

# Acute myocardial Infarction in Women: Clinical Characteristic and Short-Term and Long-Term Outcomes

STELLA M. MACÍN<sup>†</sup>, EDUARDO R. PERNA<sup>†</sup>, LORENA CORONEL, JAIME PARRA, PERLA BARRIOS, MARCELO DE LA ROSA, PABLO LIVA, JORGE BACARO, JORGE R. BADARACCO

Received: 04/03/2008  
Accepted: 11/10/2008

**Address for reprints:**  
Dr Stella Maris Macín  
Coronary Intensive Care Unit.  
Bolívar 1334  
(3400) Corrientes, Argentina  
Phone number: +54-03783-410000  
Fax: +54-03783-410030  
e-mail: macinucic@hotmail.com  
or stellam@gigared.com

## ABSTRACT

### Background

In Latin America, little is known about dissimilarities between men and women with acute coronary syndromes. We hypothesized that there are differences in acute myocardial infarction between both sexes.

### Objectives

To compare the clinical characteristics and short-term and long-term prognosis in women (group I) and men (group II) with acute myocardial infarction (AMI).

### Material and Methods

Between January 2001 and December 2004, 536 patients with AMI within 24 hours since the onset of symptoms were prospectively and consecutively admitted. One hundred and forty four (26.9%) were women (group I).

### Results

Median age was greater in group I (66 [interquartile range 25-75: 56-75] versus 60 [interquartile range 25-75: 52-68] years;  $p < 0.001$ ). The incidence of smoking habits (25% versus 46.7%;  $p < 0.001$ ) as well as of prior myocardial infarction (18.1% versus 25.3%;  $p = 0.008$ ) was lower among women; however, chronic stable angina was more frequent than in men (20.8% versus 12%;  $p = 0.01$ ). Heart rate and BUN were greater at admission (80 versus 76 bpm;  $p = 0.01$ , and 0.48 versus 0.36 g/L;  $p = 0.003$ , respectively) but ejection fraction was similar between both groups (50% versus 51%;  $p = 0.27$ ). In-hospital outcomes [death (9.7% versus 4.8%;  $p = 0.037$ ), refractory angina (9.7% versus 4.2%;  $p = 0.039$ ) and acute pulmonary edema (12.5% versus 5.4%;  $p = 0.005$ )] were worse in women than in men. In both groups, reperfusion strategies were similar: thrombolytic therapy (21.4% versus 20.3%;  $p = ns$ ) and primary angioplasty (18.1% versus 21.8%;  $p = ns$ ). Survival rates at 54 months were 77% versus 85% in groups I and II, respectively (log rank test:  $p = 0.032$ ). Univariate analysis showed that sex was a significant variable (OR=1.71;  $p = 0.035$ ). Cox proportional hazards model found the following significant variables for mortality: age (HR=1.033;  $p = 0.006$ ), as well as BUN (HR=4.275;  $p < 0.001$ ), heart rate (HR=1.018;  $p = 0.004$ ) and Killip classification (HR=2.771;  $p = 0.01$ ) at admission.

### Conclusions

Women admitted for AMI have different short-term and long-term risk profiles than men; however, they are treated in a similar fashion. After adjusting for other variables, sex did not emerge as an independent predictor of risk at follow-up.

REV ARGENT CARDIOL 2008;76:429-436.

**Key words** > Myocardial infarction - Sex - Mortality

Abbreviations >	
ARAs	Angiotensin II receptor antagonists
ECG	Electrocardiogram
EF	Ejection fraction
AMI	Acute myocardial infarction
ACEIs	Angiotensin-converting enzyme inhibitors
ACS	Acute coronary syndrome

## BACKGROUND

Despite progress in therapeutic options achieved in the last decades, prognosis of patients who have survived to the acute phase of coronary artery disease

depends on several factors, such as age, congestive heart failure, ventricular function and gender, among others. (1)

Previous studies have reported greater mortality rates in women, probably attributed to the fact that

they are older and present more comorbidities, (2-4) and to differences in the pathogenesis of coronary artery disease, in the response to therapy and in the possibility to undergo procedures and interventions such as coronary arteriography, angioplasty and coronary artery bypass graft surgery which might have an influence on prognosis. (5, 6) However, as new recommendations, such as chest pain units, primary angioplasty, antithrombotic agents and statins have been introduced and put into practice, it is possible that this tendency will change as more women may undergo interventional procedures. (7-9) In Latin America, little is known about dissimilarities between men and women with acute coronary syndromes. We hypothesized that there are differences in acute myocardial infarction (AMI) between both genders. The aim of this study was to compare the clinical characteristics and short-term and long-term prognosis in women and men with acute myocardial infarction.

