

Long-Term Prognosis of Women with Non-ST-Segment Elevation Acute Coronary Syndromes

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Background and objectives. Women with ST-segment-elevation myocardial infarction have a worse prognosis than men. However, information about the prognosis of women with non-ST-segment-elevation acute coronary syndromes (NSTEMACS) is scarce. The aim of this study was to determine if the long-term prognosis of men and women with NSTEMACS differs.

Patients and method. In a consecutive series of 300 patients admitted for a NSTEMACS and ischemic ECG changes, we compared the clinical characteristics, in-hospital and long-term follow-up of 95 women and 95 men matched for age, presence of diabetes, and past history of hypertension.

Results. The median age of patients was 69 years, 36% had diabetes, and 65% had a history of hypertension. There were no gender differences in the history of angina or hypercholesterolemia, clinical presentation, number of patients with ST-segment depression, and CK-MB elevation. However, smoking, coronary artery disease, and peripheral vascular disease were less frequent in women. Treatment at admission and at discharge was similar in men and women, as was the use of in-hospital diagnostic and therapeutic procedures (echocardiography: 80 vs 88%; coronary angiography: 57 vs 59%; percutaneous coronary intervention: 17 vs 14%; coronary surgery 13 vs. 11%). Women had a better mean ejection fraction (55 ± 13 vs $49 \pm 14\%$; $p < 0.01$) and fewer stenosed coronary vessels (1.4 ± 1.1 vs 2.2 ± 0.9 ; $p < 0.01$).

There were no differences in the frequency of recurrent angina (28 vs 25%), and of death or infarction (both 3.2%) during hospitalization. However, during a 30-month follow-up the incidence of death, myocardial infarction, or a new episode of NSTEMACS was significantly lower in women with a relative risk (RR) of 0.53 (95% CI: 0.33-0.86; $p < 0.01$).

This apparently better prognosis persisted after adjusting for clinical data and ejection fraction (RR: 0.57 (0.33-0.98); $p < 0.05$), but disappeared after adjusting for the number of diseased coronary vessels (RR: 0.71 (0.35-1.47); $p = 0.36$).

Conclusions. Women with NSTEMACS had a better long-term prognosis than men. This better prognosis was independent of the patients' clinical characteristics and treatment, and could be explained by a less severe and less extensive coronary artery disease.

Key words: *Unstable angina. Myocardial infarction. Acute coronary syndrome. Women. Prognosis.*

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Pronóstico a largo plazo de las mujeres con síndrome coronario agudo sin elevación del segmento ST

Antecedentes y objetivos. Las mujeres con infarto y elevación del segmento ST tienen un peor pronóstico que los varones. Sin embargo, existe poca información sobre el pronóstico de las mujeres con síndrome coronario agudo sin elevación del segmento ST (SCASEST). El objetivo del estudio fue conocer si el pronóstico a largo plazo de las mujeres con SCASEST es diferente al de los varones.

Pacientes y método. De un total de 300 pacientes consecutivos ingresados por SCASEST con cambios isquémicos en el ECG, se compararon las características clínicas y la evolución de las 95 mujeres con las de 95 varones seleccionados por tener la misma edad, prevalencia de diabetes mellitus e hipertensión arterial.

Resultados. La edad media de los pacientes fue de 69 años, el 36% eran diabéticos y el 65% tenía antecedentes de hipertensión arterial. No existieron diferencias entre géneros en los antecedentes de angina o hipercolesterolemia, forma de presentación clínica, frecuencia de descenso del segmento ST en el ingreso o elevación de la CK-MB. Sin embargo, las mujeres presentaron menos antecedentes de tabaquismo, enfermedad coronaria y vasculopatía periférica. El tratamiento al ingreso y al alta fue similar en ambos grupos, así como la frecuencia de procedimientos realizados (ecocardiografía: 80 frente a 88%; coronariografía: 57 frente a 59%; angioplastia: 17 frente a 14%, y cirugía: 13 frente a 11%). Las mujeres tuvieron mejor fracción de eyección (55 ± 13 frente a $49 \pm 14\%$; $p < 0,01$) y un menor número de vasos estenosados ($1,4 \pm 1,1$ frente a $2,2 \pm 0,9$; $p < 0,01$).

