine protocol were recorded.

Diabetes was defined by occasional blood glucose ≥ 200 mg/dL or fasting glucose ≥ 126 mg/dl, use of oral hypoglycemic drugs or insulin treatment or self-reported history<sup>15</sup>.

Dyslipidemia was defined by high lipid levels according to the Third National Cholesterol Education Program<sup>16</sup> or by use of lipid-lowering drugs.

Death, acute myocardial infarction (AMI) characterized by troponin T levels ≥ 0.1 µg/ml and ck-MB-mass levels ≥ 5.0 µg/ml with a characteristic rise and fall curve, congestive heart failure (CHF) occurring before discharge and length of stay in hospital were considered as in-hospital outcomes.

The local Bioethics Committee of our center approved the protocol study and all patients provided informed consent.

### Laboratory evaluation

On admission, blood venous samples were obtained before intravenous administration of any drug (except for aspirin according to chest pain unit protocol), with a delay not superior to 15 minutes. Coded plasma samples were stored at -85°C. CRP was measured via a high-sensitivity latex enhanced immunonephelometric assay on a BN II analyzer (Dade Bering, Newark, Del) at a Clinical Analyses Laboratory (LPC). The detection limit of C-reactive protein was 1.3 mg/l. The interassay coefficient of variation was 2.2%, and the intra-assay coefficient was 2.9%.

Plasma concentration of IL-6 was measured by a commercially available enzyme-linked immunosorbent assay (Quantikine human IL-6, R&D Systems, Minneapolis, MN) at Osvaldo Cruz Foundation (FioCruz). The lower detection limit of interleukin-6 was under 0.9 pg/ml. The interassay coefficient of variation was 6.4% and the intra-assay coefficient was 4.2%.

Plasma glucose, triglyceride, total cholesterol, and HDL-cholesterol were determined using enzymatic colorimetric assays (reagents obtained from Boehringer Mannheim Diagnostics, Mannheim, Germany). In subjects who had plasma triglyceride levels < 400 mg/dl, LDL-cholesterol was calculated according to the Friedewald formula. When triglyceride levels were > 400 mg/dl, LDL-cholesterol was measured by the enzymatic method on a Hitachi 902 automatic analyzer (Boehringer Mannheim, Mannheim, Germany).

HbA<sub>1c</sub> levels were determined by a immunoturbidimetric immunoassay (Roche Diagnostics GmbH, D-68298 Mannheim) with a normal range of 4.5–6, %.

### Statistical analyses

The study was designed with 80% power to detect a two-fold C-reactive protein value difference between two groups. To obtain this difference, a mean value of 2.8 mg/L and a standard deviation of 4.48 mg/L were used<sup>17</sup>. Considering a type I error of 0.05, and a type II error of 0.20, 80 patients were required.

C-reactive protein and IL-6 concentrations are presented as median and interquartile range. Baseline characteristics were compared by chi-square test or Fisher's exact test for categorical variables and Wilcoxon's rank-sum or Student's *t* test for continuous variables. Nonparametric tests were used to compare hs-CRP and IL-6 between groups (Mann-Whitney U test) and to determine correlations (Spearman's *p* test). All *p* values are 2-tailed, and values lower than 0.05 were considered statistically significant.

SPSS statistical software (version 10.0, SPSS Inc., Chicago, Illinois, USA) was used for data analysis.

## Results

### Baseline characteristics

A total of 117 consecutive patients were admitted from February to October 2005 in a reference cardiologic tertiary hospital. We excluded 24 patients who had serum cardiac markers elevation within 12 hours after admission, as well as 1 patient with Chagas heart disease, 1 patient with chest pain after alcohol libation and 1 patient with chronic renal disease.