## MATERIAL AND METHODS

### Population

This observational and prospective study enrolled 536 consecutive patients, admitted to the intensive care coronary unit in the Instituto de Cardiología de Corrientes between January 2001 and December 2004, with a diagnosis of acute myocardial infarction within 24 hours after onset of symptoms.

### Inclusion Criteria

We included patients with acute myocardial infarction, defined by two out of three criteria: 1) typical angina at rest lasting for at least 20 minutes, 2) rise in CK-MB above the reference limit, and 3) development of new Q waves.

### Exclusion Criteria

Patients admitted 24 hours after the onset of symptoms, cardiogenic shock, unstable angina, suspected myocarditis, pulmonary thromboembolism, congenital heart defects, dilated cardiomyopathy, valvular heart disease, pericardial disease and problems in maintaining follow-up were reasons for exclusion from the study.

### Study Protocol

The study protocol was approved by the Teaching and Research Committee of our institution: patients were informed of their inclusion in the project and signed the informed consent form. All patients were admitted in the Coronary Care Unit and complete clinical history with physical examination was taken. The following tests were performed: 12-lead electrocardiogram at admission and 2 hours after the reperfusion strategy used in patients with ST segment elevation; chest X-ray at admission; determination of total CK and CK-MB levels at admission, at two hours after admission or after reperfusion strategy, at 6, 12, 24 hours and every 24 hours thereafter until achieving normal levels; determination of Troponin T (biomarker of myocardial necrosis) using the electrochemiluminescence immunoassay (Roche Diagnostics, Elecsys 2010 automatic analyzer) at admission; BUN and serum creatinine levels.

Mortality: all-cause mortality was recorded at the end of follow-up.

### Follow-up and Endpoints

Patients were followed-up 6 months after the inclusion of the last patient. Assessment of patients was performed in our institution either in the out-patient clinic of coronary artery disease (82%) or by their cardiologists (13%); the remaining 5% of patients were either followed-up by a family doctor in other medical centers or were contacted by phone. Mean follow-up was  $42 \pm 9$  months.

### In-Hospital Management

Most patients received 100-325 mg/d of oral aspirin after admission. Three hundred and twenty two patients presented ST-segment elevation AMI and 112 non-ST-segment elevation AMI; 212 of them were hospitalized within 12 hours from onset of symptoms. Patients admitted within 12 hours of symptoms onset and ST-segment elevation underwent primary angioplasty or thrombolytic therapy. Nitroglycerin was administered intravenously to 95% of patients and beta blockers and angiotensin-converting enzyme inhibitors were prescribed to all patients in absence of contraindications. Coronary angiography was performed to 63% of patients with non-ST-segment elevation; 51% of them underwent angioplasty.

### Statistical Analysis

Patients were divided into two groups: group I (women) and group II (men). Patients characteristics were compared using the chi square test for qualitative variables and the results were expressed as percentages. Quantitative variables were reported as median with its corresponding interquartile interval (25-75) and were analyzed with Mann-Whitney's test. Receiver-operator characteristic (ROC) curves were constructed to determine the optimal cut-off point of BUN to predict mortality during follow-up (BUN value  $\geq 0,55$  g/L). Two Cox proportional models were constructed in order to identify independent predictors of mortality during follow-up. Both models included the following variables: gender, age, chronic stable angina, crackles, hematocrit, BUN, systolic blood pressure, heart rate, Killip class (model I) and a cut-off point of BUN  $\geq 0,55$  g/L as a qualitative variable (model II). A p value  $< 0.05$  was considered statistically significant. Survival curves were constructed using the Kaplan-Meier method and compared with the log-rank test. Data was analyzed using software SPSS 10.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

## RESULTS

### Patients Characteristics

Population data are described in Table I. One hundred and forty four (26.9%) participants were women (group I). Median age was greater in group I. Smoking habits and prior myocardial infarction were less frequent in women; however, history of chronic stable angina was more prevalent than in men.

Patients in group I had higher heart rate and greater levels of creatinine and BUN, and similar mean values of Troponin T, maximal CK-MB and ejection fraction at admission; however, there was a trend towards greater time from onset of symptoms to reperfusion in women (Table 2).

In-hospital mortality and adverse outcomes were greater in women (Table 3).

