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Characterization of acute coronary syndrome in women

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Abbreviations
ACS: acute coronary syndrome
AMI: acute myocardial infarction
CAD: coronary artery disease
CHF: congestive heart failure
CVD: cardiovascular diseases
NSTE-ACS: non-ST-segment elevation acute coronary syndrome
PCI: percutaneous coronary intervention
HBP: high blood pressure
STE-ACS: ST-segment elevation acute coronary syndrome

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ABSTRACT

Introduction: Women suffering from acute coronary syndromes (ACS) have worse prognosis and are prone to major adverse events.

Objectives: To characterize female patients with ACS admitted to the Hospital Dr. Carlos J. Finlay (Havana, Cuba) between June 2012 and June 2018.

Methods: A cross-sectional descriptive study with 1252 women was carried out. Two groups were defined: ST-segment elevation ACS (STE-ACS) and non-ST-segment ACS (NSTE-ACS). Study variables were: age groups, risk factors, angiographic characteristics and in-hospital major adverse events.

Results: Mean age was 66.2 ± 11.9 years old, NSTE-ACS predominated (73.4% vs 26,6%). High blood pressure (95.2%), tobacco smoking (37.9%) and diabetes mellitus (36.3%) were the prevailing risk factor, with significant differences in favor of NSTE-ACS (p <0.004). Glycemia values (69.1% vs 51.5%, p <0.0001) and total cholesterol (46.2% vs 16.6%, p <0.0001) were significantly higher in the NSTE-ACS. A 29.3% of cases underwent coronary angiography where a high prevalence of serious lesions of 73.3% and an incidence of left main coronary artery disease of 4.9% were found. A 23% presented major adverse events, heart failure (35.1%) and cardiogenic shock (18.1%) being the most prevalent ones. Cardiogenic shock predominated as cause of death in STE-ACS (45.1 vs 11,8; p<0,0001). Both major adverse events were directly related to mortality (3.8%).

Conclusions: There is a predominance of NSTE-ACS in women with ACS in postmenopausal ages. High blood pressure, diabetes mellitus and tobacco smoking were the main clinical characteristics. Cardiogenic shock and heart failure were the major adverse events most frequently associated to mortality.

Keywords: Acute coronary syndrome, females, Rsik factors, Complications, Cardiogenic shock

Caracterización del síndrome coronario agudo en mujeres

RESUMEN

Introducción: Las mujeres afectadas por síndromes coronarios agudos (SCA) tienen peor pronóstico y son más propensas a presentar complicaciones.

Objetivos: Caracterizar las pacientes con SCA ingresadas en el Hospital Dr. Carlos J. Finlay (La Habana, Cuba) entre junio de 2012 y junio de 2018.

Método: Estudio descriptivo transversal con 1252 mujeres. Fueron definidos 2 grupos: SCA con (SCACEST) y sin elevación del segmento ST (SCASEST). Las va-

Authors' contribution
LOCR: Idea and design of the research, raw data collection and analysis as well as final report confection.
RMGR y RRD: Idea and design of the research. Final report review.
YCF, EVC y GBA: Information search, raw data collection as well as helping in the final report confection.
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riables de estudio fueron: grupos de edad, factores de riesgo, características angiográficas y complicaciones intrahospitalarias.
Resultados: La media de edad fue 66,2 ± 11,9 años, predominó el SCASEST (73,4% vs. 26,6%). La hipertensión arterial (95,2%), el tabaquismo (37,9%) y la diabetes mellitus (36,3%) fueron factores de riesgo más prevalentes, con diferencias significativas a favor del SCASEST (p<0,004). Los valores de glucemia (69,1% vs. 51,5%; p<0,0001) y colesterol total (46,2% vs. 16,6%; p<0,0001) fueron significativamente mayores en el SCASEST. A un 29,3% de los casos se les realizó coronariografía, donde se encontró una alta prevalencia de lesiones significativas (73,3%) y una incidencia de enfermedad de tronco de 4,9%. Un 23% presentó complicaciones, las más prevalentes fueron la insuficiencia cardíaca (35,1%) y el shock cardiogénico (18,1%), esta última predominó como causa de muerte en el SCACEST (45,1 vs. 11,8; p<0,0001). Ambas complicaciones se relacionaron directamente con la mortalidad (3,8%).
Conclusiones: En las mujeres con SCA predominó el SCASEST en edades posmenopáusicas. La hipertensión arterial, la diabetes mellitus y el tabaquismo constituyeron las principales características clínicas. La insuficiencia cardíaca y el shock cardiogénico se asociaron frecuentemente a la mortalidad.
Palabras clave: Síndrome coronario agudo, mujeres, Factores de riesgo, Complicaciones, shock cardiogénico

