ORIGINAL ARTICLE

ST-segment Elevation Acute Myocardial Infarction in Women in Argentina. Subanalysis of the CONAREC XVII Registry

Infarto de miocardio con supradesnivel del segmento ST en mujeres en Argentina. Subanálisis del registro CONAREC XVII

JUAN P. COSTABEL, LUCRECIA M. BURGOS, MARÍA P. DUCZYNSKI, IGNACIO CIGALINI, CASANDRA LILEN GODOY, ELIÁN F. GIORDANINO, SEBASTIAN GARCÍA ZAMORA, GONZALO PÉREZ, NICOLÁS GONZÁLEZ, RICARDO IGLESIAS

ABSTRACT

Background: Acute myocardial infarction is one of the leading causes of death among women.
Objective: The aim of this study was to analyze the characteristics of ST-segment elevation myocardial infarction in Argentine women.
Methods: This was an observational study, performed with data from the CONAREC XVII registry.
Results: The study included a total of 694 patients, among which 150 were women with mean age of 69.2±13.7 years vs. 59.9±11.5 years in men (p=0.001). Women presented a higher prevalence of diabetes (29.3% vs. 19.9%, p=0.010) while smoking was higher in men (71% vs. 45.3%, p=0.001). No differences were found in presentation symptoms, ischemia times, or reperfusion treatments. Women had a higher prevalence of single vessel lesions, with more Killip and Kimbal C-D infarctions (15.3% vs. 7.5% (p=0.001) and higher inotropic requirements [21.3% vs. 8.6% (p=0.001)]. In addition, they presented significantly higher percentage of bleeding and mechanical complications (4.7% vs. 1.3%, p=0.017) without differences in percent mortality. However, the multivariate analysis showed no relationship between female sex and poor hemodynamic evolution or complications.
Conclusions: Women have a different cardiovascular risk profile, presenting ST-segment elevation myocardial infarctions with worse hemodynamic impact and greater in-hospital complications. Gender was not an element individually associated with this finding, but it seems to group a series of factors that imply worse tolerance to myocardial infarction.

Keywords: Acute myocardial infarction - Women - In-hospital evolution

RESUMEN

Introducción: El infarto agudo de miocardio es una de las principales causas de muerte entre las mujeres.
Objetivos: Analizar las características del infarto con elevación del segmento ST en mujeres argentinas.
Material y métodos: Estudio observacional, realizado con los datos del registro CONAREC XVII.
Resultados: De un total de 694 pacientes, 150 eran mujeres cuya edad media era de 69,2 ± 13,7 años vs. 59,9 ± 11,5 años en varones (p = 0,001). Las mujeres presentaron mayor prevalencia de diabetes (29,3% vs. 19,9%, p = 0,010) mientras que el tabaquismo fue mayor en varones (71% vs. 45,3%, p = 0,001). No se hallaron diferencias en síntomas de presentación, tiempos de isquemia, o tratamientos de reperfusión. Las mujeres tuvieron mayor proporción de lesión de único vaso, con más infartos Killip y Kimbal C-D (15,3% vs. 7,5% (p = 0,001) y mayor requerimiento de inotrópicos (21,3% vs. 8,6% (p = 0,001)). Además, presentaron significativamente mayor porcentaje de sangrado y de complicaciones mecánicas (4,7% vs. 1,3%, p = 0,017) sin diferencias en el porcentaje de mortalidad. Sin embargo, en el análisis multivariado no se encontró relación entre el sexo femenino y la mala evolución hemodinámica o complicaciones.
Conclusiones: Las mujeres presentan un perfil de riesgo cardiovascular diferente, con infartos con elevación del ST con peor impacto hemodinámico y complicaciones intrahospitalarias. El sexo no resultó constituir un elemento individualmente ligado a ello, sino que parece agrupar una serie de factores que implican peor tolerancia al infarto.