Three out of the 24 patients had diabetes. Ninety subjects who fulfilled the inclusion criteria were studied. Mean age was  $62 \pm 9$  (range 34-87) years; 42 were diabetic and 48 non-diabetic. Table 1 shows the baseline clinical and laboratory characteristics of non-diabetic and diabetic patients. There were no differences in baseline clinical characteristics between groups except for higher systolic blood pressure ( $158 \pm 31$  vs.  $143 \pm 31$  mm/Hg,  $p = 0.02$ ) and heart rate ( $75 \pm 15$  vs.  $67 \pm 12$  beats/min,  $p=0.01$ ) in diabetic patients at admission. The mean time from the onset of chest pain to admission in the chest pain unit was similar for diabetic and non-diabetic patients ( $4.3 \pm 0.6$  vs.  $4.0 \pm 0.5$  h,  $p= 0.83$ ). No differences were observed for previous treatment between diabetic and non-diabetic patients except for the use of hypoglycemic drugs and insulin.

Time since last meal until blood samples were drawn was also similar between groups ( $4.9 \pm 3.1$  vs.  $5.0 \pm 3.3$  h,  $p=0.95$ ). There were no differences in laboratory characteristics between groups except for higher admission plasma glucose ( $178 \pm 78$  vs.  $105 \pm 27$  mg/dl,  $p < 0.001$ ), fasting plasma glucose ( $130 \pm 40$  vs.  $96 \pm 12$  mg/dl,  $p < 0.001$ ), and HbA1c ( $6.3 \pm 4.2$  vs.  $3.4 \pm 1.2$  %,  $p < 0.001$ ).

### Inflammatory markers

In the entire population, median hs-CRP, IL-6 and leukocyte count was respectively 2 mg/L (interquartile range 0.8 – 4.7 mg/L), 0 pg/ml (interquartile range 0 – 0 pg/ml) and  $7900$  l/mm<sup>3</sup> (interquartile range 6327– 9895 l/mm<sup>3</sup>).

Median hs-CRP (1.78 mg/L vs 2.23 mg/L,  $p = 0.74$ ), IL-6 concentrations (0 pg/mL vs, 0 pg/mL,  $p = 0.31$ ) and the leukocyte count ( $8245$  l/mm<sup>3</sup> vs,  $7520$  l/mm<sup>3</sup>,  $p = 0.74$ ) were similar in diabetic and non-diabetic subjects (Table 2).

No difference was observed between groups when analyzed in accordance with three CRP ranges ( $< 1$  mg/L, 1 to 3 mg/L and  $> 3$  mg/L):  $< 1$  mg/L (16% vs, 14%,  $p=0.5$ ), 1-3 mg/L (10% vs. 18%,  $p=0.32$ ) and  $> 3$  mg/L (14% vs 14%,  $p=0.7$ ). The diabetic and non-diabetic groups had also similar distribution when analyzed in accordance with quartiles:  $< 0.8$  mg/L (15% vs, 12%,  $p=0.36$ ), 0.81-2.04 mg/L (12% vs. 13%,  $p=0.95$ ), 2.05-4.7 mg/L (8% vs, 16%,  $p=0.12$ ) and  $> 4.7$  mg/L (14% vs. 13%,  $p=0.66$ ).

When IL-6 levels were analyzed as a categorical variable (0 pg/mL = no and  $> 0$  pg/mL = yes), positive results were similar in both groups, (17% vs. 8%,  $p=0.12$ ).

In the entire population, C-reactive protein levels were positively correlated with total cholesterol levels, ( $r_s = 0.21$   $p=0.05$ ), LDL cholesterol levels ( $r_s = 0.22$ ,  $p=0.04$ ) and leukocytes count ( $r_s = 0.32$ ,  $p = 0.02$ ).

### In-hospital outcomes

The overall mean hospital stay was 12 days, with a median of 7 days (range 2-125 days).

During the in-hospital period there were no differences between diabetic and non-diabetic subjects with respect to occurrence of congestive heart failure (5% vs. 0%,  $p=0.21$ ), acute myocardial infarction (5% vs. 2%,  $p=0.60$ ), death (25 vs. 0%,  $p=0.47$ ) and median hospital stay (8 days vs. 7

