Inflammatory, Lipid, and Metabolic Profile in Acute Ischemic Syndrome. Correlation with Hospital and Posthospital Events

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Objective

To associate the markers of lipid profile, inflammatory profile (high-sensitivity C-reactive protein [HSCRP] and fibrinogen), and metabolic profile (glucose determination) with hospital and post-hospital events in patients with acute ischemic syndrome (AIS) and to describe the predictors of mortality in this population.

Methods

A cohort study with 199 patients with AIS (unstable angina, acute myocardial infarction (AMI) with or without ST segment elevation) admitted to the intensive care unit (ICU) of a university cardiology Hospital, from March to November 2002. The previous diseases, the medication in use, and the coronary risk factors were recorded. The clinical events considered in the hospital were reinfarction, angina, heart failure (HF), ventricular fibrillation, and death; the posthospital events considered (30 days after hospital discharge) were reinfarction, angina, HF, death, and admittance for percutaneous procedures (PTCA) or for revascularization (MRS).

Results

HSCRP and altered glycemia were significantly associated with hospital events ($P = 0.03$ and $P < 0.01$, respectively); however, they were not associated with posthospital events ($P = 0.19$ and $P = 0.61$, respectively). Lipid profile and fibrinogen did not have a statistically significant association in any of the times assessed. Using multiple logistic regression, age ($P = 0.04$), previous AMI ($P = 0.04$), myocardial infarction with ST segment elevation ($P = 0.008$) or without ST segment elevation ($P = 0.048$), and altered glycemia ($P = 0.002$) were predictors of hospital mortality.

Conclusion

Increased HSCRP and altered glycemia were associated with a greater number of hospital events, whereas age, previous AMI, AMI with or without ST segment elevation, and altered glycemia were predictors of hospital mortality.

Key words

acute ischemic syndrome, lipid profile, inflammatory markers

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The name "acute ischemic syndrome" corresponds to a wide range of clinical manifestations including unstable angina, myocardial infarction initially without elevated ST segment, myocardial infarction with ST segment elevation, and sudden death.

The physiopathology of acute ischemic syndrome is the same in all its presentations. The rupture of the plaque and thrombosis are responsible for the change of stable coronary artery disease to unstable coronary artery disease. The intensity of clinical manifestations is related to the vessel caliber, to the rupture of the plaque, to the intensity of thrombosis, and to the presence of collateral circulation [1]. Vessel occlusion depends on several factors in addition to the plaque rupture, such as vessel diameter, shape of lesion, distal vasoconstriction, platelet aggregability, and balance between homeostatic and thromboembolic endogenous factors. Coronary obstruction is usually total in acute myocardial and partial in angina pectoris and myocardial infarction without ST segment elevation [2].

Increased plasma concentration of low-density lipoprotein cholesterol (LDL-C) is directly related to the development of coronary artery disease[3] and the low plasma concentration of high-density lipoprotein cholesterol (HDL-C) has been regarded as one of the strongest independent risk factors for coronary atherosclerotic disease[4]. New evidence indicates that small elevations in triglycerides increase the risk of coronary events and the development of coronary artery disease; it also leads to the formation of new lesions[5-7]. Patients with previous myocardial infarction, high levels of total cholesterol, increased LDL-C, and low levels of HDL-C, have an increased risk of reinfarction, death from coronary disease, and death from all causes [8-12]. Randomized clinical trials [13-17], meta-analysis of previous clinical studies [18] and angiographic studies [19-20] have reported the benefits of decreasing LDL-C in patients with coronary artery disease.

Advances in understanding of the physiopathology of atherosclerosis have revealed the essential role of inflammation throughout the stages of the disease, from the onset to the advanced complications, such as rupture and thrombosis of the plate. Dyslipidemias are associated with a greater inflammatory activity; however, classical risk factors for atherosclerotic disease, such as diabetes and blood hypertension, seem also to be associated with inflammation. More recently, it became evident that inflammation markers may identify high-risk individuals for adverse outcomes that cannot be predicted by risk-factor or lipid profile analysis alone [21]. Elevated levels of highly sensitive C-reactive protein (HSPCR) have been associated with future cardiovascular events [22]. Some studies have demonstrated that HSPCR levels were predictors of early and late mortality in patients with acute coronary syndrome [23-26].