Palabras clave: Infarto agudo de miocardio - Mujeres - Evolución intrahospitalaria

Abbreviations

AMI	Angiotensine converting enzyme inhibitors	**IABP**	Intraaortic balloon pump
ACS	Acute coronary syndrome	**LV**	Left ventricular
AMI	Acute myocardial infarction	**MV**	Mechanical ventilation
ARBs	Angiotensin II receptor blockers	**RV**	Right ventricle
CK	Creatine kinase	**STEMI**	ST-segment elevation myocardial infarction
ECG	Electrocardiogram	**UP**	Upper limbs

Rev Argent Cardiol 2015;85:417-424. http://dx.doi.org/10.7775/rac.v85.i5.10771

Received: 05-15-2017 - *Accepted:* 08-15-2017

Address for reprints: Juan Pablo Costabel - e-mail:juanpablocostabel@gmail.com

Investigators of the Argentine Council of Cardiology Residents (CONAREC)

INTRODUCTION

Cardiovascular diseases represent the leading cause of mortality worldwide. For years it has been chiefly considered a male disease, but for some time now it is also known to be the main cause of death in adult women. ST-segment elevation myocardial infarction (STEMI) is a medical emergency, and has the highest mortality rate among acute coronary syndromes (ACS) in men and women.

In our country there are insufficient articles about statistics and characteristics of STEMI in women. For this reason, a descriptive analysis was made based on data from the Acute Myocardial Infarction (AMI) Registry of the Argentine Council of Cardiology Residents (XVII CONAREC Registry), (1) considering that knowing patient's performance according to gender is important to improve therapeutic conducts.

The aim of the present work was to describe STEMI demographic characteristics, presentation, treatment and outcome in women, comparing these data with that observed in men.

METHODS

A prospective study was performed analyzing the CONAREC XVII registry data from consecutive patients admitted between December 2009 and July 2010. Centers from all over the country that had a cardiology residence associated with CONAREC participated in the study. (1)

All patients >18 years admitted with presumptive diagnosis of STEMI or non-STEMI, understood as primary thrombotic episode (type I or III according to the new definition of AMI) were included. Both types of infarction required elevated cardiac injury markers (preferably troponin) with at least one of the following signs of ischemia: symptoms, electrocardiographic (ECG) abnormalities, including ST-T changes, new left bundle branch block or new Q waves, or new motility disorders on the echocardiogram. (2)

Demographic data, educational level, stress situations associated to the episode, cardiovascular risk factors, comorbidities, patient symptoms, hemodynamic status on admission, treatment and implementation times, in-hospital complications and medication at discharge were collected. (The definitions are detailed in the Appendix).

Statistical analysis

Discrete variables were expressed as percentages and continuous variables, as mean or median, with their corresponding standard deviation and interquartile range, depending on their distribution. The chi-square test was used to compare discrete variables and Student's t test or the Mann-Whitney test for continuous variables, according to sample distribution. ANOVA and Kruskal-Wallis tests were used for multiple comparisons. A two-tailed p value <0.05 was considered statistically significant. Logistic regression analysis was performed to identify risk predictors, using for the multivariate analysis the variables that in the univariate analysis had p ≤ 0.10. All the data was analyzed with IBM Statistical Package for the Social Sciences (SPSS) 21 software.

Ethical considerations

The protocol was evaluated and approved by the Ethics Committee of each participating institution and following the principles of the Declaration of Helsinki. According to the Argentine personal data protection law 25,326, all information will remain confidential..

RESULTS

A total of 694 STEMI patients were included in the study. Among them, 150 were women (21.6%) with mean age of 69.2±13.7 years vs. 59.9±11.5 years in men (p=0.001). Cardiovascular risk factor analysis showed a higher prevalence of diabetes in women (29.3% vs. 19.9%, p=0.010) versus greater smoking in men (71% vs. 45.3%, p=0.001), without significant differences in the percentage of dyslipidemia, hypertension or family history of cardiovascular disease (Table 1).

Regarding cardiovascular history, there were no differences in the percentage of vascular disease or stroke, but men presented with higher prevalence of prior angioplasty (10.8% vs. 3.3 %, p=0.002) as well as prior infarction (14.5% vs. 8.7%, p=0.037). However, there were no differences in the use of aspirin before the episode (31.4% in men vs. 34.7% in women, p=0.256) or in the use of statins, nitrates, clopidogrel or angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARBs), though women had greater previous use of diuretics (9.3% vs. 2.6%, p=0.001).