Table 1 - Baseline Characteristics

Variable	Diabetic (n=42)	Non-diabetic (n=48)	p-value
Age (yrs)	62 ± 9	63 ± 12	0.65
Men	16 (38%)	24 (49%)	0.28
<b>Physical examination</b>			
SBP (mm/Hg)	158 ± 31	143 ± 31	0.02
DBP (mm/Hg)	88 ± 18	85 ± 16	0.3
HR (beats/min)	75 ± 15	67 ± 12	0.01
BMI (kg/m <sup>2</sup> )	27 ± 3	26 ± 4	0.48
<b>History</b>			
Systemic hypertension	40 (95%)	42 (88%)	0.23
Current smoker	5 (13%)	13 (26%)	0.10
CABG	8 (18%)	8 (16%)	0.88
PTCA	14 (33%)	15 (31%)	0.85
Confirmed CAD	40 (95%)	45 (94%)	0.65
Previous AMI	20 (48%)	16 (33%)	0.17
Hyperlipidemia	35 (83%)	38 (80%)	0.73
ST-seg depression > 0.1 mV	7 (17%)	8 (17%)	0.96
Intermediary troponin T	7 (17%)	8 (17%)	0.96
TIMI risk	3 (0-6)	2 (0-4)	0.21
<b>CAD (number of involved vessels)</b>			
Normal	14 (34%)	16 (33%)	0.94
1	8 (20%)	11 (23%)	0.70
2	15 (37%)	16 (33%)	0.75
3	3 (7%)	4 (8%)	0.86
<b>Chest pain characteristics</b>			
Pain at admission	32 (77%)	29 (61%)	0.10
Pain duration (h)	1.5 ± 2.7	1 ± 1.2	0.90
Δ T (h)	4.3 ± 0.6	4 ± 0.5	0.83
<b>Previous medications</b>			
Aspirin	31(74)	39 (81)	0.45
β-blocker	26 (62)	27 (56)	0.67
Statin	23 (55)	29 (60)	0.7
ACE	19 (45)	15 (31)	0.20
<b>Laboratory</b>			
Admiss. plasma glucose (mg/dl)	178 ± 78	105 ± 27	< 0.001
Fasting plasma glucose (mg/dl)	130 ± 40	96 ± 12	< 0.001
HbA <sub>1c</sub> (%)	6.3 ± 4.2	3.4 ± 1.2	< 0.001
Total cholesterol (mg/dl)	182 ± 48	190 ± 58	0.48
HDL-cholesterol (mg/dl)	41 ± 14	41 ± 10	0.97
LDL-cholesterol (mg/dl)	98 ± 41	112 ± 54	0.18
Triglycerides (mg/dl)	208 ± 128	180 ± 103	0.26

Continuation of Table 1 - Baseline Characteristics

Ck-mb mass (µg/ml)	2.37 ± 1.0	2.4 ± 1.5	0.86
Troponin T(µg/ml)	0.01(0.01-0.09)	0.01 (0.01-0.14)	0.58

Values expressed as mean ± SD or number (%) or median (minimum-maximum); SBP - systolic blood pressure; DBP - diastolic blood pressure; HR - heart rate; BMI - body mass index; CABG - coronary artery bypass grafting; PTCA - percutaneous transluminal coronary angioplasty; CAD - coronary artery disease; AMI - acute myocardial infarction; ST-seg - ST segment; ΔT - time from onset of chest pain to admission; ACE - angiotensin-converting enzyme; Admiss. - Admission.

Table 2 - Comparison of Inflammatory Biomarkers

Variable	Diabetic (n=42)	Non-diabetic (n=48)	P-value
CRP (mg/l)	1.78 (0.16-15)	2.23 (0.22-21)	0.74
IL-6 (pg/ml)	0 (0-40)	0 (0-17)	0.31
Categorical IL-6	7 (17%)	4 (8%)	0.12
WBC (leukocytes/mm <sup>3</sup> )	8245 (3350-13100)	7520 (5170-16930)	0.74

Values expressed as number (%) or median (minimum-maximum).; RP - C-reactive protein; IL-6 - interleukin-6; WBC - white blood cells;

days, p=0.44). When combined outcomes were analyzed, events were also similar in both groups (12% vs. 2%, p=0.06, RR=5.7; 95% CI 0.7 to 56) (Table 3).