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Received 15 April 2002.
Accepted for publication 15 July 2002.

ABBREVIATIONS

CK-MB: creatin kinase MB fraction.

NSTEACS: non-ST segment elevation acute coronary syndrome.

RR: relative risk.

Durante la hospitalización no se observaron diferencias en la incidencia de angina recurrente (28 frente a 25%) ni en la de mortalidad o infarto (3,2% en ambos casos). Sin embargo, en el seguimiento a 30 meses la incidencia acumulada de mortalidad, infarto o nuevo episodio de SCASEST fue significativamente menor en las mujeres con un RR (IC del 95%) de 0,53 (0,33-0,86; $p < 0,01$). Este mejor pronóstico se mantuvo al corregir los resultados por los demás datos clínicos y la fracción de eyección (RR = 0,57; IC del 95%, 0,33-0,98; $p < 0,05$), pero desapareció al corregir por el número de vasos estenosados (RR = 0,71; IC del 95%, 0,35-1,47; $p = 0,36$).

Conclusiones. Las mujeres con SCASEST y cambios electrocardiográficos en el ingreso presentan una evolución mejor que los varones a largo plazo. Este mejor pronóstico es independiente de las características clínicas y del tratamiento realizado y parece explicarse por una menor extensión y gravedad de la enfermedad coronaria.

Palabras clave: Angina inestable. Infarto de miocardio. Síndrome coronario agudo. Mujeres. Pronóstico.

INTRODUCTION

The epidemiological characteristics and clinical presentation of ischemic heart disease differ between women and men; while the incidence of heart disease is much higher in men, the most frequent clinical manifestation in men is myocardial infarction and in women is chest pain.¹ In addition, the overall mortality rate for ischemic heart disease is 3 times higher in men, a difference that tends to dissipate after the age of 55 years.¹ In spite of these differences, the majority of the large cardiologic studies have generally involved men and the results extrapolated to women.

Only in the last 10 years, by means of comparative studies, has been paid greater attention to the different characteristics of ischemic heart disease presenting in women. The initial studies performed described the presence of a worse prognosis for women with ST-segment elevation acute myocardial infarction.²⁻⁵ These differences were attributed, in part, to a later-in-life presentation of ischemic heart disease in women, a higher prevalence of cardiovascular risk factors (especially arterial hypertension and diabetes), delayed di-

agnosis, and a lesser use of diagnostic and therapeutic interventions.⁶⁻¹² In addition, various studies on patients treated with angioplasty or coronary surgery have shown a worse prognosis in women than in men.¹³⁻¹⁷

There are few studies that have analyzed the difference in prognosis between types of patients with unstable angina or ST-segment elevation myocardial infarction, and the results of such studies are contradictory.¹⁸⁻²⁰ Our study was designed to determine if the short-term and long-term prognosis for women with a non-ST segment elevation acute coronary syndrome (NSTEACS) is different from that of men.

PATIENTS AND METHOD

We designed a prospective observational study that included all the patients with the diagnosis of unstable angina or a non-ST elevation myocardial infarction who presented in the emergency department of our hospital from March 1996 to February 1997. Unstable angina was defined as the presence of ischemic pain associated with the presence of ischemic abnormalities recorded on ECG upon admission: ST segment depression ≥ 1 mm or the presence of negative T-waves of ≥ 3 mm in at least 2 contiguous leads. An infarct without ST segment elevation was diagnosed in presence of prolonged angina without ST segment elevation and with elevation of the MB fraction (activity) of the creatin phosphokinase enzyme (CK-MB) over the normal values as defined by the laboratory in our center. We collected data on the clinical presentation, prior history, tests performed and treatment administered, as well as the patient's hospital course and long-term outcome.

Patients

During the study, an initially conservative strategy of treatment was followed during the first 48 hours, in which indications for revascularization were established in relation to the recurrence of symptoms and signs of ischemia or the results of a stress test performed prior to discharge,^{19,21} except for patients who upon admission presented with signs of persistent ischemia on ECG, that were submitted to early coronary angiography. Pharmacological treatment, tests to be performed, and interventions were established in advance in a protocol that was distributed to the various units of the cardiology service.