When consulting for recent stressful situations, 28% of patients globally reported a linked episode as trigger factor. Job instability was the most frequent trigger in men, while divorce, family problems, and death of loved ones were more frequent in women.

The analysis of episode presentation revealed no differences in symptom profile classification nor in the arrival time at the treatment center, with a median prehospital delay (pain-medical care) of 120 minutes (60-240) in men and 165 minutes (90-360) in women, p=0.27. There were no differences in door-to-balloon time: 90 minutes (60-150) in men vs. 90 minutes (60-120) in women (p=0.589), with 55% of men under the recommended 90 minutes vs. 58% in women (p=0.71). Total ischemic time was 240 minutes (155-360) in men vs. 270 minutes (172-465) in women (p=0.19).

No gender differences were found in the administration of aspirin, thienopyridines, heparin, and IIb/IIIa receptor inhibitors on admission. Men were prescribed more frequently with nitroglycerin (67% vs. 58.7% p=0.04), ACEI/ARBs (46% vs. 35% p=0.02), beta-blockers (58.1% vs. 40.7% p=0.001) and lidocaine (2.6%, with no use in women p=0.049) while women required more frequently diuretics and inotropic agents. (Table 2)

The analysis of reperfusion showed no differences in the percentage of the different forms of primary angioplasty (77% in men vs. 72% in women, p=0.232) as well as in the use of fibrinolytics (14.5% in men vs. 14% in women, p=0.435), with streptokinase predominance in 85-86% of patients in both groups. There were no differences in the frequency of positive rep-

Table 1. Baseline characteristics according to gender

Variable	Men N=544	Women N=150	p
Age, years	59.9±11.5	69.2±13.7	0.001
Stressful situations			0.007
Family/divorce	46 (8.4%)	22 (14.6%)	
Work instability	78 (14.3%)	7 (4.7%)	
Death of a beloved one	21 (3.8%)	11 (7.3%)	
Surgery	3 (0.6%)	2 (1.3%)	
Does not refer	395 (72.6%)	108 (72%)	
Risk factors			
Diabetes	108 (19.9%)	44 (29.3%)	0.010
Dyslipidemia	279 (51.3%)	79 (52.7%)	0.418
Hypertension	337 (62.1%)	370 (68%)	0.110
Family history	107 (19.7%)	31 (20.7%)	0.433
Smoking	386 (71%)	68 (45.3%)	0.001
Renal failure	18 (3.3%)	13 (8.7%)	0.012
Peripheral vascular disease	27 (5%)	7 (4.7%)	0.540
Previous angioplasty	59 (10.8%)	5 (3.3%)	0.002
Previous infarction	79 (14.5%)	13 (8.7%)	0.037
Previous aspirin	171 (31.4%)	52 (34.7%)	0.256
Previous ACEI/ARBs	204 (37.5%)	63 (42%)	0.31
Previous betablockers	126 (23.2%)	30 (20%)	0.41
Statins	120 (22.1%)	28 (18.7%)	0.36
Diuretics	14 (2.6%)	14 (9.3%)	0.001
Clopidogrel	27 (5%)	8 (5.3%)	0.85
Nitrates	15 (2.8%)	0 (0%)	0.051

Family history: Family history of coronary artery disease. ACEI: Angiotensin converting enzyme inhibitors. ARBs: Angiotensin II receptor blockers.

erfusion criteria or in the frequency of primary rescue or deferred angioplasty (p=0.1).

In relation to the characteristics of infarction, the number of affected vessels, including the culprit vessel, was significantly lower in women, with a higher proportion of single-vessel injury (57.6% vs. 48.5%, p=0.001) (Table 3). When analyzing the hemodynamic impact of infarctions, women had significantly greater Killip and Kimbal class C-D infarction than men (15.3% vs. 7.5%, p=0.001), although peak troponin and total creatine kinase showed no differences. Consistent with these data, the need for inotropic agents was greater in women, (21.3% vs. 8.6%, p=0.001), added to the fact that they required more frequently a Swan Ganz (14% vs. 7.7%, p=0.01) and mechanical ventilation (14.7% vs. 9.2%, p=0.001).

