ORIGINAL ARTICLE

CME

Gender Differences in the Treatment of Acute Coronary Syndromes: Results From the Epi-Cardio Registry

JAVIER MARIANI [1,†], LAURA ANTONIETTI [2,†], CARLOS TAJER [MTSAC,1], MAXIMILIANO DE ABREU[1], ADRIAN CHARASK [MTSAC], MARIO SILBERSTEIN[1], JUAN GAGLIARDI [MTSAC, 1], HERNÁN DOVAL [MTSAC,1]

Received: 03/22/2013
Accepted: 03/27/2013

Address for reprints:
Dr. Javier Mariani
Rivadavia 2358 - PB 4
(C1034ACP) CABA, Argentina
Tel. 54 11 4952-4112

ABSTRACT

Background
Controversial evidence has been reported regarding gender bias in the management of patients with acute coronary syndromes; thus, it is relevant to have data related to this topic in our country.

Objective
The aim of this study was to assess gender differences in the management of acute coronary syndromes in cardiovascular care units participating in the Epi-Cardio registry.

Methods
We included 8997 records of patients with diagnosis of acute coronary syndromes. Propensity score adjusted analyses and sensitivity analysis were performed.

Results
In patients with non ST-segment elevation acute coronary syndromes, women were independently associated with lower in-hospital indication of coronary angiography (OR 0.73, 95% CI 0.65 to 0.82), and lower use of IIb/IIIa inhibitors than men.
After adjusted analyses, there were no significant differences between men and women in the use of reperfusion therapy for myocardial infarction or in in-hospital mortality.
At discharge, women were significantly less likely than men to receive prescriptions for beta-blockers and statins, and more likely to receive prescriptions for benzodiazepines.

Conclusions
These findings suggest gender bias in the treatment of patients with acute coronary syndromes, evidenced by selection of a more conservative strategy and lower prescription of drugs recommended for secondary prevention in women. Differences between genders in the approach of acute coronary syndromes should be studied more deeply, as the underutilization of evidence-based therapies could have an impact on women's clinical outcomes.

Rev Argent Cardiol 2013;81:287-295. http://dx.doi.org/10.7775/rac.v81.i4.2330

Key words > Acute coronary syndromes – Gender - Ischemic heart disease - Women

Abbreviations >

AMI	Acute myocardial infarction	**NSTE-ACS**	Non ST-segment elevation acute coronary syndrome
ACS	Acute coronary syndrome		

INTRODUCTION

More than 20 years have elapsed since awareness of differences in the way doctors managed coronary disease in men and women. (1, 2) Authors described differences at all stages of medical care, to the detriment of women who suffered greater delay in diagnosis and less use of validated therapeutic strategies. In recent decades cardiology treatments have shown a tendency to greater standardization based on the evidence from large controlled trials, but recent data suggest that disparity between men and women in addressing heart disease still persists, even in relation to the

SEE RELATED ARTICLE: Rev Argent Cardiol 2013;81:277-278 - http://dx.doi.org/10.7775/rac.v81.i4.2997.

[1] Grupo de Estudio, Docencia e Investigación Clínica (GEDIC).
[MTSAC] Full Member of the Argentine Society of Cardiology
[2] Hospital El Cruce de Alta Complejidad en Red Dr. Néstor Kirchner
[†] To apply as Full Member of the Argentine Society of Cardiology

diagnosis and treatment of acute coronary syndromes (ACS). (3, 4)

Some observational studies have found that in the event of ACS women are less likely to be referred for coronary angiography (5) and revascularization, and receive less evidence-based prescriptions than men. (6-9) Differences persist even after adjusting for age and comorbidities, and may in part account for the progressive higher mortality observed in women in certain jobs. (4, 10) These findings have been challenged by other publications that have not observed such differences in more recent cohorts or patients from other parts of the world. (11 -14) Our local environment has no updated data on this phenomenon to establish its incidence and possible constraints.

The phenomenon is complex because lower prescription or aggressive therapy may be established on medical grounds related to different ACS demographic factors in men and women or otherwise by cultural reasons and a real gender bias. If the latter were the case, lack of validated measures would have negative consequences on the clinical outcome and morbimortality of women.

Our objective was to assess whether there is gender bias in the therapeutic approach of a contemporary cohort of ACS patients, representative of a wide spectrum of practices in Argentina. To this end, the differential indication of diagnostic and therapeutic strategies used during hospitalization and prescriptions at hospital discharge were analyzed both in men and women in this cohort of the Epi-Cardio registry.