Several clinical and epidemiologic studies have associated fibrinogen levels with cardiovascular diseases [27-29].

In diabetic patients, cardiovascular events account for 80% of the causes of mortality, and about 75% of the hospital admissions are due to disease complications [30]. The presence of diabetes is particularly harmful in women, especially in those with low levels of HDL-C. They have a greater risk of coronary artery disease than do men with the same condition [31].

The objective of our study was to assess the possible correlation of inflammation (HSCRP and fibrinogen), lipid profile, and metabolic profile (glycemia) with hospital and posthospital events in patients with acute ischemic syndrome, in the intensive care unit (ICU) at a university hospital. The predictors of mortality during hospital admission will also be described.

Methods

A cohort study was performed in the ICU of a cardiology referral center, from March to November 2002.

Patients no more than 10 hours after the onset of acute ischemic syndrome admitted to the ICU were included in the study. These patients fasted for 12 hours to provide samples for laboratory testing, and they all gave written consent to participate in the study that had been approved by the Ethics Committee of the hospital.

Exclusion criteria were onset of acute ischemic syndrome lasting longer than 10 hours, absence of 12-hour-fasting, and the presence of chronic inflammatory pathology.

Two hundred patients with acute ischemic syndrome were assessed and followed up during their hospital stay. One patient was excluded from the study at admittance because he was diagnosed with neoplasia.

Regarding the clinical profile, data were obtained from anamneses and physical examination on admittance. Variables studied were age, sex, skin color, weight, and height (indicated by the patient), when admitted to the ICU. Body mass index (BMI) was assessed using the height/weight formula[2]. Previous diseases, the medication in use, risk factors for coronary disease, and the therapeutics adopted were recorded.

Risk factors investigated were familial history of ischemic heart disease, smoking, diabetes mellitus, dyslipidemia, sedentary lifestyle, systemic blood hypertension, and alcohol consumption. Positive familial history included those that had first-degree relatives (age<55 years old in males and<65 years old in females) with a diagnosis of coronary artery disease or another type of atherosclerotic disease. Those patients who smoked regularly were considered smokers, and those who had quit smoking for at least one year were considered former-smokers. Patients who had a previous diagnosis of diabetes, those using hypoglycemic medication, and those with a fasting glycemia >126 mg/dL, in previous examinations or during admission were considered diabetic. Patients with systolic blood pressure >140 mm Hg and diastolic blood pressure > 90 mm Hg, or with a diagnosis of systolic blood hypertension before hospital admission, and those using antihypertensive medication were considered as having systemic blood hypertension. Those patients who did not exercise regularly were considered sedentary individuals. Dyslipidemia was determined by the presence of increased serum levels of LDL-C or low serum levels of HDL-C or a serum increase in triglycerides (LDL-C >130 mg/dL, HDL-C <40 mg/dL, and TG >150 mg/dL), or all of these. Patients with BMI >25 kg/m^2 were considered overweight. Regarding the use of alcohol, the investigation concerned its regular use.

The diagnosis of hospital and posthospital complications was based in the patients' charts. All the complications described in the charts were recorded; however, only the following were considered hospital events: acute myocardial re-infarction, chest angina, heart failure, ventricular fibrillation (recovered cardiac and respiratory arrest), and death. After the first month of hospital discharge, the patients were called, and the charts were reviewed for posthospital events. Posthospital events analyzed were acute myocardial infarction, angina, HF, and readmission for procedures (PTCA and MRS).

Five percent of the sample was lost to follow-up after hospital discharge (11 patients without telephone numbers, and without data for new appointments in the chart).

Blood samples were collected and assessed in the clinical analysis laboratory. Plasma cholesterol and triglycerides were assessed 3 times, using enzymatic kits (*Boehringer Mannheim Diagnostics*). HDL-C was determined, using the heparine-2M Mncl2 method and assessed with the same enzymatic kit used for total plasma cholesterol. LDL-C and VLDL-C were estimated using Friedwald's formula in mg/dL. When triglycerides were over 400, LDL was assessed using the enzymatic method, in a *Hitachi 902 appliance*. From the lipid and proteic variables, TC/HDL-C ratio and LDL/HDL-C were calculated. Non-HDL cholesterol was calculated with the formula NON-HDL= total cholesterol - HDL-C.