We evaluated a total of 300 consecutive patients with the diagnosis of NSTEACS. Of these patients, we selected the 95 women who presented with ischemic changes on ECG upon admission and compared them with 95 men, adjusting for age (± 2 years), history of arterial hypertension and diabetes.

Diagnostic techniques

An echocardiogram was performed within the first 72 hours after admission in order to measure left ventricular ejection fraction (EF) and to rule out the presence of valvulopathies or cardiomyopathies. A Hewlett-Packard model SONOS 5500 echocardiograph was used. Tests performed were systematically reviewed by experienced medical personnel.

A conventional stress test or a cardiac perfusion scintigraphy stress test was performed the third day after admission on all patients who were clinically stable following of a modified Bruce protocol. For those patients in whom we could not perform a conventional stress test due to physical or cardiological causes, a pharmacological stress test with dipyridamole in conjunction with cardiac perfusion scintigraphy was performed.

Indications for coronary angiography and revascularization

The presence of refractory angina and hemodynamic instability were considered to be indications for immediate catheterization. Indications for elective coronary angiography were: the presence of signs of acute persistent ischemia on ECG; the recurrence of anginal pain with ECG changes that did not fit the profile of refractory angina during the hospital stay; the presence of signs of severe ischemia during the stress test; the presence of ventricular dysfunction (EF<40%); and the inability to perform a stress test as a result of cardiac causes (recurrent angina or heart failure).

A stress test was considered positive, affecting the decision to perform cardiac catheterization, in presence of severe signs of ischemia defined by the occurrence of angina or ≥ 1 mm ST segment depression at a workload of 5 METS or less, ST segment depression of more than 2 mm or in more than 4 leads or persistent (more than 5 minutes in the post-exercise period), or a decrease in systolic arterial pressure of more than 10 mm Hg during exercise. In the patients in whom myocardial perfusion scintigraphy was performed, coronary angiography was considered to be indicated in presence of a perfusion defect, whether it was reversible or not, in 2 or more vascular areas, or in only 1 area if extensive and reversible.

Coronary revascularization was considered for those patients in whom coronary angiography was performed and who presented with appropriate coronary features..

Ischemic events

To achieve the final objectives of this study we counted only spontaneous ischemic events. Coronary revascularization was considered as an additional ther-

apeutic procedure. A myocardial infarction or reinfarction in the cases of acute myocardial infarction (AMI) without ST segment elevation was diagnosed in the presence of an elevation of CK-MB values greater than the maximum normal limit. In the setting of revascularization surgery, we required a CK-MB elevation of more than 5 times the maximum limit of normal to diagnose a perioperative AMI.

Follow-up

After discharge, all patients were followed clinically by means of telephone interview. As a final study goal, we established the incidence of death, AMI or readmission for a new episode of NSTEMI during both the hospital stay and during the 30-month follow-up period.

Statistical analysis

Qualitative variables are expressed as numbers and percentages, and quantitative variables as mean \pm standard deviation (SD). The comparison of variables was performed using the χ^2 test and the exact Fisher test for qualitative values and the Student *t* test for the quantitative values. We established a confidence interval (CI) of 95% and we considered a *P* value of *P*<.05 to be significant. The cumulated incidence of events was calculated during the 30-month follow-up period by constructing Kaplan-Meier survival curves that were compared using the log-rank test. Multivariate analysis was performed using the Cox proportional hazards model.²² Adjustment for possible confounding variables between men and women was made in 3 stages. In the first stage, we included only the clinical variables that, on binary analysis, had *P* values <.15 both in the comparison of baseline variables by gender and when analyzing the prognosis at 30 months. In the second stage, we added the EF. Finally, in the third stage, we added the information obtained from coronary angiography with respect to the number of stenosed vessels. The analysis was also repeated on the entire group of 300 patients studied. We calculated the adjusted relative risk (RR) with its corresponding 95% CI for both the bivariate analysis and the multivariate analysis. The data was analyzed with the SPSS statistical package version 10.0.