**Table 1.** Demographic characteristics in men and women

Variable	Women (group I)	Men (group II)	p
Patients, n (%)	144 (26.9)	392 (73.1)	-
Age, years [median ( IQR 25-75)]	66 (56.25-75)	60 (52-68.75)	0.001
Chronic stable angina (%)	30 (20.8)	47 (12)	0.01
Hypertension (%)	48 (33.3)	108 (27.6)	0.19
Dyslipemia (%)	54 (37.5)	155 (39.5)	0.42
Obesity (%)	31 (21.5)	79 (20.3)	0.81
Diabetes (%)	39 (27.1)	84 (21.4)	0.16
Smoking habits (%)	36 (25)	183 (46.7)	< 0.001
Previous myocardial infarction (%)	26 (18.1)	99 (25.3)	0.008

IQR: interquartile range 25-75.

**Table 2.** Vital signs and lab tests in groups I and II

Variable	Women (group I) [median (IQR 25-75)]	Men (group II) [median (IQR 25-75)]	p 95% CI
SBP (mm Hg)	120 (16.5)	128 (110-145)	0.02
Heart rate (bpm)	80 (68.5-95.75)	76 (70-89)	0.02
BUN, g/L	0.48 (0.40-0.68)	0.36 (0.29-0.50)	0.003
Creatinine, mg/dl	1.11 (0.78-.37)	1.02 (0.85-1.29)	0.02
Hematocrit, %	40 (37-42)	42 (13-15)	0.31
cTnT at admission, ng/dl	0.50 (0.24-1.23)	0.45 (0.25-0.80)	0.68
CPK-MB, U/L	82 (49-163)	85 (54-214)	0.10
Ejection fraction, n (%)	50 (46-55)	51 (45-54)	0.27
Time to reperfusion, min	420 (360-460)	300 (240-340)	0.04

SBP: Systolic blood pressure. cTnT: cardiac Troponin T IQR: interquartile range 25-75.

**Table 3.** In-hospital events in both groups

Variable	Women (group I)	Men (group II)	p 95% CI
Muerte hospitalaria, %	9.7	4.8	0.037
Angina refractaria, %	9.7	4.2	0.039
Edema agudo de pulmón, %	12.5	5.4	0.005
Fibrilación auricular, %	7.6	3.6	0.04

### Treatment

In this series of patients included within 24 hours after onset of symptoms, the use of reperfusion strategies was similar between both groups; thrombolysis (21.4% versus 20.3%;  $p = ns$ ), primary angioplasty (18.1% versus 21.8%;  $p = ns$ ), and early revascularization surgery (3.1% versus 2.9%;  $p = ns$ ). Interventional strategy with angioplasty was similar among patients with non-ST-segment elevation (51.8% versus 50.9%;  $p = ns$ ).

No significant differences were observed in the use of ACEIs-ARAs (89% versus 88.7%;  $p = ns$ ), aspirin (95.2% versus 94.3%;  $p = ns$ ), clopidogrel (23.5 versus 24.2;  $p = ns$ ) and statins (62% versus 65%;  $p = ns$ ). Patients in group I showed a trend towards a

greater use of furosemide (29.2% versus 21.4%;  $p = 0.04$ ) and lower administration of beta blockers (65.6% versus 72.8%;  $p = 0.04$ ).

### Predictors of Mortality and Survival Analysis

In women, in-hospital mortality rates, as well as complications during hospitalization, such as refractory angina, acute pulmonary edema and atrial fibrillation were almost than double those in men (Table 3).

Age (HR = 1.033, 95% CI 1.010-1.058;  $p = 0.006$ ), heart rate (HR = 1.018, 95% CI 1.006-1.031), BUN (HR = 4.275, 95% CI 1.006-1.031) and Killip classification (HR = 2.771; 95% CI 1.276-6.016) at admission were identified as independent predictors of mortality during follow-up (Table 4). Patients with BUN

Female gender (OR = 1.71; p = 0.035, 95% CI 1.039-2.839)

Variabl	OR	95% CI	p
Gender (F/M)	1.214	0.82-1.62	ns
Age, years	1.033	1.010-1.058	0.006
BUN, mg/dl	4.275	1.006-1.031	< 0.001
Heart rate (bpm)	1.018	1.006-1.031	0.004
Maximal Killip class			< 0.001
B	2.771	1.276-6.016	0.010
C	2.738	1.136-6.596	0.025
D	28.441	14.261-56.719	< 0.001

**Table 4.** Modelo proporcional de Cox (I)

Variable	OR	95% CI	p
Gender (F/M)	1.214	0.82-1.62	ns
Age, years	1.028	1.007-1.050	0.010
BUN $\geq$ 55 g/L (Yes/No)	6.197	3.415-11.243	< 0.001
Heart rate (bpm)	1.017	1.004-1.030	0.011
Maximal Killip class			< 0.001
B	2.586	1.183-5.655	0.017
C	3.535	1.619-7.719	0.002
D	30.178	14.680-62.039	< 0.001

**Table 5.** Cox proportional model (II)

of 0.55 g/L or greater had a 6-fold increase in the risk of mortality (OR = 6.197, 1.007-1.050) (Table 5, model 2).