Glucose was dosed using commercially available kits (*Boehringer Mannheim Diagnostics*). Fibrinogen was assessed with a *CA 500 automated coagulation analyzer.* Highly sensitive C-reactive protein was dosed using the *Behring BN II Nephelometer*

All laboratory specimens were collected in a single sample, after a 12-hour fast within the first 24 hours of the onset of an ischemic coronary event. Considering that most of the population studied was admitted to the hospital with ischemic syndrome of < 6 hours evolution, the mean time for specimen collection was 18 hours, and the maximum time was 22 hours.

Sample size was estimated with the EPI-INFO 6.0 program, in 182 patients, with an alpha error of 0.05%, power of 80% and an incidence of events of 40% in the exposed population an RR of 2.0.

The statistical analysis was performed using the *Statistical Package for Social Sciences* (SPSS) 10.0 software. Numerical variables are described as mean and standard deviation, or medians and interquartile intervals (25-75%). Categorical variables are described as proportions. Chi-square tests were used for categorical variables and the Student *t* test or Mann Whitney's test for numerical variables. For the comparison between more than 2 groups (clinical syndromes), ANOVA and Kruskal-Wallis were used. For all comparisons, a 5% significance level was considered. Additionally, a multivariate analysis was performed with multiple logistic regression to assess the predictor factors of events and mortality, including the variables with P < 0.10 in the bi-variate analysis considered in the theoretical model. HF and AVC variables were discharged because of the low frequency of these diagnoses.

Results

One hundred and ninety-nine patients with acute ischemic syndrome were assessed; 35% (69) were females and 65% (130) were males. Mean age of patients was 61±12 years old.

Regarding the type of acute ischemic syndrome, 17% (34) were admitted due to unstable angina, 12% (23) due to acute myocardial infarction without ST segment elevation, and 71% (142) due to acute myocardial infarction with ST segment elevation. The most common types of acute myocardial infarctions were extensive anterior infarction in 21% (42) of the patients, and dorsal or posterior myocardial infarction in 19% (37) of the patients.

Table I demonstrates the general characteristics of patients at the beginning of the study, the analysis of the possible association of these characteristics, and the occurrence of hospital and posthospital events. Of the characteristics assessed (sex, age, AMI, type of AIS, previous cardiovascular disease, coronary risk factors, and medications used), age (P = 0.03), diagnosis of acute myocardial infarction with or without ST segment elevation (P= 0.05), and the previous diagnosis of stroke (P = 0.03) and HF (P=0.02) were associated with the development of hospital events. None of the general characteristics assessed demonstrated a statistically significant association with posthospital outcome.

It is important to note that 60% (118) of the patients from the population studied were hypertensive, 60.5% (129) were dyslipidemic, 42% (84) were smokers, and 55% had AMI above 25 kg/m^2. Forty percent of the patients were diagnosed with multiple metabolic disorders (tab. I).

Regarding lipid profile, 39.5% (79) of the patients had a normal lipid profile, 21.5% (43) had an increase in the total cholesterol, 17.0% (34) had hypertriglyceridemia, 11.5% (23) had low HDL-C, and 10.5% (21) had mixed dyslipidemia. Mean total cholesterol was 192 mg/dL, that of LDL-C was 118 mg/dL, that of HDL-C 46 mg/dL, and that of triglycerides was 137 mg/dL. Mean non-HDL cholesterol was 146 mg/dL, and the total cholesterol/HDL-C ratio was 4.36. No statistically significant difference was noted between the lipid variables and hospital and posthospital events (tab. II). Only 11% of the patients were taking statins before the onset of acute ischemic syndrome (tab. II)

Metabolic (glycemia) and inflammatory (fibrinogen and HSCRP) variables are presented in table III.