When subjects who had in-hospital events were compared with those without events, median hs-CRP was similar in both groups for CHF (8.1 mg/L vs 2.4 mg/L, p=0.47), AMI (7.8 mg/L vs 1.7 mg/L, p=0.81) and cardiovascular death (5.66 mg/L vs 2.04 mg/L, p=0.41). No difference was likewise observed for respectively median IL-6 and leukocyte count to CHF (0 pg/mL vs 0 pg/mL, p = 0.58; 9590 l/mm<sup>3</sup> vs 7460 l/mm<sup>3</sup>, p = 0.53), AMI (0 pg/mL vs 0 pg/mL, p = 0.58; 7925 l/mm<sup>3</sup> vs 7860 l/mm<sup>3</sup>, p = 0.5) and death (0 pg/mL vs 0 pg/mL, p = 0.70; 11500 l/mm<sup>3</sup> vs 7900 l/mm<sup>3</sup>, p = 0.22).

There was no correlation between length of stay in hospital and hs-CRP levels (rs=0.02, p=0.86), IL-6 (rs=0.09, p=0.44) or leukocyte count (rs=0.21, p=0.85).

## Discussion

There are few clinical studies comparing inflammation markers between diabetic and non-diabetic subjects with acute coronary syndrome, especially involving exclusively patients with unstable angina.

Moreno et al<sup>18</sup> found that, in diabetic patients, coronary tissue exhibits a larger content of lipid-rich atheroma, macrophage infiltration, and subsequent thrombosis than tissue from patients without diabetes, suggesting that there is an increased vulnerability for plaque disruption and thrombosis in patients with diabetes mellitus. The same author reviewed the pathogenesis of diabetes atherosclerosis<sup>19</sup> and supported the idea that patients with diabetes mellitus have

Table 3 - In-Hospital Outcomes in Diabetic and non-Diabetic Patients

Variable	Diabetic (n=42)	Non-diabetic (n=48)	Valor de p
CHF	2 (5%)	0 (0%)	0.21
AMI	2 (5%)	1 (2%)	0.60
CV death	1 (2%)	0 (0%)	0.47
hospital STAY (day)	8 (3-125)	7 (2-44)	0.44
Combined outcomes	5 (12%)	1 (2%)	0.06

Values as expressed as number (%) or median (minimum-maximum).; HF - congestive heart failure; AMI - acute myocardial infarction; CV - cardiovascular.

more inflammatory activity than the general population with atherosclerosis.

However, in this study no differences were observed in hs-CRP and IL-6 concentrations between diabetic and non-diabetic patients with unstable angina.

Aggarwal et al<sup>13</sup>, evaluating inflammatory activity measuring hs-CRP levels in 75 patients with acute coronary syndrome before, during and after coronary stenting in diabetic and non-diabetic individuals, concluded that diabetic patients with acute coronary syndrome had increased inflammatory activity before the procedure but after 24 hours there were no differences between diabetic and non-diabetic patients. Nevertheless the authors in their methodology did not describe fundamental information to conclude that in fact they had studied a population with acute coronary syndrome. Data on the time from onset of chest pain to admission or even the stenting procedure (first blood sample) was not informed. Moreover the author included patients with stable angina and non-ST elevation acute myocardial infarction when the necrosis factor could act as a confounding variable<sup>20</sup> and differently from our study, which used validated criteria to define diabetes, the authors did not even describe glucose levels.

Analyzing the CRP levels between the two groups, we observed before stenting procedure that diabetic patients had two-fold inflammatory activity than non-diabetic patients but after coronary stenting (endothelial aggression) there were no differences in hs-CRP concentrations between the two groups. Gottsauner et al<sup>21</sup> found that the persistence of elevated C-reactive protein plasma levels 96 h after stent implantation might reflect a prolonged inflammatory reaction to coronary stent implantation.

The role of acute endothelial aggression as a stimulus to an intense inflammatory response could be also present in unstable angina and would justify our findings and enhance the significance of our results.