Complications during hospitalization evidenced greater percentage of major and minor bleeding in women, despite double antiplatelet therapy and IIb/IIIa inhibitors was not different. Mechanical complications (ventricular septal defect, severe mitral regurgitation and free wall rupture) were more prevalent in women (4.7% vs. 1.3%, p=0.017), as well as 2-3 degree atrioventricular (AV) block (8.7% in women vs. 2.6% in men, p=0.002), with higher requirement for transient pacemaker (p=0.018). In-hospital semiquantitative left ventricular (LV) function assessment did not differ in relation to gender, as well as hospitalization times and global mortality.

Univariate analysis of worst hemodynamic impact predictors, defined as Killip and Kimball C-D on admission, showed association with female gender. However, in the multivariate analysis, it was not a significant determinant, as were age, diabetes, and previous infarction; while hypertension behaved as an inversely associated cause (Table 4). In order to define poor in-hospital outcome, a combined endpoint grouping death, reinfarction, mechanical or electrical complications, mechanical ventilation or use of intraaortic balloon pump (IABP) was designed. In the multivariate analysis, female gender was not significant, while age was associated to the event (Table 5).

DISCUSSION

The present work showed that female gender has a different risk profile than male gender, associated with worse hemodynamic impact at infarct presentation and greater in-hospital complications. However, despite this statement, multivariate analyses showed that gender in itself was not an independent risk predictor.

Table 2. Treatment according to gender

Medication administered	Men N=544	Women N=150	p
Aspirin	533 (98%)	145 (96.7%)	0.34
Clopidogrel			0.44
- 75mg	58 (10.7%)	13 (8.7%)	
- 300mg	201 (36.9%)	61 (40.7%)	
- 600mg	212 (39.7%)	62 (41.3%)	
Prasugrel	29 (5.3%)	7 (4.7%)	0.74
Anticoagulants			0.91
- Sodium heparin	202 (37.1%)	53 (35.3%)	
- Low molecular weight heparin	125 (23%)	33 (22%)	
- Fondaparinux	9 (1.7%)	2 (1.3%)	
IIb/IIIa inhibitors	43 (7.9%)	13 (8.7%)	0.76
Nitroglycerin	368 (67.6)	88 (58.7%)	0.04
Diuretics	96 (17.6%)	38 (25.3%)	0.035
ACEI/ARBs	250 (46%)	53 (35.3%)	0.02
Betablockers	316 (58.1%)	61 (40.7%)	0.001
Inotropics	47 (8.6%)	32 (21.3%)	0.001
Amiodarone	27 (5%)	3 (2%)	0.1
Lidocaine	14 (2.6%)	0 (0%)	0.049

ACEI: Angiotensin converting enzyme inhibitors. ARBs: Angiotensin II receptor blockers.

The literature regarding cardiovascular risk factors shows that, at the time of infarction, women tend to be older and have higher comorbidities than men. (5, 6) In this sense, our study revealed that women were, on average, almost 10 years older at the time of their coronary event, and that this is assumed to be linked to the protective effect that estrogen provides on the vascular endothelium. (7) On the other hand, women had a higher percentage of diabetes, which is probably associated with older age and overweight, something described in the results of the GUSTO study where women presented with 22% of diabetes vs. 14% in men ($p < 0.0001$) or in the Argentine cohort of the GRACE study described by Barros et al., where 23.8% of women had diabetes compared to 20.9% of men ($p=0.01$) (8, 9). In both studies, as in others publications, it is observed that women tend to smoke less and to have less history of infarction at the time of presentation, which could influence the presence of collateral circulation, with a paradoxical protective effect during an acute coronary occlusion (10, 11). In 1995 Ciruzzi et al. published an infarction registry where 37.9% of women were smokers or ex-smokers at the time of the event compared with 72.5% of men, and that this condition was associated with a reduction in age at the time of infarction of 15.48 years in women vs. 9.57 years in men ($p<0.001$).