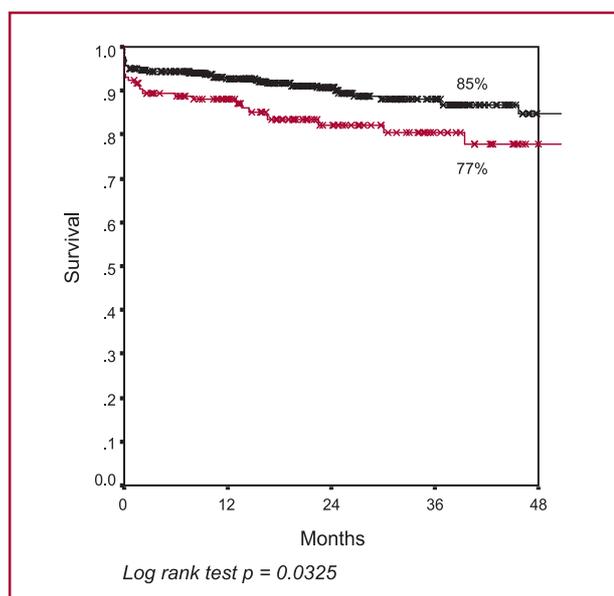
Survival at 48  $\pm$  10 months was lower in women (77% versus 85%, long rank test: p = 0.032) (Figure 1). Complete follow-up was achieved in 97.5% of patients.

## DISCUSSION

According to the results of this observational study, performed on an unselected population of patients with acute myocardial infarction presenting within 24 hours after symptoms onset, women had different risk profiles than men. Gender did not emerge as an independent predictor of risk.

### Risk Factors and Prognosis in Women with Myocardial Infarction

It is well known that in women with myocardial infarction, risk factors differ from those reported in men; the prevalence of diabetes and hypertension is greater and smoking habits are less frequent. (10) In this study, basal characteristics differ in women and men: while women were older and presented greater prevalence of chronic stable angina, smoking habits and history of previous myocardial infarction was more frequent in men. These findings are consistent with those of several studies previously published (11-13)



**Fig. 1.** Survival in both groups.

that reported worse in-hospital outcomes in women related to the presence of more comorbidities, older age and longer time intervals from symptoms onset to medical consultation, among others. (14) Women

in the present study were *older* than men and there was a *trend towards a greater time delay to reperfusion*; however, use of reperfusion techniques was similar. In this sense, time delay from onset of symptoms to reperfusion (mean time 5.5 hours) was greater in women than in men (420 versus 300 min). Although this difference was not statistically significant, this information should be taken into account in terms of epidemiology. In this way, the general population and especially women with myocardial infarction should be encouraged to seek medical help early (within 3 hours after onset of symptoms), as early intervention is essential to preserve ventricular function. (14) In fact, mean time to consultation is almost the double, especially in women. (15, 16)

Interestingly, the use of reperfusion strategies was similar in both groups. This finding differs from other series that reported that women were less likely to undergo invasive and reperfusion therapies. (16-18) Therefore, and in spite of the use of similar treatments, many of the differences seen between men and women with myocardial infarction may be partially explained by gender differences. (19) In this way, some conditions that are only present in women explain the physiopathological differences with men, for example early menopause, Raynaud's phenomenon, migraine, vasospastic disorders and vasculitis. Hormones may also play a key role in vascular physiopathology: women are used to experience significant fluctuations in hormone levels such as reduction in estrogen concentrations during premenopause with changes in the balance between estrogens and androgens. Estradiol is the predominant estrogen before menopause; thereafter, estrogens are the result of the conversion from androgens in the adipose tissue. (19, 20) In addition, estrogens may have a protective role on vulnerable plaques preventing the progression of atherosclerotic lesions. Rupture and subsequent thrombosis of less severe plaques may prevent the development of ischemic preconditioning and collateral circulation, worsening the prognosis of myocardial infarction. Gender-related differences in ACS may be associated with variations in thrombolytic and fibrinolytic activity. Heart failure is more frequent in women probably due to diastolic dysfunction. (21)