INTRODUCTION

Cardiovascular diseases (CVD) are the top cause of death in the world. It is estimated that 23.6 millions of people will die from ischemic heart disease in 2030[1]. This disease has a major impact on the individual who suffers from it, affecting his or her life quality and it is directly responsible for significant economic costs[2]. The CVD have a different incidence, evolution and prognosis in the population depending on gender. Society has not recognized these differences until few years ago, which has remarkably affected women. Thus, three out of every ten deaths that take place in female population are directly related to ischemic heart disease[1-3].

This disease is the top cause of death in both genders and it is more frequent after 50 years old in women in a 2:1 ratio. In recent decades the incidence of acute myocardial infarction (AMI) has increased in women between 35 and 54 years old. According to the World Health Organization (WHO), out of 16.7 million deaths per year worldwide, approximately seven million are caused by ischemic heart disease. Nearly 68 000 women died in Spain due to CVD during 2015 and this very same year 56 000 men died due to the same cause. This shows that 10 000 more women die due to CVD than men[4-10]

In Cuba, CVD are also the top cause of death, followed by malignant tumors and cerebrovascular disease. Specifically, in females, ischemic heart disease is the top cause of death in age groups over 60 years old. The considerable increase in the number of females who died during 2016 from the 40-59 age group is noteworthy, with a rate of 29.1 per 100.000 inhabitants[11-14].

Female patients are a special population group because of how CVD manifests differently from what is classically described. In addition, the onset of coronary artery disease (CAD) in women has been brought forward due to the increase of risk factors at present, which means that its evolution has changed in an unfavorable way. Bearing in mind that preventive actions in term of health education, changes in lifestyle and habits, as well as clinical evolution of CAD, can be exercised on almost all risk factors, it is necessary to determine the clinical and demographic characteristics of women with acute coronary syndrome (ACS) admitted to our department during the study period.

METHOD

A descriptive, cross-sectional study was carried out including 1 252 female patients admitted to the Coronary Care Unit of the *Hospital Carlos J. Finlay* (Havana, Cuba), with a diagnosis of ACS between June 2012 and June 2018. The study's population consisted of all admitted patients and only those in whom, for whatever reason, the results of all study variables could not be obtained were excluded.

Coronary angiography was performed according

to the indications established in the department, with prior signature of the informed consent.

Every patient´s data was collected from the medical records and recorded in the department`s database. The information was processed on microcomputers using Microsoft Office 2007 Word and Excel systems. MedCalc statistical software was also used.

Univariate statistical procedures were used with the calculation of central tendency measures (mean and median) and dispersion (standard deviation and range) for quantitative variables. For the qualitative variables frequency distributions with percentage calculation were used. Bivariate statistical methods were also used for comparisons of two groups and determination of the relationship among variables with the Chi square test in its different variants. For quantitative variables, Student's t-test was used to compare two means with unequal and unknown variance with a significance level of 5%.

Once the relationship among variables was established and the result was considered as a possible risk, the cross-product test (OR) was used to determine its significance and strength with a 95% confidence interval, calculated by Woolf's method. The results were presented in tables and they were always collective in order to respect the individuality and the confidentiality established by medical ethics.

RESULTS

Table 1 shows the clinical forms of ACS according to age groups. There was a predominance of patients with a diagnosis of non-ST-segment elevation ACS (NSTE-ACS) (73.4%) and 60-79 years old patients predominated in both groups (56.7% for STE-ACS vs. 54.4% for NSTE-ACS).

When cardiovascular risk factors were associated with the clinical forms of the disease (**Table 2**), high blood pressure (95.2%), tobacco smoking (37.9%) and type II diabetes mellitus (36.3%) were the most prevalent ones, with significant differences in patients with NSTE-ACS (p<0.004). There was a remarkable presence of smokers in the STE-ACS group (45.6% vs. 35.1%, p<0.0001). It should be highlighted that 36.1% of patients presented the association of three or more risk factors, with no significant differences for both clinical forms (p=0.83).