It is interesting to note that in our study, we used a very careful methodology to include UA patients. All subjects were rigorously labeled by validated criteria as unstable angina to avoid interference of the necrosis factor as a confounding variable. Were admitted in a reference emergence unit to cardiologic patients which the pos-test probability is higher



than 80% to patients with typical chest pain and age equal or superior to 60 years. Moreover, at the end of the study 94% of the patients had the atherosclerotic disease confirmed by coronary angiography. Lastly, the homogeneity between groups was demonstrated by the lack of statistically significant differences in baseline characteristics.

Our findings with statistically significant differences (SBP and HR) may be explained by the trend towards more severe chest pain at admission in the diabetic group, contrary to the original concept<sup>22</sup> that is currently being highly questioned<sup>23</sup>.

Contrary to our study, Sanchez et al<sup>24</sup> observed that diabetic patients with non-ST elevation acute coronary syndrome showed higher inflammatory activity than non-diabetic ones. Nevertheless, diabetic patients had a higher leukocyte count than non-diabetic subjects, and the authors included no instrument in their methodology to detect silent infectious process, especially in diabetic women<sup>25</sup>. In our study, we conducted urinalysis in all the patients and explored the upper airways, including the auditory canal, to exclude silent infections. Moreover, there were no differences in leukocyte count measured at admission between diabetic and non-diabetic patients, suggesting no differences in previous inflammatory condition due to systemic infectious process.

Moreover, Sanchez did not describe admission and fasting blood glucose and lipid profile. It is important to underscore that the metabolic state of diabetes is characterized by hyperglycemia and dyslipidemia and is associated to endothelial lesion and consequently to increased inflammation markers<sup>19,26,27</sup>.

Regarding the positive correlation between hs-CRP concentrations and leukocyte count, Danesh et al<sup>28</sup> described a strong association between leukocyte count and coronary artery disease development and Stewart et al<sup>29</sup> observed higher mortality reduction associated to the use of pravastatin in those patients who showed increased leukocyte count values at admission.

In this study, upon analyzing all included patients with unstable angina, a weak correlation was observed between hs-CRP and total and LDL cholesterol, but superior to that found in previous studies<sup>30,31</sup> that did not include patients with acute coronary syndrome.

In our study, we did not observe higher in-hospital outcomes between diabetic and non-diabetic patients despite literature findings<sup>32</sup>, probably because of the reduced follow-up period (median 8 days) and few patients included (small sample), to find more in-hospital outcomes such as CHF, AMI and death (reduced power) in patients with unstable angina.

Another limitation was the fact that the mean time from onset of chest pain to admission in the emergency room (4 h) until collection of blood samples to measure hs-CRP may have been insufficient to find the inflammatory process in course.

However, this occurrence would not explain the similar hs-CRP results between two groups.

Our findings suggest that events involved in an acute coronary screening, such as unstable angina, propitiate an important, yet similar, inflammatory response between diabetic and non-diabetic patients, suggesting that inflammation response resulting from an acute coronary syndrome is more intense and acute than the inflammation response resulting from diabetes where the process is more continuous and slower and endothelial aggression is lasting. Another possibility is that the use of statin (in our study similar in both diabetic and non-diabetic patients) may be more effective in diabetic patients, since more intense anti-inflammatory effect was described in individuals with enhanced inflammatory activity<sup>29</sup>. It is important to underscore that our diabetic patients were well controlled (mean Hba1c=6.3%) and this finding may have decreased hyperglycemia impact on endothelial aggression.

Regarding everything we discussed in our study, some questions must be answered: Are the inflammation characteristics observed in diabetes different from those in acute coronary syndrome? Is there any way to evaluate this? Is the statin effect higher among diabetic than among non-diabetic patients? Could this superior effect explain the equality of inflammation activity between groups when they were admitted in the study with acute coronary syndrome? Is the inflammatory response in an acute coronary syndrome so intense that it could equilibrate inflammation activity between diabetic and non-diabetic patients?

Our findings allow us to conclude in this group of patients that inflammation activity is similar between diabetic and non-diabetic patients with unstable angina and in these patients hs-CRP showed a positive correlation with total and LDL cholesterol as well as with leukocyte count. These findings also underscore the importance of CRP as an endothelial aggression marker in acute coronary syndrome, as well as of the multifactorial aspect of the atherothrombosis process.

#### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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#### Study Association

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