In contrast to numerous reports, this work did not show differences in the ischemic symptoms which classify the presentation, with only a trend towards longer consultation time, probably influenced by the incorporation of patients solely with STEMI, who generally have a more florid presentation facilitating the diagnosis (12-14). The same occurred with the pharmacological treatments established, the rate of reperfusion therapy used or the implementation time, since this type of syndromes leave less room for doubt concerning the clinical condition, unlike non-STEMI cases, where multiple studies report a lower percentage of revascularization in women or longer time to implementation. (13, 15, 16)

When analyzing the hemodynamic impact of infarction, it was observed that for a similar infarct size measured by echocardiogram and peak markers, women had more Killip and Kimball C-D myocardial infarctions, despite a comparable number of affected vessels. This could be related to a greater degree of diastolic dysfunction linked to female gender, age and higher prevalence of diabetes, conditions that would worsen hemodynamic tolerance. This situation could also be explained by differences in thrombotic and fibrinolytic activity both in men and women, as well as by the presence of higher collateral circulation in men (5, 6, 14, 17-19). Moreover, the presentation seems to be associated with greater need for inotropic agents during hospitalization and a lower indication of betablockers, which is reasonable.

In turn, women had a higher percentage of major and minor bleeding, which is systematically repeated in the literature. The explanation could be found in the lack of adjustment of antithrombotic medications, which may be excessive for women with lower body weight and creatinine clearance.

Information from more than 20,000 patients in-

Table 3. Presentation mode and outcome

Variable	Men N=544	Women N=150	p
Presentation			0.324
Precordial oppression	78.1%	78%	
Upper limb pain	26.1%	23.3%	
Asymptomatic	1.5%	2.7%	
Vagal symptoms	40.6%	42.7%	
Epigastralgia	13.1%	14%	
Others	14.5%	20%	
Door-to-balloon time, min	80 (60-140)	85 (50-120)	0.43
Pain-to-door time, min	120(60-240)	165 (90-360)	0.27
Reperfusion			
Angioplasty	419 (77%)	108 (72%)	0.232
Fibrinolytics	79 (14.5%)	21 (14%)	0.435
Angioplasty			
Primary	327 (79.8%)	92 (87.6%)	0.1
Rescue	38 (9.3%)	7 (6.7%)	
Deferred	45 (11%)	6 (5.7%)	
Affected vessels			0.001
1 vessel	264 (48.5%)	86 (57.6%)	
2 vessels	164 (30.1%)	33 (22.4%)	
3 vessels	110 (20.3%)	20 (13.6%)	
Main left coronary artery	48 (8.8%)	10 (6.6%)	
Killip and Kimbal			0.002
A	421 (77.4%)	93 (62%)	
B	82 (15.1%)	34 (22.7%)	
C	16 (2.9%)	43 (6%)	
D	25 (4.6%)	14 (9.3%)	
Bleeding			0.035
Major	18 (3.3%)	9 (5.8%)	
Minor	28 (5.1%)	15 (10%)	
Complications			
Reinfarction	12 (2,2%)	3 (2%)	0.,587
AF	48 (5,3%)	17 (6,3%)	0.310
VT	53 (5.8%)	12 (4.4%)	0.234
Mechanical complications	7 (1.3%)	7 (4.7%)	0.017
2-3 AV-block	14 (2.6%)	13 (8.7%)	0.002
Temporary pacemaker	21 (3.9%)	13 (8.7%)	0.018
RV hemodynamics	23 (4.2%)	13 (8.7%)	0.030
Infections	34 (6.3%)	15 (10%)	0.083
Swan Ganz	50 (9.2%)	22 (14.7%)	0.016
MV	20 (3.7%)	7 (4.7%)	0.04
IABP	7 (4.7%)	20 (3.7%)	0.3
LV function			
Moderate-severe	155 (28%)	50 (33.3%)	0.781
Hospital stay, days	6 (4-7)	5.5 (4-7)	0.461
Mortality	43 (7.9%)	18 (12%)	0.174
Death causes			
Infections	5 (11.6%)	1 (5.6%)	0.35
Heart failure	24 (55.8%)	9 (50%)	
Mechanical complications	3 (7%)	0 (0%)	
Arrhythmia	11 (25.6%)	8 (44.4%)	