The 56.2% of the sample presented high basal blood glucose levels (**Table 3**) with a predominance in the STE-ACS group (69.1% vs. 51.5%, p< 0.0001). A similar situation took place regarding total cholesterol (46.2% vs. 16.6%, p<0.0001). The hypertriglyceridemia was documented in 36.6% of patients and it was more prevalent in the NSTE-ACS group (15.9% vs. 44.1%, p<0.0001).

Only a 29.3% of patients underwent coronary angiography (**Table 4**). The 73.3% of them presented a significant CAD with predominance of two or more vessel disease (37.3%). Left main coronary artery (LMCA) disease was significant in patients with NSTE-ACS (4.3% vs. 5.1%, p<0.0001). Percutaneous coronary intervention (PCI) was performed in a 44.7% of all patients who underwent coronary angiography.

Table 1. Distribution of patients according to age groups and clinical presentation form of the acute coronary syndrome.

Age groups (years)	Clinical forms		Total (66.2 ± 11.9)	p
	STE-ACS (66.9 ± 11.9)	NSTE-ACS (65.9 ± 11.9)		
20 - 39	0	7 (0.8)	7 (0.6)	0.39
40 - 59	94 (28.2)	279 (30.4)	373 (29.8)	
60 - 79	189 (56.7)	500 (54.4)	689 (55.0)	
80 ≥	50 (15.1)	133 (14.4)	183 (14.6)	
Total	333 (26.6)*	919 (73.4)*	1252 (100)	

Data express n (%).
* Percentage calculated based on the total of the row. The rest of them were calculated per columns.
STE-ACS/NSTE-ACS: ST-segment elevation/non- ST-segment elevation acute coronary syndrome.
Source: Database.

Table 2. Distribution according to the presence and association of the different cardiovascular risk factors depending on the clinical forms of the acute coronary syndrome.

Risk factor	Clinical forms		Total (n=1252)	p
	STE-ACS (n=333)	NSTE-ACS (n=919)		
High blood pressure	305 (91.6)	853 (92.8)	1158 (92.5)	> 0.05
Type II diabetes mellitus	123 (36.9)	331 (36.0)	454 (36.3)	> 0.05
Previous infraction	62 (18.6)	228 (24.8)	290 (23.2)	> 0.05
Dyslipidemia	23 (6.9)	260 (28.3)	283 (22.6)	**0.004**
Tobacco smoking	152 (45.6)	323 (35.1)	475 (37.9)	**< 0.0001**
Number of risk factors per patient				
1	93 (27.9)	249 (27.1)	342 (27.3)	
2	109 (32.8)	321 (34.9)	430 (34.3)	0.83
≥ 3	120 (36.0)	331 (36.0)	451 (36.1)	

Data express n (%).
STE-ACS/NSTE-ACS: ST-segment elevation/non-ST-segment elevation acute coronary syndrome.

Table 3. Distribution of the studied sample according to the variables of fasting blood glucose values and lipid profile depending on the forms of presentation of the ACS.

Variables	Clinical forms		Total (n=1252)	p
	STE-ACS (n=333)	NSTE-ACS (n=919)		
Fasting blood glucose ≥ 5.5 mmol/L	230 (69.1)	473 (51.5)	703 (56.2)	<0.0001
Total cholesterol ≥ 5.2 mmol/L	154 (46.2)	153 (16.6)	307 (24.5)	<0.0001
Triglycerides ≥ 2.1 mmol/L	53 (15.9)	405 (44.1)	458 (36.6)	<0.0001

Data express n (%).
STE-ACS/NSTE-ACS: ST-segment elevation/non-ST-segment elevation acute coronary syndrome.

Table 4. Distribution of patients according to the results of the coronary angiography/PCI depending on the presentation forms of the acute coronary syndrome.