Regarding glycemia, 19.6% of the patients had a previous diagnosis of diabetes. In our sample, 42.5% (85) had glycemia > 126 mg/dL, with a 142 mg/dL mean. Altered glycemia was significantly associated with hospital events (P < 0.01); however, it was not associated with posthospital events (P = 0.61). Among the patients with glycemia >126 mg/dL, 57% (48 patients) had

Table I - General characteristics of hospital and porthospital events

General features	Hospital events			Post hospital events		
	With (n=77)	Without (n=122)	P	With (n=49)	Without (n=130)	P
Sex n (%)						
Female	26 (33.8)	43 (35.2)	0.95	18 (27.7)	47 (72.3)	1.00
Male	51 (66.2)	79 (64.8)		31 (27.2)	83 (72.8)	
Age (mean in years±SD)	63±12.4	59.4±11.3	0.03	60±11.8	60±11.6	0.88
BMI n(%)						
≤25	36 (40.4)	53 (59.6)	0.69	17 (21.0)	64 (79.0)	0.10
>25	40 (36.7)	69 (63.3)		32 (33.0)	65 (67.0)	
Diagnoses n (%)						
AI	07 (20.6)	27 (79.4)	0.05	06 (20.7)	23 (79.3)	0.66
AMI without elevation	11 (47.8)	12 (52.2)		05 (26.3)	14 (73.7)	
AMI with elevation	59 (41.5)	83 (58.5)		38 (29.0)	93 (71.0)	
Previous diseases n (%)						
Carotid	03 (3.9)	01 (0.8)	0.30	02 (100)	00	0.07
AMI	21 (27.3)	19 (15.6)	0.07	10 (28.6)	25 (7.4)	1.00
PVD	13 (16.9)	15 (12.3)	0.48	08 (34.8)	15 (65.2)	0.54
Stroke	07 (9.1)	02 (1.6)	0.03	02 (33.3)	04 (66.7)	0.66
DM	17 (22.1)	22 (18.0)	0.60	12 (36.4)	21 (63.6)	0.28
HF	04 (5.2)	00	0.02	00	02 (100)	1.00
Risk factors n (%)						
SBH	43 (55.8)	75 (62.0)	0.47	35 (30.4)	80 (69.6)	0.29
Alcohol	16 (21.9)	31 (25.6)	0.68	34 (29.1)	83 (70.9)	0.60
Dyslipidemias	50 (66.7)	79 (64.8)	0.90	19 (28.4)	48 (71.6)	0.95
Obesity	28 (37.3)	44 (36.1)	0.97	24 (25.3)	71 (74.7)	0.61
FH	37 (49.3)	70 (57.4)	0.34	22 (25.0)	66 (75.0)	0.59
Smoking	34 (45.3)	57 (46.7)	0.96	23 (24.0)	73 (76.0)	0.35
Sedentary lifestyle	44 (58.7)	61 (50.0)	0.30			
Previous med. n (%)						
ACE inhibitors	24 (31.6)	36 (29.5)	0.88	21 (37.5)	35 (62.8)	0.05
AAP	33 (42.9)	48 (39.3)	0.73	25 (36.2)	44 (63.8)	0.05
Statins	09 (11.7)	13 (10.7)	1.00	08 (42.1)	11 (57.9)	0.21
Diuretics	22 (28.6)	26 (21.3)	0.32	15 (33.3)	30 (66.7)	0.39
Anticoagulant	02 (2.6)	01 (0.8)	0.56	00	03 (100)	0.56
Hypoglycemic medication	08 (10.4)	14 (11.5)	0.99	06 (30.0)	14 (70.0)	0.79
Insulin	04 (5.2)	01 (0.8)	0.07	02 (50.0)	2 (50.0)	0.30
Nitrate	23 (30.0)	26 (21.3)	0.23	13 (30.2)	30 (69.8)	0.77
Beta-blockers	24 (31.2)	37 (30.3)	1.00	14 (25.9)	40 (74.1)	0.92
Anti-inflammatory	02 (2.6)	05 (4.1)	0.71	03 (42.9)	04 (57.1)	0.39

BMI - body mass index; UA - unstable angina; AMI - acute myocardial infarction; AMI - without elevation = acute myocardial infarction without ST segment elevation; AMI - with elevation AMI with ST segment elevation; PVD - peripheral vascular disease; DM - diabetes mellitus; HF - heart failure; SBH - systemic blood hypertension; FH - familial history of atherosclerotic disease; ACE inhibitors - angiotensin converting enzyme inhibitors; PA - platelet anti-aggregating.