METHODS

Software characteristics and multicenter network configuration

Epi-Cardio is a multicenter registry of Cardiovascular Intensive Care Unit discharge summaries directed to clinical epidemiological assessment, which started in 2005 with the participation of 54 centers of Argentina. It uses a software program independently developed, distributed free of charge to intensive care and coronary care units. The program generates discharge summary forms to be used in daily practice and data is simultaneously stored in a database for later processing. Periodically, each center database is submitted to the coordinator center (GEDIC) for central analysis.

Database contents

The program registers demographic information, personal history, risk factors, treatments at admission, in-hospital studies, outcome, records of medical procedures, and diagnosis and treatment prescribed at discharge. It has specific fields for the main cardiovascular diseases, where particularly relevant information for each clinical condition is recorded.

Current analysis

We performed a retrospective analysis of the Epi-Cardio database, selecting all the registries with diagnosis of ACS, including acute myocardial infarction (AMI) and non ST-segment elevation acute coronary syndromes (NSTE-ACS), having complete gender information.

Analyzed data included risk factors, personal history, coronary angiography, percutaneous coronary intervention and/or thrombolytic therapy, in-hospital complications, mortality and treatments prescribed at discharge.

Evaluation analyses for medications prescribed at discharge were restricted to patients not dying during hospitalization and who had at least one prescription registered in the database (to avoid including patients with missing data in all prescriptions in the “not treated” field).

Statistical analysis

Data were expressed as mean and standard deviation (SD) for continuous variables with normal distribution and median and interquartile range (IQR) for non-normal distribution. Normality was evaluated through visual inspection of quantile-quantile plots and the Shapiro-Wilks test. Categorical variables were described using absolute numbers and percentages. Continuous variables of both genders were compared using Student´s t test for normal data and the Mann-Whitney U-test for non-normal data. Categorical variables were compared using Pearson´s chi-square test. Multivariate logistic regression models with the inclusion of potential confounders were used to assess the influence of gender on the utilization of in-hospital procedures, mortality and treatments prescribed at discharge.

To further explore the relationship between gender and prescribed treatments at discharge and compensate for the non-randomized study design, a sensitivity analysis was performed based on propensity score. (16) This analysis consisted in building a propensity score, i.e. the conditional probability of belonging to gender A=a, given a vector of covariates (confounders). Then a 1:1 matching was performed between subjects of each gender so that the difference between both propensity scores was < 30%. This resulted in two groups with similar confounder distribution. Finally, both groups were directly compared (without further adjust) using Student´s t test for dependent samples or the Wilcoxon signed-rank test for continuous samples, and the McNemar test to compare categorical data.

All analyses were two-tailed and a p value < 0.05 was considered statistically significant.

RESULTS

Between August 2005 and May 2012, 71054 patients from 54 coronary care units were included in the Epi-Cardio registry, 9022 (12.69%) of whom had ACS. The final sample consisted of 8997 (12.66%) hospitalized patients, as in 25 registries gender data was not available.

Out of the total number of patients, 28.6 % (n = 2575) were women and 71.4% (n = 6422) were men. Table 1 describes patient characteristics at the time of admission. Women were older than men, and had greater prevalence of hypertension, diabetes and diabetes requiring insulin, history of chronic angina and of chronic heart failure than men. Men had greater prevalence of smoking, and history of previous infarction, percutaneous coronary intervention and myocardial revascularization surgery

Non ST-segment elevation acute coronary syndromes were more frequent than AMI with ST-segment elevation in both genders, a tendency that was more marked in women (67.9%) than in men (58.3%, p < 0.001).

Table 1. Patient characteristics at admission (overall and by gender)