Cathegories	Clinical forms		Total (n=367)	p
	STE-ACS (n=92)	NSTE-ACS (n=275)		
Coronary angiography*	92 (27.6)	275 (29.9)	367(29.3)	0.28
CAD (stenosis > 50%)	84 (91.3)	185 (67.3)	269 (73.3)	0.03
LMCA	4 (4.3)	14 (5.1)	18 (4.9)	< 0.0001
One-vessel CAD	42 (45.7)	72 (26.2)	114 (31.1)	0.03
Two or more vessel CAD	38 (41.3)	99 (36.0)	137 (37.3)	0.08
PCI	63 (68.5)	101 (36.7)	164 (44.7)	0.04

Data express n (%).
STE-ACS/NSTE-ACS: ST-segment elevation/non- ST-segment elevation acute coronary syndrome.
* The percentages of this row were calculated based on the number of cases of each group (STE-ACS [n=333], NSTE-CAS [n=919]) as well as on the total (n=1 252).
CAD: coronary artery disease, LMCA: left main coronary artery, PCI: percutaneous coronary intervention.

A 23% of all the studied women presented at least one major adverse event (**Table 5**). Congestive heart failure (35.1%), cardiogenic shock (9.7%) and post-infarction angina (18.1%), were the most prevalent ones, with significant differences of CHF in the NSTE-ACS group (p=0.007). Cardiogenic shock was significantly higher in the STE-ACS group (16.7% vs. 3.3%, p<0.0001).

Table 6 shows data regarding mortality and its causes according to the different clinical forms of the ACS. There were 48 deaths, which represents a 3.8% of the total. The STE-ACS was significantly associated to a higher mortality (9.3% vs. 1.8%, p<0.0001) due to any cause. The CHD and the cardiogenic shock were the major adverse events most frequently associated to the patients' fatal outcome. It is noteworthy the predominance of cardiogenic shock as cause of death in the STE-ACS group (45.1% vs. 11,8%).

DISCUSSION

The current study included 1 252 female patients with a diagnosis of ACS during six consecutive years.

Table 5. Distribution of patients according to the occurrence of major adverse events and the clinical forms of the acute coronary syndrome.

Major adverse events	Clinical forms		Total (n=288)	p
	SCACEST (n=138)	SCASEST (n=150)		
Heart failure	34 (24.6)	67 (44.7)	101 (35.1)	**0.007**
Shock	23 (16.7)	5 (3.3)	28 (9.7)	**< 0.0001**
Post-infraction angina	31 (22.4)	21 (14.0)	52 (18.1)	0.092
Reinfraction	9 (6.5)	4 (2.7)	13 (4.5)	0.206
Bleeding	5 (3.6)	10 (6.7)	15 (5.2)	0.36
Respiratory	4 (2.9)	8 (5.3)	12 (4.2)	0.47
Atrial fibrillation	0	17 (11.3)	17 (5.9)	-
Ventricular fibrillation	12 (8.7)	5 (3.33)	17 (5.9)	0.094
Others	9 (6.5)	13 (8.6)	22 (7.6)	0.07

Data express n (%).
STE-ACS/NSTE-ACS: ST-segment elevation/non- ST-segment elevation acute coronary syndrome.

Table 6. Distribution of patients according to fatal major adverse events according to the clinical forms of the acute coronary syndrome.

Fatal major adverse events	Clinical forms		Total (n=48)***	p
	STE-ACS (n=31)*	NSTE-ACS (n=17)**		
Heart failure	6 (19.4)	5 (29.4)	11 (22.9)	< 0.0001
Shock	14 (45.1)	2 (11.8)	16 (33.3)	< 0.0001
Reinfraction	3 (9.7)	1 (5.9)	4 (8.3)	< 0.0001
Bleeding	2 (6.5)	0	2 (4.2)	-
Respiratory	1 (3.2)	2 (11.8)	3 (6.3)	< 0.0001
Ventricular fibrillation	4 (12.9)	4 (23.5)	8 (16.7)	< 0.0001
Others	1 (3.2)	3 (17.6)	4 (8.3)	< 0.0001

Data express n (%).
STE-ACS/NSTE-ACS: ST-segment elevation/non- ST-segment elevation acute coronary syndrome.
* 31/333 (9.3%)
** 17/919 (1.8%)
*** 48/1252 (3.8%)

A predominance of HBP, diabetes mellitus and tobacco smoking predominated with a higher incidence in the 60-79 years old age group, with a mean age of 66.2 ± 11.9 years old. This finding is clearly related to the already well-known increase in the prevalence of CAD as women grow older, especially in the postmenopausal stage[15,16].