Table II - Mean of lipid variables and presence or absence of hospital and posthospital events

Laboratory variables Mean±SD	Hospital events With (n=77)	Hospital events Without (n=122)	p	Posthospital events With (n=49)	Posthospital events Without (n=130)	P
Total cholesterol (mg/dL)	192.52 (±49.82)	192.20 (±41.78)	0.96	196.87 (±36.41)	194.23 (±47.04)	0.69
HDL-C (mg/dL)	47.55 (±11.95)	45.26 (±9.59)	0.16	46.20 (±10.93)	46.43 (±10.64)	0.90
CT/HDL-C	4.18 (±1.10)	4.39 (±1.08)	0.17	4.46 (±1.13)	4.32 (±1.11)	0.47
LDL-C calc. (mg/dL)	118.13 (±40.55)	119.23 (±35.86)	0.84	111.57 (±29.63)	121.49 (±39.41)	0.63
Non-HDL cholesterol (mg/dL)	144.96 (±45.41)	146.94 (±39.74)	0.74	150.67 (±36.04)	147.80 (±43.81)	0.65
Triglycerides (mg/dL)	134.09 (±110.04)	139.37 (±88.76)	0.71	153.67 (±127.86)	133.67 (±86.19)	0.23

Table III - Inflammatory and glycemia variables, hospital and posthospital events

Laboratory variables	Hospital events With (n=77)	Hospital events Without (n=122)	p	Posthospital events With (n=49)	Posthospital events Without (n=130)	p
Glycemia (mg/dL) mean (±SD)	157.37 (±69.24)	132.45 (±62.94)	0.01	143.40 (±70.99)	138.11 (±59.56)	0.61
Fibrinogen (mg/dL) mean (±SD)	247.09 (±82.13)	252.41 (±62.83)	0.61	251.08 (±69.77)	248.67 (±74.05)	0.84
HSCRP (mg/L) median (25-75)	0.79 (0.33-1.84)	0.47 (0.24-1.07)	0.03	0.69 (0.26-1.76)	0.52 (0.25-1.05)	0.19

HSCRP - High sensitivity C-reactive protein, median (25-75).

hospital events (4 acute myocardial reinfarction, 21 HF, 7 deaths) (fig.1), and 19% (15 patients) had posthospital events, 14 were hospital admittances (2 acute myocardial reinfarction, 4 HF, and 5 angina). Of the patients who died in the hospital, 70% had elevated glucose.

Median HSCRP was 0.55 mg/L (0.24-1.84), demonstrating a statistically significant association with hospital events (P=0.03), the same did not occur with posthospital events (P=0.19). Figure 2 shows the ratio between HSCRP levels and the incidence of hospital events where the same values occurred in patients with angina, heart failure, and those who died. However, in a multivariate analysis, HSCRP was not a predictor of hospital mortality.

Fibrinogen was > 277 mg/dL in 41% of patients, with a mean of 251 mg/dL. The difference for the association of fibrinogen with the incidence of hospital and posthospital events was not significant. (tab. III).

The most frequent events during hospital admittance were heart failure in 23.1% (46) of patients, angina in 8.5% (17) of patients, ventricular fibrillation in 11.6% (23) of patients, and reinfarction in 5.5% (11) of patients.

At hospital discharge, 76% (152) of patients were asymptomatic, 19% (38) were clinically stable, and 5% (10) died. Of these patients, 71.4% (142) underwent PTCA, 54% underwent primary PTCA, 2.5% (5) underwent PTCA and MRS, and 5% (10) of the patients underwent MRS.

Of the 48 patients who experienced events 1 month after hospital discharge, 36 were admitted again, 11 patients (5.5%) because of angina, 7 patients (3.5%) because of heart failure, and 5 patients (2.5%) because of acute myocardial re-infarction. Additionally, 5 patients were admitted again to the hospital for procedures (MRS/PTCA). One sudden death occurred at home.