However, despite these differences due to biological factors the impact of this bias is important. Compared to previous studies, our series failed to show significant differences in the use of reperfusion strategies in women, and multivariate analysis demonstrated that female gender was not an independent variable. Using a simulation model of similar use of angioplasty in men and women, as Milcent et al. have established, the difference in mortality reduces in one third. (20) The results obtained in the present series support the hypothesis that greater mortality rates in women are associated with bias phenomena and not with strict biological differences; in addition, women mortality

rates decreased when they were adjusted by age. These findings allow us to ask ourselves whether the presence of biological differences between men and women are real and, if so, do women have worse outcomes than men? In fact, myocardial infarction in women occurs 10 years later with an incidence of one woman out of four men. (20)

### Predictors of Mortality

Most studies agree that female gender increases the risk of death in acute myocardial infarction. Indeed, the present study reported a 1.7-fold increase in mortality risk in *women*; (3, 6, 9, 10, 20) however when the analysis for confounders such as age was performed, this difference was no longer statistically significant. Most of the series that included patients with ST-segment-elevation acute myocardial infarction demonstrated increase in short-term and long-term mortality. (3, 11, 20, 22) Myocardial infarction is extremely rare in young women; however, its presence was underestimated in the Framingham study. (23) Women present not only greater mortality risk, but also more complications during hospitalization and are less likely to undergo reperfusion interventions; however, the independent relationship between gender and adverse outcomes is controversial despite these therapies are underused. (24-27) Previous series have reported that the use of less aggressive therapies in women is responsible for high mortality rates; (28-30) nevertheless, in the present study the percentage of reperfusion therapies with thrombolytic agents or percutaneous coronary interventions in men and women was similar, and excess mortality remains unclear. This difference may be explained by the presence of small and tortuous coronary vessels and by other biological differences that may reflect physiopathological and anatomical differences between men and women. (19)

Age was a strong predictor of mortality in the present study: for each increase in age by one year, the mortality rate increased 1.033 times. This finding coincides with the results of international trials and registries. (31) This is an interesting piece of information that points out that high mortality rates in women are more related with age than with the gender itself.

BUN at admission was another important marker of prognosis. A cut-off point greater than 0.55 g/L was associated with a 4 to 6-fold increase in mortality risk, reflecting more severe patients with greater comorbidities. The role of renal function has recently become important in patients with ACS. (32) The VALIANT study reported that, in patients with myocardial infarction, glomerular filtration rates lower than 81ml/min are associated with an increase in adverse outcomes, even after adjustment for different variables. (33) Our study supports to perform a precise assessment of the presence of renal failure, as mild stages of renal impairment with normal creatinine

level and a glomerular filtration rate of about 60 ml/min have a negative impact in the prognosis of patients with ACS. (32)

Heart rate at admission was also a marker of prognosis, with a risk increase of 1% for each increase in heart rate by 1 beat per minute. These findings are similar to previous reports. (34)

According to previous studies, Killip class was also associated with worse short-term and long-term outcomes. Thus, Killip class B or C increased the risk 2.7 times, while Killip class D produced a 28-fold increase. (35) In patients with severe heart failure mortality rates are greater due to its association with comorbidities. A previous study reported that in-hospital mortality was 6 times greater in patients with heart failure and survival at 10 years was only 10% compared to 30% in the group without heart failure. (35)

### Survival

Survival curves show that female gender has worse outcomes. It should be noted that both curves have already separated at the first month and this difference continued until the end of follow-up.

### Study Limitations

Despite this study shows data of the "real world", this registry of acute myocardial infarction within 24 hours after symptoms onset includes different reperfusion strategies that might have some influence on long-term outcomes. Another limitation is the small size of the sample and population heterogeneity.

### Clinical implications

This study confirms the presence of gender differences in acute coronary syndromes; it clearly identifies a group of patients with worse in-hospital outcomes and lower 4-year survival, and these differences are more related to clinical characteristics than to gender in itself, as female gender was not an independent predictor.

The clinical usefulness of these findings contributes to describe outcomes of patients with acute myocardial infarction associated with gender differences; in addition, it emphasizes the necessity to improve time delay after symptoms onset to medical consultation, to develop a line of research on pathophysiological characteristics and work groups focused on studying these population. (21, 31-42)

### CONCLUSIONS

Women admitted for acute myocardial infarction have different short-term and long-term risk profiles than men; however, they are treated in a similar fashion. After adjusting for other variables, sex did not emerge as an independent predictor of risk at follow-up.