Variables	Overall (n=8997)	Women (n=2575)	Men (n=6422)	p value
Age in years, mean (SD)	62.4 (12.6)	66.7 (13.3)	60.6 (11.9)	<0.001
Hypertension, n (%)	5592 (62.2)	1792 (69.6)	3800 (59.2)	<0.001
Dyslipidemia, n (%)	4050 (45.0)	1151 (44.7)	2899 (45.1)	ns
Diabetes, n (%)	1826 (20.3)	595 (23.1)	1231 (19.2)	<0.001
Insulin*	305 (16.7)	127 (21.3)	178 (14.5)	<0.001
Current smoking, n (%)	2807 (31.2)	478 (18.6)	2329 (36.3)	<0.001
Previous infarction, n (%)	1606 (17.9)	359 (13.9)	1247 (19.4)	<0.001
Previous percutaneous coronary intervention, n (%)	1262 (14.0)	294 (11.4)	968 (15.1)	<0.001
Previous CABG, n (%)	580 (6.4)	137 (5.3)	443 (6.9)	0.006
Previous CHF, n (%)	342 (3.8)	128 (5.0)	214 (3.3)	<0.001
Previous chronic angina, n (%)	821 (9.1)	292 (11.3)	529 (8.2)	<0.001
Systolic BP, mean (SD)	134.8 (26.5)	135.9 (28.2)	134.4 (25.8)	0.029
HR, median (IQR)	75.0 (60.0 to 80.0)	75.0 (63.0 to 85.0)	75.0 (60.0 to 80.0)	0.001**
Clinical condition, n (%)				
AMI	3502 (38.9)	826 (32.1)	2676 (41.7)	<0.001
NSTE-ACS	5495 (61.1)	1749 (67.9)	3746 (58.3)	
Enzymes and ECG in NSTE-ACS (5495 patients)				
Presence of ECG changes, n (%)	2777 (50.5)	899 (51.4)	1878 (50.1)	ns
Type of change T wave	1621 (58.4)	556 (61.8)	1065 (56.7)	0.010
ST	1156 (41.6)	343 (38.2)	813 (43.3)	
Elevated enzymes, n (%)	2037 (37.1)	547 (31.3)	1490 (39.8)	<0.001
Elevated enzymes and ECG, n (%)	1426 (26.0%)	382 (21.8)	1044 (27.9)	<0.001

SD: Standard deviation. CABG= Coronary artery bypass grafting. CHF= chronic heart failure. BP= blood pressure. HR= heart rate. IQR: Interquartile range. AMI: Acute myocardial infarction. NSTE-ACS: Non ST-segment elevation acute coronary syndrome. ECG: Electrocardiogram. ns: not significant.
*Percentage over total diabetic patients.
** Mann-Whitney U-test.

There were no gender differences in NSTE-ACS either in the presence or absence of electrocardiographic changes. However, differences were present in the type of electrocardiographic change: women presented with greater frequency changes in the T wave and men in the ST segment. Moreover, men presented more frequently elevated cardiac enzymes (39.8% vs. 31.3%, $p < 0.001$), and the combination of elevated enzymes with electrocardiographic changes (27.9% vs. 21.8%, $p < 0.001$).

Unadjusted analyses

Table 2 shows use of procedures, in-hospital mortality and prescribed treatments at discharge. Women underwent less angiographies (52.5% vs. 62.7%) and percutaneous coronary interventions (30.8% vs. 44.2%) and had lower use of IIb/IIIa inhibitors (6.7% vs, 9.9%) compared to men. In patients with AMI, reperfusion therapy was lower in women than in men (62.2% vs. 66.1%).

Overall in-hospital mortality was 3.7% (n = 94) in women and 2.7% (n = 173) in men ($p = 0.016$), at the expense of greater difference in women mortality in the group with AMI (8.5% vs. 4.3%). In NSTE-ACS patients, mortality was 1.4% in women and 1.6% in men.

At discharge, fewer women were prescribed with statins, beta-blockers and thienopyridines compared to men. Conversely, women were prescribed more frequently calcium blockers, nitrates, benzodiazepines, with no difference in the use of renin-angiotensin system inhibitors (ACEI) or angiotensin receptor blockers (ARB).

Adjusted analyses

After adjusting for potential confounders, women were still associated with lower use of coronary angiography (OR 0.73; 95% CI 0.65- 0.82) and IIb/IIIa inhibitors (OR 0.64; 95% CI 0.47- 0.87) among patients with NSTE-ACS, though this association disappeared with use of reperfusion therapy in patients with AMI (OR 1.02; 95% CI 0.84-1.23) (Figure 1). Similarly, no significant differences were found in adjusted analyses for in-hospital mortality (OR 0.89; 95% CI 0.65-1.25).