RESULTS

Clinical characteristics

Mean patient age was 69 years, the prevalence of arterial hypertension was 65% and of diabetes mellitus was 36%. Unstable angina was the final diagnosis in 80% of patients and non-ST-segment elevation myocardial infarction in 20%. Baseline clinical characteristics of the patients included are shown in Table 1.

There were no gender differences in the prevalence of hipercolesterolemia or the history of angina or of coronary revascularization. Nevertheless, men were more often smokers (30% of men vs 6% of women; $P<.01$) and had a higher frequency of peripheral vascular disease (36% of men vs 16% of women; $P<.05$).

The pain that led to hospital admission was more prolonged in women than in men (115 ± 151 min for women vs 75 ± 84 min in men; $P<.05$) and was considered as being typical of a coronary event in 93% of women and 96% of men (NS) (Table 2). Most of the episodes occurred at rest, were prolonged, and had been present within prior 48 hours. No differences were observed in the type of ECG changes at the time of admission or in the elevation level of the serological markers of necrosis.

Treatment and tests performed

There were no significant differences with regard to medical treatment administered at admission (Table 3). Aspirin was administered to 100% of patients, heparin to 90% of patients, and beta-blockers to 73% of patients. A stress test was performed on more than half of the patients. No significant differences were observed between men and women with regard to the presence of angina or ischemic changes during the stress test, although man had a higher frequency of positive perfusion stress tests. No differences were observed either in the number of coronary angiographies or in the number of revascularization procedures that were performed (Table 3).

The EF measured by echocardiography was $55\% \pm 13\%$ for women and $49\% \pm 14\%$ for men ($P<.01$). Only 13% of women presented with an EF lower than 40%, vs 29% in men ($P<.05$). Among the patients who were catheterized, the number of diseased coronary vessels was significantly lower among women (1.4 ± 1.1 vessels vs 2.2 ± 0.9 vessels for men; $P<.01$) as a

TABLE 1. Clinical characteristics

	Women (n=95)	Men (n=95)
Age, mean \pm SD	69 \pm 10	69 \pm 10
Risk factors		
Diabetes mellitus	34	35
Arterial hypertension	64	60
Hypercholesterolemia	49	42
Smoking	6	28**
History of heart disease	54	69*
Myocardial infarction	27	38
Angina	48	51
Coronary surgery	11	13
Coronary angioplasty	8	9
Cerebrovascular accident	11	5
Peripheral vascular disease	15	34**

* $P<.05$. ** $P<.01$.

TABLE 2. Presentation of angina and clinical data obtained at admission

	Women (n=95)	Men (n=95)
Typical pain	88	91
Hours pain-admission	2.7 \pm 15	2.4 \pm 7
Maximum duration of angina, min	115 \pm 151	75 \pm 84*
≥ 2 pain episodes during previous 24 hours	36	36
Type of angina		
Progressive	30	36
Prolonged pain at rest	70	69
Pain at rest+persistent ECG changes	53	48
Braunwald classification		
Severity of angina		
I. Progressive on exercise	6	9
II. At rest >48 h	4	4
III. At rest <48 h	85	82
Etiology of angina		
A. Primary	83	88
B. Secondary	5	1
C. Post-infarction	6	6
Previous treatment*		
1. Without treatment	49	46
2. Standard treatment	37	23
3. Maximum treatment	9	26
Physical examination at admission		
Systolic arterial pressure	152 \pm 30	149 \pm 29
Heart rate	81 \pm 14	78 \pm 18
ECG upon admission		
ST changes ≥ 0.5 mm	71	77
Negative T-waves	53	52
Biochemical markers		
CK-MB elevation	19	21
Troponin I elevation (n=96)	10	17

CK-MB indicates creatin kinase MB fraction.

* $P<.05$.

result of, above all, a greater number of women without significant coronary lesions (28% of women vs 4% of men; $P<.05$).

Hospital course

During the hospital stay, coronary angioplasty was performed in 17% of women and on 14% of men (NS), and surgery was performed in 14% of women and in 12% of men (NS). Ten percent of the procedures were performed in an emergency setting (Table 3). During this time, 4 patients died, 3 had a myocardial infarction, and 51 had recurrent angina, 31 of whom had transient ischemic changes on ECG. There was no gender differences between the sexes regarding the incidence of adverse clinical events during the hospital course (Table 4).