In multiple regression logistics, the factors that remained as predictors of hospital mortality were age, previous acute myocardial infarction with or without ST segment elevation, and altered glycemia (tab. IV).

Discussion

The ratio between lipid profile and risk of cardiovascular diseases has been well demonstrated in clinical and observational studies[32-34]. These studies have demonstrated that the decrease in cholesterol, especially in LDL-C, helped to prevent coronary artery disease and to reduce coronary events, both in primary (WOSCOPS, AFCAPS/TexCAPS), and in the secondary prevention (4S,CARE, LIPID and HPS) [13-17,35].

Although in this study mean serum levels of total cholesterol (192 mg/dL), of LDL-C (118 mg/dL), HDL-C (46 mg/dL), and triglycerides (137 mg/dL) were not considered increased, it is important to note that 60.5% of patients had some alteration in lipid levels (21.5% had increased total cholesterol, 17% had hypertriglyceridemia, 11.5% had low HDL-C, and 10.5% had mixed dyslipidemia). Additionally, this is a high cardiovascular risk population with several risk factors as follows: 60% were hypertensive, 42% were smokers, 53.8% had a familial history of atherosclerotic disease, 42.5% had altered glycemia, and 55% had BMI above 25 kg/m^2. These data reinforce those of the literature and call attention to the importance of associating risk factors to determine the risk of coronary events of an individual rather than assessing one isolated risk factor. Several studies have indicated that cholesterol levels decrease during acute myocardial infarction [36-41]. Lipid and lipoprotein variation after acute myocardial infarction occur within 24-48h after the onset of precordial pain and are made evident by decreases in total cholesterol (24% to 70% baseline), in LDL-C (31%), HDL-C (12-18%), and by increases in triglyceride levels (25%). In this study, samples were collected before the acute ischemic syndrome had evolved for 24 hours (mean time was 22h), to eliminate the possibility of an acute-phase reaction. A point to be considered to explain the results obtained is the current knowledge that individuals with comparable serum levels of LDL-C and HDL-C can also have fairly different levels of risk for coronary artery disease because of the differences in subclass distribution of these lipoproteins; however, this was not the objective of our study [42]. Patients with a predominance of small/dense LDL and/or small HDL had a very atherogenic profile.

Clinical studies have demonstrated that systemic inflammation markers are strong predictors of clinical events in coronary artery disease [43]. CRP is a predictor of cardiovascular events. Liuzzo et al [24] studied patients with stable angina, unstable angina, and acute myocardial infarction, using a cut point for normal/high

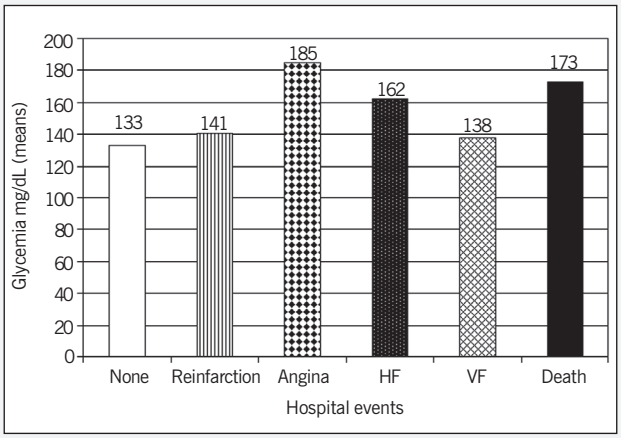

Fig. 1 - Glycemia and incidence of hospital events. HF: heart failure; VF: ventricular fibrilation.