AF: Atrial fibrillation. VT: Ventricular tachycardia. RV: Right ventricle. AV: Atrioventricular block. MV: Mechanical ventilation IABP. Intraaortic balloon pump. LV: Left ventricular

Variable	OR	95 % CI	p
Age	1.044	1.019-1.062	0.001
Female gender	1.381	0.798-2.388	0.249
Diabetes	1.687	1.021-2.687	0.041
Hypertension	0.571	0.338-0.963	0.036
Renal failure	1.276	0.603-2.698	0.524
Previous AMI	2.089	1.218-3.585	0.007
Smoking	1.175	0.707-1.951	0.533
Dyslipidemia	1.252	0.763-2.053	0.373

AMI: Acute myocardial infarction

Table 4. Multivariate analysis for Killip and Kimball C-D on admission

Variable	OR	95 % CI	p
Age	1.021	1.007-1.034	0.003
Female gender	1,.03	0.711-1.498	0.869
Diabetes	1.271	0.892-1.811	0.184
Previous infarction	0.817	0.579-1.152	0.901
Hypertension	1.108	0.756-1.608	0.249
Renal failure	1.02	0.563-1.86	0.161
Dyslipidemia	1.135	0.828-1.555	0.431

Table 5. Multivariate analysis for global in-hospital complications: death, reinfarction or postinfarction angina, mechanical or electrical complications, mechanical ventilation or use of aortic balloon pump.

cluded in the GRACE registry indicates that women are 43% more likely to suffer major bleeding during hospitalization, a risk that became higher in STEMI patients (OR 1.71). (20, 21) Likewise, women have higher rates of puncture site complications during primary angioplasty and greater bleeding related to reperfusion with thrombolytics. (22)

Women are at greater risk of developing high-grade atrioventricular block, a finding similar to that found in the Krumholz study, which could be linked to the lower presence of collateral circulation. In addition, they presented a higher percentage of mechanical complications, an association previously described in the literature, especially in older, non-smoking, and with single-vessel disease women. (15)

It is interesting to note that the multivariate analysis found no significant relationship between gender and the worst hemodynamic impact valued as Killip and Kimball C-D. This would show that gender is not a weakness in itself, but rather groups a series of factors that imply worse tolerance to infarction, such as age and diabetes. The analysis of the factors associated with the occurrence of complications showed something similar, with no significant association of gender in the multivariate analysis, complications being again an expression of older age and percentage of bleeding. The literature shows ambivalent results in this regard, probably linked to the different composition of the patients included in the studies (unstable angina, STEMI and non-STEMI cases).

Limitations

Possibly our sample is not large enough to detect some differences, due to the fact that women represented only one fifth of the subjects analyzed. This situation is common to most of the works and registries, and reinforces the need for more information to better characterize the occurrence and evolution of ACS among women.

On the other hand, our analysis was performed on data obtained between 2009 and 2010, which represents the practice of that period and could vary from the one performed today.

CONCLUSIONS

The comparison between men and women shows that the latter have a different cardiovascular risk profile, with worse hemodynamic impact and greater in-hospital STEMI complications. Gender was not an element individually linked to it, but rather seems to group a series of factors, such as age and diabetes, that imply worse tolerance to infarction.