### RESUMEN

#### Infarto agudo de miocardio en mujeres: características clínicas y evolución a corto y a largo plazo

#### Introducción

En América latina se conoce poco acerca de las diferencias entre varones y mujeres con síndrome coronario agudo. La hipótesis del presente trabajo es que el sexo presenta diferente riesgo cardiovascular en el infarto agudo de miocardio.

#### Objetivos

Comparar características clínicas y pronóstico a corto y a largo plazo en mujeres (grupo I) y en varones (grupo II) con infarto agudo de miocardio (IAM).

#### Material y métodos

Desde enero de 2001 hasta diciembre de 2004 se admitieron en forma prospectiva y consecutiva 536 pacientes con IAM dentro de las 24 horas de evolución. De ellos, 144 (26,9%) eran mujeres (grupo I).

#### Resultados

La mediana de edad del grupo I fue mayor (66 [rango intercuartil 25-75: 56-75] versus 60 [rango intercuartil 25-75: 52-68] años;  $p < 0,001$ ). Las mujeres fumaban menos (25% versus 46,7%;  $p < 0,001$ ), tenían menos infarto previo (18,1% versus 25,3%;  $p = 0,008$ ) y más angina crónica estable (20,8% versus 12%;  $p = 0,01$ ). Al ingreso, las mujeres estaban más taquicárdicas (80 versus 76 lat/min;  $p = 0,01$ ), con mayor nivel de urea (0,48 versus 0,36 g/L;  $p = 0,003$ ) y similar Fey (50% versus 51%;  $p = 0,27$ ). Tuvieron peor evolución hospitalaria: muerte (9,7% versus 4,8%;  $p = 0,037$ ), angina refractaria (9,7% versus 4,2%;  $p = 0,039$ ) y edema agudo de pulmón (12,5% versus 5,4%;  $p = 0,005$ ). Las estrategias de reperfusión en ambos grupos fueron: trombolíticos (21,4% versus 20,3%;  $p = ns$ ) y angioplastia primaria (18,1% versus 21,8%;  $p = ns$ ). La supervivencia a los 54 meses fue del 77% versus el 85% en los grupos I y II, respectivamente (*log rank test*:  $p = 0,032$ ). El sexo fue una variable significativa en el análisis univariado (OR = 1,71;  $p = 0,035$ ). En el modelo proporcional de Cox, las variables significativas de mortalidad fueron edad (HR = 1,033;  $p = 0,006$ ) y, al ingreso, urea (HR = 4,275;  $p < 0,001$ ), frecuencia cardíaca (HR = 1,018;  $p = 0,004$ ) y Killip (HR = 2,771;  $p = 0,01$ ).

#### Conclusiones

Las mujeres admitidas por IAM tienen un perfil de riesgo diferente que los varones, tanto a corto plazo como a largo plazo, a pesar de que son tratadas en forma similar. El sexo no fue un predictor de riesgo independiente en el seguimiento luego de ajustar con otras variables.

**Palabras clave >** Infarto de miocardio - Sexo - Mortalidad

### BIBLIOGRAPHY

1. Yung R, Brilakis E, Reeder G, Gersh BJ. Modern management of acute myocardial infarction. *Curr Probl Cardiol* 2006;31:769-817.
2. Fukuoka Y, Dracup K, Moser DK, McKinley S, Ball C, Yamasaki K, et al. Is severity of chest pain a cue for women and men to recognize