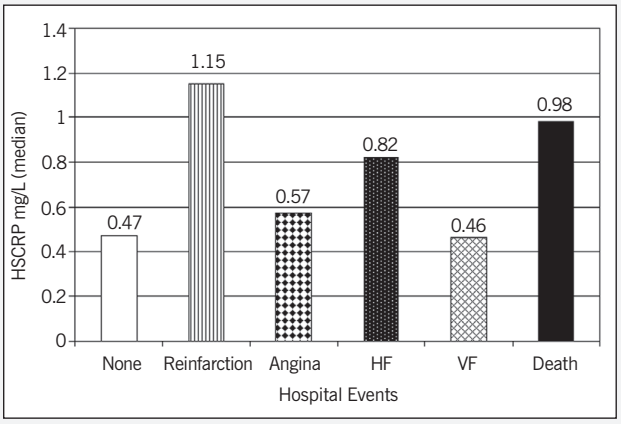

Fig. 2 - HSCRP and incidence of hospital events.HF: heart failure; VF: ventricular fibrilation.

Table IV - Hospital mortality predictors

Variable	P	*Odds Ratio*	Confidence Interval (95%)
Age	0.04	1.03	1.00 – 1.06
Previous AMI	0.04	2.3	1.04 – 5.0
AMI with ST segment elevation	0.008	5.7	1.6 – 2.04
AMI without ST segment elevation	0.48	2.7	1.01 – 7.4
Glycemia (>111 and <126mg/dL)	0.04	2.5	1.04 – 6.1
Glycemia >126mg/dL	0.002	3.5	1.6 – 7.9

HSCRP at 3 mg/L. Patients with unstable angina had greater serum concentrations of HSCRP than those patients with stable angina, more ischemic episodes, and greater risk of death than those patients with low HSCRP (4.8±2.5/1.8 ±2.4; P=0.02). In patients with acute myocardial infarction, more increased levels of HSCRP are correlated with a greater area of myocardial necrosis[44,45]. In a retrospective study of 37 patients with acute myocardial infarction, HSCRP ≥2 mg/L correlated with a greater risk of myocardial rupture [46]. In patients with unstable angina, HSCRP correlates with a greater risk of coronary events (acute myocardial infarction, need for angioplasty or myocardial revascularization surgery, or sudden death) [47-49].

Our study reinforces the data from the literature. HSCRP was significantly associated with a greater incidence of hospital events. No significant difference occurred between HSPCR levels and the incidence of posthospital events.

CRP levels increased after acute myocardial infarction, reflecting the level of tissue lesion. Kushner et al [50] found a small increase in CRP after acute myocardial infarction, twice as much as the mean in 8h and a peak at 2-4 days, returning to baseline after 3-4 weeks. In acute ischemic syndrome, CRP may increase modestly,[51] and this increase seems to be restricted to patients with tissue necrosis demonstrated by the levels of troponin [52]. An isolated measure of CRP, after infarction, is not predictive of future events[53], unless it is found right after the onset of symptoms and before the acute phase reaction [54]. Definition of increased levels of HSCRP has varied in different studies. These differences are because of the patients' characteristics, including age, obesity, smoking, DAC extension, regional differences (prevalence of *C. pneumoniae* or positivity for *cytomegalovirus*), use of medications that can affect CRP levels (aspirin, statins, estrogens) [55]. In the classification of risk for future cardiovascular events, HSCRP levels have been considered low when they were < 1 mg/L; mild when they were 1 to 3 mg/L; and increased when they were > 3 mg/dL. In our study, HSCRP was between 0.05 and 2.90 mg/L in approximately 90% of patients. Despite being an acute-phase marker, CRP has an individual variability similar to that associated with cholesterol tracking. Several investigators have recommended 2 measures of CRP using the mean or the lower value to determine vascular risk. This is a practice that is in accordance with cholesterol evaluation[21]. In the present study, HSCRP was assessed within the first 24h of the onset of the picture and by only one determination.

Fibrinogen, an acute-phase marker, plays an important role in platelet compliance and aggregation. ECAT (*European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study*) [27] and PROCAM (*Prospective Cardiovascular Münster*) studies [56] demonstrated an interaction between total cholesterol, LDL-cholesterol, and fibrinogen. In the ECAT study, the presence of moderate and high levels of fibrinogen increased the cardiovascular risk in individuals with hypercholesterolemia, whereas low levels of fibrinogen identified patients with smaller risk of events even in the presence of increased concentrations of cholesterol. In the PROCAM study, a greater risk of events in individuals with increased fibrinogen and LDL-C was observed. Becker et al [29] verified that a fibrinogen level in the plasma >300 mg/dL is associated with an increase in death, acute myocardial infarction and spontaneous ischemia in patients with angina and infarction without ST segment elevation.