Conflicts of interest

None declared
(See author´s conflicts of interest forms on the web / Supplementary Material)

REFERENCES

1. Pérez GE, Costabel J, González N, Zaidel E, Altamirano M, Schiavone M, et al. Acute Myocardial Infarction in Argentina. Rev Argent Cardiol 2013;81:390-9. http://doi.org/sg9
2. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third Universal Definition of Myocardial Infarction. Global Heart 2012;7:275-95. 10.1016/j.gheart.2012.08.001
3. Meyers HP, Limkakeng AT, Jaffa EJ, Patel A, Theiling BJ, Rezaie SR, et al. Validation of the modified Sgarbossa criteria for acute coronary occlusion in the setting of left bundle branch block: A retrospective case-control study. Am Heart J 2015;170:1255-64. http://doi.org/f76n5r
4. Steg PG, James SK, Atar D, Badano LP, Lundqvist CB, Borger MA, et al. ESC Guidelines for the management of acute myocardial in-

farction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur Heart J 2012;33:2569-619. http://doi.org/zkn
5. Kosuge M, Kimura K, Ishikawa T, Ebina T, Hibi K, Tsukahara K, et al. Differences between men and women in terms of clinical features of ST-segment elevation acute myocardial infarction. Circulation J 2006;70:222-6. http://doi.org/bs3cdj
6. Baratta S, Burna F, Ferroni F, Ho Bang J, Calvo G, Cecchi A, et al. Rev Argent Cardiol 2000;68:539-49.
7. Williams JK, Adams MR, Klopfenstein HS. Estrogen modulates responses of atherosclerotic coronary arteries. Circulation 1990;81:1680-7. http://doi.org/fpwtr7
8. Hochman JS, Tamis JE, Thompson TD, Weaver WD, White HD, Van de Werf F, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators. N Engl J Med 1999;341:226-32. http://doi.org/bb7rx5
9. Barros M, Casellas LF, Coria N, Duronto EA, Beck E, Bozovich GE. Women with acute coronary syndromes are less invasively treated than men in the acute phase in an Argentine population. Rev Argent Cardiol 2013;81:299-300. http://doi.org/cgv4
10. Gholizadeh L, Davidson P. More similarities than differences: an international comparison of CVD mortality and risk factors in women. Health Care Women Iint 2008;29:3-22. http://doi.org/bn45hv
11. Chen KY, Rha SW, Li YJ, Jin Z, Minami Y, Park JY, et al. 'Smoker's paradox' in young patients with acute myocardial infarction. Clin exp Pharmacol Physiol 2012;39:630-5. http://doi.org/f33rs4
12. Ciruzzi M, Soria P, Fortunato M, Zylbersztejn H, Talamona S, Gagliardi E. Influencia del sexo, tabaquismo y antecedentes de enfermedad coronaria en la edad de aparición del primer infarto de miocardio. Rev Argent Cardiol 1995;63:17-23.
13. Mariani J, Anotonietti L, Tajer C, De Abreu M, Charask A, Silberstein M, et al. Gender differences in the treatment of acute coronary syndromes: results of the Epi-Cardio Registry. Rev Argent Cardiol 2013;81:307-15. http://doi.org/cgv5
14. Dey S, Flather MD, Devlin G, Brieger D, Gurfinkel EP, Steg PG, et al. Sex-related differences in the presentation, treatment and outcomes among patients with acute coronary syndromes: the Global Registry of Acute Coronary Events. Heart (British Cardiac Society) 2009;95:20-6. http://doi.org/fscg8n
15. Dreyer RP, Dharmarajan K, Kennedy KF, Jones PG, Vaccarino V, Murugiah K, et al. Sex Differences in 1-Year All-Cause Rehospitalization in Patients After Acute Myocardial Infarction Clinical Perspective. Circulation 2017;135:521-31. http://doi.org/f9p8m7
16. Valero-Masa MJ, Velásquez-Rodríguez J, Diez-Delhoyo F, Devesa C, Juárez M, Sousa-Casasnovas I, et al. Sex differences in acute myocardial infarction: Is it only the age? Int J Cardiol 2017;231:36-41. http://doi.org/cgv6
17. Akhter N, Milford-Beland S, Roe MT, Piana RN, Kao J, Shroff A. Gender differences among patients with acute coronary syndromes undergoing percutaneous coronary intervention in the American College of Cardiology-National Cardiovascular Data Registry (ACC-NCDR). Am Heart Journal 2009;157:141-8. http://doi.org/bb62hp
18. Milcent C, Dormont B, Durand-Zaleski I, Steg PG. Gender differences in hospital mortality and use of percutaneous coronary intervention in acute myocardial infarction: microsimulation analysis of the 1999 nationwide French hospitals database. Circulation 2007;115:833-9. http://doi.org/dw3629
19. Fang J, Alderman MH. Gender differences of revascularization in patients with acute myocardial infarction. Am J Cardiol 2006;97:1722-6. http://doi.org/fjw5sb
20. Hochman JS, McCabe CH, Stone PH, Becker RC, Cannon CP, DeFeo-Fraulini T, et al. Outcome and profile of women and men presenting with acute coronary syndromes: a report from TIMI IIIB. TIMI Investigators. Thrombolysis in Myocardial Infarction. J Am Coll Cardiol 1997;30:141-8. http://doi.org/fsb7pw
21. Alexander KP, Chen AY, Newby LK, Schwartz JB, Redberg RF, Hochman JS, et al. Sex differences in major bleeding with glycoprotein IIb/IIIa inhibitors: results from the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) initiative. Circulation 2006;114:1380-7. http://doi.org/djvbn4
22. Lansky AJ, Hochman JS, Ward PA, Mintz GS, Fabunmi R, Berger PB, et al. Percutaneous coronary intervention and adjunctive pharmacotherapy in women: a statement for healthcare professionals from the American Heart Association. Circulation 2005;111:940-53. http://doi.org/cbxt58