- acute myocardial infarction symptoms as cardiac in origin? *Prog Cardiovasc Nurs* 2007; 22:132-7.
3. Heer T, Schiele R, Schneider S, Gitt AK, Wienbergen H, Gottwik M, et al. Gender differences in acute myocardial infarction in the era of reperfusion (the MITRA Registry). *Am J Cardiol* 2002; 89:511-7.
  4. Blanco P, Gagliardi J, Higa C, Dini A, Guetta J, Di Toro D, Botto F, Sarmiento. Infarto agudo de miocardio. Resultados de la Encuesta SAC 2005 en la República Argentina. *Rev Argent Cardiol* 2007;75:163-70.
  5. Chang AM, Mumma B, Sease KL, Robey JL, Shofer FS, Hollander JE. Gender bias in cardiovascular testing persists after adjustment for presenting characteristics and cardiac risk. *Acad Emerg Med* 2007;14:599-605.
  6. Perers E, Caidahl K, Herlitz J, Karlsson T, Hartford M. Impact of diagnosis and sex on long-term prognosis in acute coronary syndromes. *Am Heart J* 2007;154:482-8.
  7. Song XT, Chen YD, Pan WQ, Lü SZ; For the CRACE investigators. Gender based differences in patients with acute coronary syndrome: findings from Chinese Registry of Acute Coronary Events (CRACE). *Chin Med J (Engl)* 2007;120:1063-7.
  8. Blomkalns AL, Chen AY, Hochman JS, Peterson ED, Trynosky K, Diercks DB, et al; CRUSADE Investigators. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) National Quality Improvement Initiative. *J Am Coll Cardiol* 2005;45: 832-7.
  9. Aguado-Romeo MJ, Márquez-Calderón S, Buzón-Barrera ML; Medical Practice Variations Andalusian Group Hospital mortality in acute coronary syndrome: differences related to gender and use of percutaneous coronary procedures. *BMC Health Serv Res* 2007;7:110.
  10. MacIntyre K, Stewart S, Capewell S, Chalmers JW, Pell JP, Boyd J, et al. Gender and survival: a population-based study of 201,114 men and women following a first acute myocardial infarction. *J Am Coll Cardiol* 2001;38:729-35.
  11. Nabel EG, Selker HP, Califf RM, Canto JG, Cao JJ, Desvigne-Nickens P, et al. Women's ischemic syndrome evaluation: current status and future research directions: report of the National Heart, Lung and Blood Institute workshop. *Circulation* 2004;109:e50-e52.
  12. Matsui K, Fukui T, Hira K, Sobashima A, Okamatsu S, Hayashida N, et al. Impact of sex and its interaction with age on the management of and outcome for patients with acute myocardial infarction in 4 Japanese hospitals. *Am Heart J* 2002;144:101-7.
  13. Hanratty B, Lawlor DA, Robinson MB, Sapsford RJ, Greenwood D, Hall A. Sex differences in risk factors, treatment and mortality after acute myocardial infarction: an observational study. *J Epidemiol Community Health* 2000;54:912-6.
  14. Mahon NG, McKenna CJ, Codd MB, O'Rourke C, McCann HA, Sugrue DD. Gender differences in the management and outcome of acute myocardial infarction in unselected patients in the thrombolytic era. *Am J Cardiol* 2000;85:921-6.
  15. King KB, McGuire MA. Symptom presentation and time to seek care in women and men with acute myocardial infarction. *Heart Lung* 2007;36:235-43.
  16. Rathore SS, Wang Y, Radford MJ, Ordin DL, Krumholz HM. Sex differences in cardiac catheterization after acute myocardial infarction: the role of procedure appropriateness. *Ann Intern Med* 2002;137:487-93.
  17. Heer T, Schiele R, Schneider S, Gitt AK, Wienbergen H, Gottwik M, et al. Gender differences in acute myocardial infarction in the era of reperfusion (the MITRA Registry). *Am J Cardiol* 2002;89:511-7.
  18. Barakat K, Wilkinson P, Suliman A, Ranjadayalan K, Timmis A. Acute myocardial infarction in women: contribution of treatment variables to adverse outcome. *Am Heart J* 2000;140:740-6.
  19. Anderson RD, Pepine CJ. Gender Differences in the treatment for acute myocardial infarction. Bias or Biology. *Circulation* 2007; 115:823-6.
  20. 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.
  21. Hurtado Martinez J, Pinar Bermudez E, Teruel Carrillo F, Gimeno Blanes JR, Lacunza Ruiz J, Valdesuso R, et al. Mortalidad a corto y largo plazo en mujeres con infarto de miocardio tratado con angioplastia. *Rev Esp Cardiol* 2006; 59:1113-22.
  22. Vaccarino V, Krumholz HM, Berkman LF, Horwitz RI. Sex differences in mortality after myocardial infarction: is there evidence for an increased risk for women? *Circulation* 1995;91:1861-71.
  23. Lundberg V, Wikstrom B, Bostrom S, Asplund K. Exploring sex differences in case fatality in acute myocardial infarction or coronary death events in the northern Sweden MONICA Project. *J Intern Med* 2002;251:235-44.
  24. de Gevigney G, Mosnier S, Ecohard R, Rabilloud M, Cao D, Excoffier S, et al. Are women with acute myocardial infarction managed as well as men? Does it have consequences on in-hospital mortality? Analysis of an unselected cohort of 801 women and 1,718 men. *Acta Cardiol* 2001;56:169-79.
  25. Hanratty B, Lawlor DA, Robinson MB, Sapsford RJ, Greenwood D, Hall A. Sex differences in risk factors, treatment and mortality after acute myocardial infarction: an observational study. *J Epidemiol Community Health* 2000;54:912-6.
  26. Vaccarino V, Rathore SS, Wenger NK, Frederick PD, Abramson JL, Barron HV, et al. Sex and racial differences in the management of acute myocardial infarction, 1994 through 2002. *N Engl J Med* 2005;353:671-82.
  27. Rathore SS, Wang Y, Radford MJ, Ordin DL, Krumholz HM. Sex differences in cardiac catheterization after acute myocardial infarction: the role of procedure appropriateness. *Ann Intern Med* 2002; 137:487-93.
  28. Mehili J, Kastrati A, Dirschinger J, Bollwein H, Neumann FJ, Schomig A. Differences in prognostic factors and outcomes between women and men undergoing coronary artery stenting. *JAMA* 2000; 284:1799-805.
  29. Lagerqvist B, Safstrom K, Stahle E, Wallentin L, Swahn E. Is early invasive treatment of unstable coronary artery disease equally effective for both women and men? FRISC II Study Group Investigators. *J Am Coll Cardiol* 2001;38:41-8.
  30. Vicente Bertomeu-Gonzalez, Julio Nuñez, Eduardo Nuñez, Lorenzo Facila Juan Sanchis, Vicent Bodý, Mauricio Pellicer, et al. Prognostic effect of renal dysfunction after ST-segment elevation myocardial infarction with and without heart failure. *International Journal of Cardiology* 2006;112:159-65.
  31. Schoenenberger AW, Radovanovic D, Stauffer JC, Windecker S, Urban P, Eberli FR, et al. Acute Myocardial Infarction in Switzerland Plus Investigators. Age-related differences in the use of guideline-recommended medical and interventional therapies for acute coronary syndromes: a cohort study. *J Am Geriatr Soc* 2008;56:510-6.
  32. Carda Barrio R, de Agustín JA, Manzano MC, García-Rubira JC, Fernández-Ortiz A, Vilacosta I, et al. In-hospital prognostic value of glomerular filtration rate in patients with acute coronary syndrome and a normal creatinine level. *Rev Esp Cardiol* 2007; 60:714-9.
  33. Lewis EF, Velazquez EJ, Solomon SD, Hellkamp AS, McMurray JJ, Mathias J, et al. Predictors of the first heart failure hospitalization in patients who are stable survivors of myocardial infarction complicated by pulmonary congestion and/or left ventricular dysfunction: a VALIANT study. *Eur Heart J* 2008;29:748-56.
  34. Macín SM, Perna ER, Coronel ML, Kriskovich JO, Bayol PA, Franciosi VA, et al. Influence of admission glucose level on long-term prognosis in patients with acute coronary syndrome. *Rev Esp Cardiol* 2006;59:1268-75.
  35. Macín SM, Perna ER, Augier N, Cialzeta J, Fariás EF, Fontana M, et al. Clinical characteristics and long-term outcome in patients