In our study, a statistically significant difference did not occur regarding the level of fibrinogen between events and the absence of events, in both hospital and posthospital events. Mean fibrinogen found in unstable angina was 262 mg/dL, in acute myocardial infarction it was 245 mg/dL, and in infarction with ST segment elevation it was 262 mg/dL. Patients experiencing hospital events had, on average, 242 mg/dL of fibrinogen, and patients with posthospital events had 251 mg/dL of fibrinogen.

In the study performed, 42% of patients had altered glycemia (>110 mg/dL), and only 19% had a previous diagnosis of diabetes. Among the patients with altered glycemia, 86% (72 patients) had infarction as an acute ischemic syndrome manifestation. Mean glycemia during hospital events was 157 mg/dL, and during posthospital events it was 143 mg/dL. Glycemia was significantly associated with hospital events (P = 0.01) and with hospital mortality (P = 0.002). Among the deaths occurring in the hospital phase, 70% of the patients had elevated glucose.

Epidemiologic studies [57] demonstrates that individuals with

diabetes mellitus present have a relative risk for cardiovascular disease increased 2 to 4 times, when compared with individuals without diabetes. Some studies show that, in patients with diabetes, the risk of cardiovascular disease increases with the elevation of glucose concentration in the plasma. Patients with uncontrolled diabetes, increase in fasting glycemia, or increase in glycated hemoglobin, have an increased risk of cardiovascular disease and mortality, when compared with individuals with controlled glycemia. [58-60]. Haffner et al [61] assessed cardiovascular mortality for an 8-year period in diabetic and nondiabetic patients, with or without previous acute myocardial infarction; they concluded that the mortality of a diabetic individual without previous infarction is equal to the mortality of a nondiabetic individual with previous acute myocardial infarction. Wahab et al[62] determined that blood glucose is an independent risk factor of mortality in acute myocardial infarction, in the thromboembolic age, in 1664 patients. They concluded that hyperglycemia is associated with a worse evolution of acute myocardial infarction even in patients without a previous diagnosis of diabetes and that hyperglycemia added greater risk, regardless of body mass index or history of increased glucose, suggesting that its status *per se* may contribute to an adverse outcome or may be a key marker. Several studies [63-65] suggest that hyperglycemia, in nondiabetic patients is, in fact, undiagnosed diabetes. Furthermore, studies suggest a role of stress in the increase of glucose in acute myocardial infarction; however, it is not clear whether this leads to a worse evolution or whether it is only a marker of a worse prognosis. Stress hyperglycemia may be a marker of extensive myocardial damage [66]. Hyperglycemia, both acute and chronic, is also related to involvement of endothelial function[67,68], catecholamine release, decrease in insulin sensitivity [69] and osmotic diuresis. The last leads to a decrease in myocardial contractility [70].

In our study, hospital mortality was 5%, and posthospital mortality was 0.5% in 60 days. In the logistic regression, the mortality predictors were age, previous acute myocardial infarction with or without ST segment elevation, and altered glycemia.

Our data reinforce the importance of differentiating the role of risk factors for a disease and that of the factor predictive of events (prognostic factor). We have studied a population with several classic risk factors for coronary disease, such as dyslipidemia, smoking, systemic blood hypertension, positive familial history of ischemic heart disease, but these risk factors do not contribute to worsen the prognosis of this group of patients. The increase of inflammatory markers, such as HSCRP, and metabolic markers, such as glycemia were related to a greater incidence of hospital events. Regarding increased glycemia, it also contributed to a greater risk of hospital mortality. Therefore, casual factors are not necessarily correlated to a worse prognosis of acute ischemic syndrome.

In conclusion, this study did not find any association between lipid profile and fibrinogen with the hospital and posthospital outcome in patients with acute ischemic syndrome. High sensitivity C-reactive protein and altered glycemia were associated with a greater incidence of hospital events but were not significantly associated with posthospital events. The mortality predictors were age, previous acute myocardial infarction with or without ST segment elevation, and altered glycemia.

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