Long-term course

Treatment recommendations at the time of hospital discharge were similar for both groups (Table 3). Clinical follow-up was performed for a median of 26

TABLE 3. Treatment and diagnostic tests performed at admission

	Women (n=95)	Men (n=95)
Pharmacological treatment		
At admission		
Aspirin	94	95
Heparin	82	87
i.v. nitroglycerine	59	52
Beta-blockers	71	66
Calcium antagonists	50	65
At discharge		
Aspirin	82	88
Tienopyridine	10	14
Beta-blockers	49	48
Calcium antagonists	52	53
Diagnostic tests		
Stress tests (n=103)	48	55
ECG Ext (n=37)	15	22
Isotopic Ext (n=26)	9	17
Dipyridamol Ext (n=40)	24	16
Positive stress test		
Angina or ST depression (n=63)	14	22
Cardiac scintigraphy (n=66)	16	22*
Echocardiography (n=160)	76	84
Mean EF	55±13	49±14**
EF<40%	10	24*
Coronary angiography (n=107)	54	53
Number of stenosed vessels, mean	1.4±1.1	2.2±0.9**
0	15	2
1	14	14
2	12	12
3	10	21
LM	2	5
Procedures		
Angioplasty	16	13
Elective	10	9
Emergency	6	4
Coronary surgery	13	11
Elective	7	8
Emergency	6	3

ExT: exercise test, LM: left main coronary vessel; EF, ejection fraction.

* $P<.05$; ** $P<.01$.

months. During this time, revascularization procedures were performed in 56 patients (31%), 40 (22.5%) during the initial hospitalization and 16 (8%) after discharge (6 angioplasty procedures and 12 by-pass surgeries). During the entire follow-up period, 30 patients died (16%), 8 had a myocardial infarction (4%), and 42 (22%) presented with another episode of NSTEMACS that required another hospitalization. In total, 72 patients (40%) died, had a myocardial infarction or a new episode of NSTEMACS.

At 30 months follow-up, the cumulative incidence of adverse events was significantly lower in women than in men, with a RR (95% CI) of 0.53 (0.33 to 0.86; $P<.01$), a difference that was observed after the first 6 months (Figure 1). After performing the multivariate analysis, the RR of adverse cardiac events for women compared to men was 0.60 (0.36 to 0.99; $P<.05$) after

TABLE 4. Hospital course

	Women	Men	RR (95% CI)	P
Recurrent angina	27	24	1.09 (0.78-1.51)	NS
with ECG changes	15	16	0.96 (0.66-1.40)	NS
Death or AMI	3	3	1 (0.44-2.25)	NS
Death, AMI, or recurrent angina with ST segment changes	17	17	1 (0.69-1.45)	NS

AMI: acute myocardial infarction

adjustment for baseline clinical features, and 0.57 (0.33 to 0.98; $P<.01$) after adjustment for clinical data and EF. Nevertheless, when the number of stenosed vessels was included, the differences no longer remained statistically significant, with a RR of 0.71 (95% CI, 0.35 to 1.47; $P=.36$).

After repeating the analysis on the entire group of 300 patients studied, the results remained unchanged, and women presented an RR of ischemic events of 0.59 (0.37 to 0.95) after adjustment for clinical data, 0.64 (0.38 to 0.99) after the addition of EF, and 0.70 (0.48 to 1.26) after including the number of stenosed vessels in the analysis.