with heart failure complicating acute myocardial infarction. *Rev Esp Cardiol* 2005;58:789-96.

**36.** Gan SC, Beaver SK, Houck PM, MacLehose RF, Lawson HW, Chan L. Treatment of acute myocardial infarction and 30-day mortality among women and men. *N Engl J Med* 2000;343:8-15.

**37.** Schwarz PE, Lindström J, Kissimova-Scarbeck K, Szybinski Z, Barengo NC, Peltonen M, et al. The European Perspective of Type 2 Diabetes Prevention: Diabetes in Europe - Prevention Using Lifestyle, Physical Activity and Nutritional Intervention (DE-PLAN). *Project Exp Clin Endocrinol Diabetes* 2008;16:167-72.

**38.** Coons JC, Battistone S. 2007 Guideline update for unstable angina/non-ST-segment elevation myocardial infarction: focus on antiplatelet and anticoagulant therapies. *Ann Pharmacother* 2008;42:989-1001.

**39.** Cho L, Hoogwerf B, Huang J, Brennan DM, Hazen SL. Gender differences in utilization of effective cardiovascular secondary prevention: a Cleveland clinic prevention database study. *J Womens Health (Larchmt)* 2008;17:515-21.

**40.** Macin SM, Perna ER, Farias E, Augier N, Agüero M, Fontana M, et al. Myocardial infarction in women: clinical, epidemiological and prognostic differences in relation with men. *Heart Disease. New Trends in Research, Diagnosis and Treatment* 2001;17:259-60.

**41.** Kalra S, Duggal S, Valdez G, Smalligan RD. Review of acute coronary syndrome diagnosis and management. *Postgrad Med* 2008;120:18-27.

**42.** De Luca G, Suryapranata H, Marino P. Reperfusion strategies in acute ST-elevation myocardial infarction: an overview of current status. *Prog Cardiovasc Dis* 2008;50:352-82.