APPENDIX

Definitions:

- ST-segment elevation myocardial infarction (STEMI): presence of ST-segment elevation measured at J point in two contiguous leads: ≥0.25 mV in men under 40 years, ≥0.2 mV in men over 40 years, or ≥0.15 mV in women in leads V2-V3 and/or ≥0.1 mV in other leads. (2) Moreover, ST-segment elevation was interpreted as presumably new complete left bundle branch block or with positive criteria according to Sgarbossa's work. (3)
- Dyslipidemia: total cholesterol values >200 mg/dl, triglycerides >150 mg/dl, under treatment with lipid-lowering drugs or self-referential.
- Diabetes: fasting blood glucose >126 mg/dl, oral glucose tolerance test (PTOG) >200 mg/dl at 2 hours, or random blood glucose >200 mg/dl prior to the episode. Patients: under treatment with hypoglycemic agents or insulin. Self-referential.
- Smoking: usual or occasional consumption of tobacco within the year prior to the episode. Ex-smoking: presenting a minimum of one year of tobacco abstinence.
- Hypertension: self-referential, blood pressure ≥140/90 mmHg (130/80 mmHg in diabetic and with baseline chronic renal failure (CRF) patients or in patients under antihypertensive treatment.
- Gout: patients with at least one acute gout episode.
- Sedentarism: lack of regular physical activity; self-referential.
- Post-Acute Myocardial Infarction Angina (PIAMA): chest pain 24 hours after and within 30 days post infarction, in the case of STEMI.
- Re-AMI: 24 hours and up to 7 days after the episode, chest pain for more than 20 minutes and/or new or recurrent changes in the ECG (supra ST or infra ST >1 mm in two or more contiguous leads) and CK-MB x 2 or 50% increase from the previous value.
- TIMI Bleeding (Thrombolysis in myocardial infarction) (4):
  1. Major: >5 g/dL drop in hemoglobin (Hb) or >15% in hematocrit (HCT), or fatal bleeding, or cardiac tamponade, or brain hemorrhage confirmed by computed tomography (CT) or magnetic resonance imaging (MRI).
  2. Minor: fall in Hb between >3 mg/d to ≤5 mg/dl or more than 10% in HCT, with known bleeding site, hematuria, hematemesis, hemoptysis; or when there is no bleeding with >4 gr/dl drop in Hb or >12% in HCT.
- Stroke: new neurological focus lasting more than 24 hours and/or compatible CT or MRI image.
- Sustained ventricular tachycardia (TVS): regular tachyarrhythmia with QRS >120 msec compatible with ventricular tachycardia according to Brugada criteria, lasting more than 30 seconds or with hemodynamic decompensation.
- Renal failure: creatinine clearance calculated by the Cockcroft Gault equation <60 ml/min.