DISCUSSION

Our data show that women with NSTEMACS have a better long-term prognosis than men. These results were obtained despite the fact that we selected for the study only patients with ischemic changes on ECG on

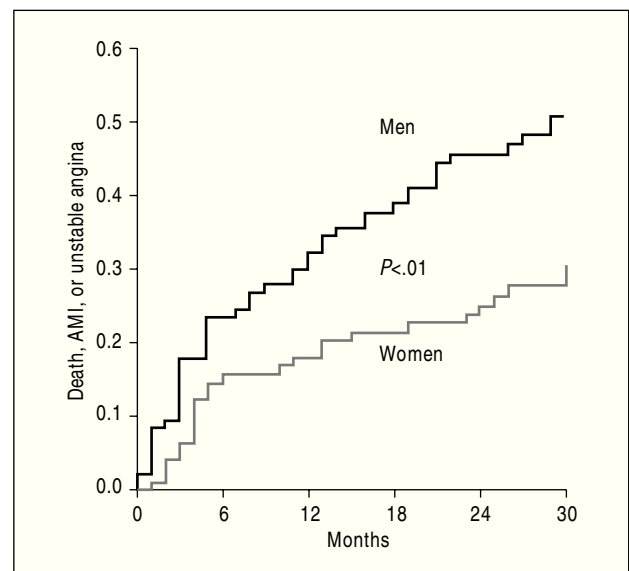


Fig. 1. Adjusted incidence of mortality, myocardial infarction, or new episode of acute coronary syndrome without ST segment elevation at 30 months for women in the study and for men of the same age and with the same prevalence of diabetes and arterial hypertension.

admission and after adjusting for the other clinical variables with an established prognostic value. Nevertheless, when taking into account differences in coronary anatomical features, the differences were no longer statistically significant. These results concur with previous studies performed on patients with unstable angina and non-ST segment elevation myocardial infarction,²³⁻²⁵ and provide important information to better understand and clinically manage this syndrome in women.

Gender differences in the prognosis of acute coronary syndromes

The Framingham study¹ was the first study to report gender differences in mortality rate after a myocardial infarction; these results were supported by later studies.^{2-5,11} While some studies have attributed these differences to the older age of women and their higher prevalence of arterial hypertension and diabetes,^{6,7} other studies have found that the difference in mortality rate is independent of these factors,⁵ especially in patients younger than 75 years of age.⁴ Some studies have suggested, nevertheless, that the higher mortality rate for women with myocardial infarction is a consequence of a proven higher prehospitalization mortality rate for men.^{1,26}

With regard to NSTEMACS, the existing evidence is scarce and contradictory. Thus, while in the TIMI IIb study¹⁹ no differences were observed in the prognosis at 42 days, in the GUSTO IIb study¹⁸ a tendency to excessive risk was noted at 30 days for women with ST-segment elevation myocardial infarction, a neutral effect in women with non-ST segment elevation myocardial infarction, and a significant (35%) decrease in women with unstable angina. Finally, in the FRISC II study,²⁰ which compared the efficacy of an initial invasive treatment strategy for NSTEMACS vs a conservative treatment strategy, the prognosis for women was better than for men in the conservative treatment group, with similar results in the invasive treatment group.

In our study, as in others,¹⁹ we did not observe differences in prognosis during the hospital stay. However, we did observe differences in the survival curves beginning in the first 6 months of follow-up and continuing through the follow-up period. In the only study performed on the long-term prognosis according to gender,²³ the multivariate analysis showed a significant (23%) risk reduction in women as compared with men. Nevertheless, in contrast to our study, the prognosis of patients was not adjusted for the number of stenosed coronary vessels and the EF.

The results of our study are notable because, in contrast to other studies,⁶⁻¹⁰ both men and women received the same treatment and underwent the same number of diagnostic and therapeutic procedures. Multiple stud-

ies have reported that the management of patients with acute coronary syndromes seems to be different in men and women, with a lower number of revascularization procedures being performed on women. In spite of the fact that in a recent study no significant differences were observed,¹⁷ data from clinical registries show the opposite.^{7,12} These differences have been attributed to the older age of the studied women,²⁷ to a larger number of concomitant illnesses, and to a management bias. The latter could result in a worse prognosis in women if lower frequency of the procedures with known diagnostic and therapeutic value are performed. The recent observation that the mortality rate of women with myocardial infarction treated with primary angioplasty was lower than that of men after adjustment for the remaining variables¹⁷ reinforces the importance of this treatment bias that was not found in our study.