In the study by Gonzalez and Gonzalez[17] on smoker women with ACS, elderly was a peculiar finding and it was generally associated with mortality. Other studies show that women with high-risk NSTE-ACS are older and have more diabetes mellitus and HBP, receive recommended medication less frequently, and they undergo coronary angiography and percutaneous coronary revascularization procedures less frequently. Due to their more unfavorable clinical characteristics, major adverse events such as death, reinfarction, heart failure, stroke and bleeding are frequent[17-20], all of which coincide with our results.

The NSTE-ACS is more prevalent than the STE-ACS in women. In this study a predominance of the NSTE-ACS (73.4% vs. 26.6%) in postmenopausal stages was demonstrated. Redondo *et al.*[21] and other authors[22-24] report data from a study on the long-term prognosis of patients with NSTE-ACS and coronary arteries without significant stenosis, and they emphasize that the most frequent form of presentation of ACS in women is without ST-segment elevation and, when this happens, it is usually severe; therefore, the incidence of major adverse events is higher.

The probability of presenting an ACS is closely related to the number and association of risk factors, and in women this is increased, which gives them a more adverse prognosis. In addition, women are at a disadvantage in the adoption of the recommended diagnostic and therapeutic measures, which can influence prognosis[17,25-28].

In a research carried out in Spain including 48 369 patients with ACS, a 24.3% were women. In patients with NSTE-ACS, women had a higher mean age than men and a much more unfavorable risk profile with a higher prevalence of HBP, dyslipidemia and type II diabetes mellitus[29,30]. Similar results were found in our study, where HBP and diabetes mellitus predominated, with no significant differences with respect to the type of ACS.

A 37.9% of the total of our patients were smokers, with a significant predominance in the STE-ACS group (45.6% vs. 35.1%, p<0.0001). It is frequent the association in young women between a diagnosis of STE-ACS and tobacco smoking as the only causative factor. Smoking doubles the risk of ACS in women, with a relative risk of 2.4 compared to the 1.43 for men, and smoking cessation is associated with a reduction in the risk of death due to AMI of around 65%[31-34]. Alonso *et al.*[34] and other authors have reported that among women with STE-ACS there were higher rates of HBP (60.2% vs. 38%, p <0.001) and diabetes mellitus (38.4% *vs.* 20.3%, p<0.001) compared to men; while no significant differences were found in the prevalence of dyslipidemia[34-37.]

Hyperglycemia in the acute phase of ACS in diabetic and non-diabetic patients has been associated to major adverse events such as: CHF, cardiogenic shock, ventricular arrhythmias and death. In the studied sample, more than half of women had high blood glucose values at the moment of the admission (56.2%), with a significant predominance of patients with STE-ACS (69.1% vs. 51.5%, p<0.0001). Otten *et al.*[38], as well as other authors[39-41], show in their studies that impaired fasting blood glucose is an independent predictor of in-hospital adverse events in female patients with ACS. In general, it is accepted that high basal blood glucose values are proportional to the severeness and extent of the myocardial ischemia and necrosis, with a strong impact on short and long-term survival.

As for the lipid profile variables, in our study only total cholesterol and triglyceride values were evaluated due to limitations for the determination of lipoproteins, so that the research lacks of the additional information they provide. Nevertheless, both cholesterol and triglycerides are indicators of the impact on risk in women with ACS, as suggested by López *et al.*[42] who compared the differences between genders and their impact on the evolution and prognosis of ACS.

Coronary angiography is the golden standard for evaluating the coronary anatomy, which has drastically changed the understanding, stratification and treatment of CAD[37,43]. Its performance is significantly lower in women due to the aforementioned reasons. In this research, from a total of 1 252 patients, only 367 (29.3%) were angiographically assessed. This could be due to the fact that the form of presentation of pain in women is often insidious and overlapping, to delays in seeking medical attention and, in addition, to the fear of a higher risk of major adverse events compared to men in this type of examination[38,44,45]. The GUSTO IIB study reported that coronary angiography was performed in 41.7% of women (compared to 59.3% in men) and the incidence of

coronary arteries without significant lesions was approximately the double in females. In our study, the incidence of non-obstructive CAD was less than 30%. Considering that most of the patients did not have their coronary tree evaluated, the real situation of CAD in these patients cannot be known with certainty, which also represents a limitation of this study, as happened in the work of Tamis-Holland *et al.*[46].

When assessing CAD, of the women who underwent coronary angiography, 73.3% had significant coronary lesions, with predominance in the STE-ACS group. Two-vessel CAD was demonstrated in 37.3% of cases and there was a prevalence of left main coronary artery involvement of 4.9%, especially in patients with NSTE-ACS. In the study by Borges Moreno *et al.*[47] it was found that the number of vessels affected increases with aging: 15.4% in patients between 60 and 69 years old, and 13.6% in those older than 70 years old.

The clinical outcome after a PCI in women is a challenge, since it is associated with an increase in major adverse events during and after the procedure. Women present more often a diffuse coronary artery disease which is very unfavorable for the PCI[37,45]. In this study, of all patients undergoing coronary angiography, only 44.7% underwent PCI, with a predominance of STE-ACS (68.5% vs. 36.7%, p=0.04) and most of them were primary angioplasties. Young patients with AMI have a favorable evolution after the acute event, with fewer major adverse events; even so, there are differences regarding gender, and it is women who, after suffering an ACS, have a worse evolution with more major adverse events, including those taking place during the PCI, in contrast to men[48,49].

When analyzing the major adverse events in the studied patients, CHF (35.1%), post-AMI angina (18.1%) and cardiogenic shock (9.7%) were the predominant adverse events. This last one was more frequent in patients with STE-ACS (16.7%), whereas CHF occurred more in patients with NSTE-ACS (44.7%). Patients with NSTE-ACS are at greater risk of major adverse events given the extent and severeness of the ischemia accompanying total occlusion of an epicardial coronary artery. Barrabes *et al.*[50] report an increased risk of severe ventricular dysfunction and cardiogenic shock in women with STE-ACS. Borrás *et al.*[51] identified that in patients of both genders with ACS, CHF was the most frequently fatal in-hospital major adverse event in females; and Domínguez-Cervantes *et al.*[52] state that the most frequent major adverse events found in women with ACS were cardiac arrhythmias (14.8%), CHF (10.0%) and reinfarction (6.0%), results somewhat similar to ours.

Cardiac arrhythmias are frequent during the ACS, and those with a ventricular origin are of worst prognosis. In our series, atrial fibrillation was documented more frequently in the group of patients with NSTE-ACS (11.3%), whereas ventricular fibrillation was observed as a major adverse event in both study groups, but mostly in the series of patients with STE-ACS (8.7%), results that coincide with those of other authors[53-55].

The 48 deaths (3.8%) found in the current study can be defined as a low mortality due to ACS, if compared with other international studies[56-59]. Death predominated in patients with STE-ACS (9.3% vs. 1.8%, p<0.0001).

Li *et al.*[60] reported that in 253 patients with a diagnosis of STE-ACS the most frequent cause of death was the cardiogenic shock in 57.7% of cases, similar to what happened in our research. In this study, 36% of the patients died during hospitalization; and elderly, high basal blood glucose levels, and CHF were considered independent predictors of mortality[61].

A paper published in 2015[62] evaluated the incidence of STE-ACS mortality in patients older than 60 years old and it found that 15.3% died within the first 30 days of the acute event. Mortality increased significantly with aging (60-69 years old [7.1%], 70-79 years old [10.9%] and 31.6% in patients aged 80 years old and older; p<0.001) and it was women who had the highest mortality when several risk factors and the presence of cardiogenic shock were associated. Both the GUSTO-IIb and CRUSADE studies found that women with NSTE-ACS had a higher crude in-hospital mortality than men (5.6% vs. 4.3%), with a higher percentage of reinfractions (4.0 vs. 3.5%) and CHF (12.1 vs. 8.8%), although these differences disappeared when adjusted with other clinical variables[18,46].

CONCLUSIONS

In women with acute coronary syndrome admitted to our department, age between the fifth and sixth decades of life and non-ST-segment elevation acute coronary syndrome were the predominant clinical characteristics. High blood pressure, tobacco smoking and diabetes mellitus were the main risk factors, and high basal levels of blood glucose and triglycer-

ides predominated in patients without ST-segment elevation. The predominant angiographic and procedure-related characteristics were low coronary angiography, significant coronary artery disease in patients with non-ST-segment elevation acute coronary syndrome, lesions in two or more vessels and percutaneous coronary intervention in patients with ST-segment elevation. Post-infarction angina, congestive heart failure and cardiogenic shock were the most frequently found major adverse events, and these last two were the most frequently associated with mortality.

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