Extension and severity of the coronary artery disease

In our study, we analyzed a group of women with NSTEMACS that were compared to an identical number of men matched for age and history of diabetes and arterial hypertension, which are the principal confounding variables in studies on coronary heart disease according to gender.^{1-20,23-27} It is well established that women have a higher incidence of atypical angina than men. For this reason, the current clinical practice guidelines²⁸ distinguish between the suspicion and the clear presence of unstable angina according to the absence or presence of ischemic signs on the ECG recorded on admission or the elevation of serological markers of myocardial necrosis. To avoid this bias, in our study we selected only patients with typical angina and ECG changes. In spite of this, women had better EF and a lesser number of stenosed coronary vessels. The high prevalence (28%) of coronary arteries without significant lesions observed in the women in our study is similar to that found in other clinical trials that used the same inclusion criteria, such as the TIMI IIb study¹⁹ (25%) and the GUARANTEE registry⁷ (25%). In the GUSTO IIb study,¹⁸ the percentage was 9% in women with a non-ST segment elevation myocardial infarction and 31% in women with unstable angina. In accordance with our results, it should be pointed out that in the FRISC II study,²⁰ the difference in prognosis between women and men in the conservative arm disappeared when women with normal coronary arteries were withdrawn from the analysis.

Clinical implications

In the FRISC II study²⁹ a significant interaction was observed between sex and management strategy, indicating that, as opposed to men, women with

NSTEACS did not benefit from an initial invasive treatment strategy. Therefore, while in the non-invasive treatment group the incidence of infarct and the combination of death or infarct were significantly lower in women than in men, in the invasive treatment strategy group there was a non-significant trend toward a worse prognosis in women. It should be pointed out that in this group, a lower number of revascularization procedures were performed in women (67% vs 82%; $P<.001$) according to their lower prevalence of significant coronary disease. Several studies and clinical registries have reported a greater frequency of complications and a worse prognosis among women who underwent percutaneous coronary interventions^{13,14} or coronary surgery,¹⁵ especially among women less than 60 years of age.¹⁶

On the other hand, the importance of coronary thrombosis in the pathophysiology of NSTEMACS seems to be different in man and women. In the PRISM-PLUS study,³⁰ the prevalence of coronary thrombus on coronary angiography performed 48 to 72 hours after admission was 50% lower in women than in men. In addition, in a recent meta-analysis of the efficacy of glycoprotein IIb/IIIa antagonists in patients with NSTEMACS, the administration of these drugs was associated with a 15% increase in the incidence of death or myocardial infarction in women in contrast to a 19% risk reduction in men.³¹ These differences in the effect of this type of medication according to sex were consistent even after adjustment for baseline clinical differences, but disappeared in the subgroup of patients who had positive troponin values, an indirect marker for coronary thrombosis.

Taken together, these results suggest that the pathophysiology of NSTEMACS may be different for men and women, with a less extensive and severe coronary artery disease in women, and a possible lower prevalence of ulcerated plaques and thrombotic load in women, as suggested by the results of our study. These results also suggest that treatment of NSTEMACS might be different in some aspects for men and women, especially with regards to whether the initial treatment strategy is invasive or conservative, and also, that the initial risk stratification is particularly important in women.

Study characteristics and limitations

The method of data analysis that was performed by pairing each woman with a man of the same age and prevalence rate for arterial hypertension and diabetes, ensures that no bias occurred as a result of baseline differences in patients' characteristics. In addition, the multivariate analysis allowed for final adjustment of the clinical and angiographic variables and the EF.

Although the number of patients studied was relatively small, it included all the women admitted over 1

year with NSTEMACS who had ischemic changes on the ECG recorded on admission. We did not perform coronary angiography on all patients; therefore, the disappearance of statistical significance when adjusting for the number of stenosed vessels could be due to a lack of statistical power. However, the relative risk of ischemic events for women as compared with men did not remain the same after adjusting for angiographic data, but decreased in parallel to the differences observed in coronary anatomy. Finally, the extension of the follow-up to 30 months increased the power of the statistical analysis by registering a high incidence of ischemic events and ensuring the validity of the results.

CONCLUSIONS

Women with NSTEMACS and electrocardiographic changes upon admission have a better long-term outcome than men. This improved prognosis is independent of clinical characteristics and treatment performed, and appears to be attributable to a lesser extent and severity of coronary artery disease in women.

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