Figure 1 shows analysis results of medications

Table 2. Treatments, procedures and in-hospital results

Variables	Total (n=8997)	Women (n=2575)	Men (n=6422)	p value
Coronary angiography, n (%)	5382 (59.8)	1353 (52.5)	4029 (62.7)	<0.001
Percutaneous coronary intervention, n (%)	3631 (40.4)	792 (30.8)	2839 (44.2)	<0.001
Reperfusion, n (%)*	2283 (65.2)	514 (62.2)	1769 (66.1)	0.041
Primary percutaneous coronary intervention**	1357 (59.5)	311 (60.6)	1046 (59.2)	ns
Thrombolytics**	923 (40.5)	202 (39.4)	721 (40.8)	
IIb/IIIa inhibitors, n (%)	344 (3.8)	58 (2.3)	286 (4.5)	<0.001
Percutaneous coronary intervention with IIb/IIIa†	333 (9.2)	53 (6.7)	280 (9.9)	0.006
CABG, n (%)	294 (3.3)	52 (2.0)	242 (3.8)	<0.001
Mortality, n (%)	267 (3.0)	94 (3.7)	173 (2.7)	0.016
NSTE-ACS	83 (1.5)	24 (1.4)	59 (1.6)	ns
AMI	184 (5.3)	70 (8.5)	114 (4.3)	<0.001
Treatments at discharge††, n (%)				
Aspirin	7282 (94.9)	2027 (94.3)	5255 (95.1)	ns
Statins	6784 (88.4)	1821 (84.7)	4963 (89.8)	<0.001
Beta-blockers	6544 (85.2)	1745 (81.2)	4799 (86.8)	<0.001
ACEI	4859 (63.3)	1291 (60.0)	3568 (64.6)	<0.001
ARB	554 (7.2)	211 (9.8)	343 (6.2)	<0.001
ACEI / ARB	5391 (70.2)	1496 (69.6)	3895 (70.5)	ns
Thienopyridines	5444 (70.9)	1404 (65.3)	4040 (73.1)	<0.001
Clopidogrel	5361 (69.8)	1389 (64.6)	3972 (71.9)	<0.001
Calcium blockers	946 (12.3)	321 (14.9)	625 (11.3)	<0.001
Nitrates	808 (10.5)	267 (12.4)	541 (9.8)	0.001
Benzodiazepines	1190 (15.4)	385 (17.9)	805 (14.6)	<0.001

CABG= coronary artery bypass grafting. NSTE-ACS: Non ST-segment elevation acute coronary syndrome. AMI: Acute myocardial infarction. ACEI= angiotensin-converting enzyme inhibitors. ARB= angiotensin receptor blockers. ns: not significant.
*Calculated among 3502 patients with acute myocardial infarction.
**Percentages were calculated among 2280 patients with acute myocardial infarction who underwent reperfusion therapy and were informed about the procedure used.
†Calculated on 3631 patients who underwent percutaneous coronary intervention.
††Calculated on 7677 patients discharged alive and at least with one medication prescribed at discharge.

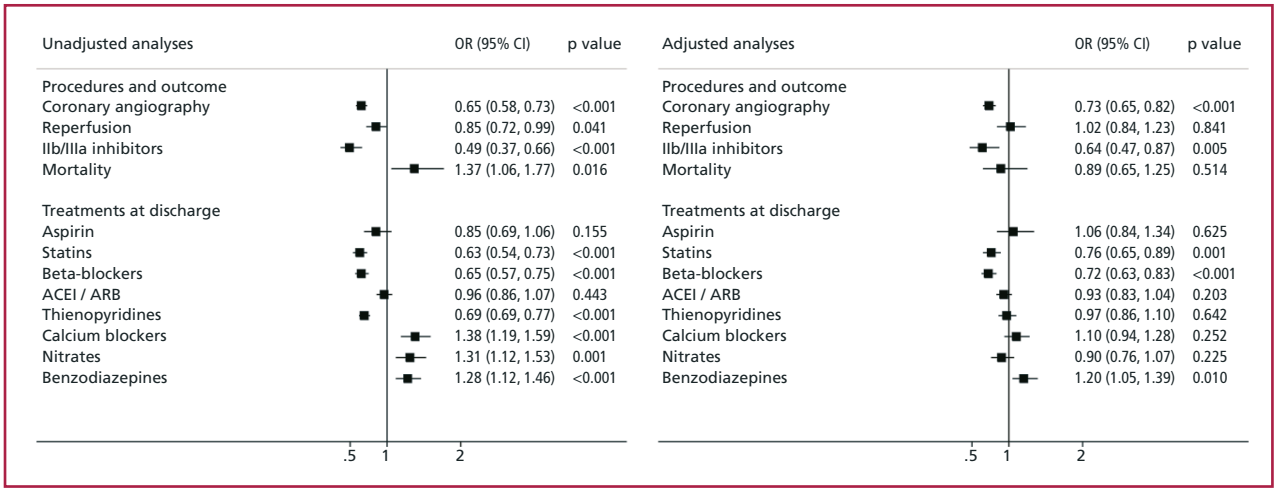

Fig. 1. Unadjusted and adjusted analyses of in-hospital treatments, mortality and treatments prescribed at discharge.

prescribed at discharge. After adjusting for covariates, women had significantly lower probability of receiving prescriptions for beta-blockers or statins and greater probability of receiving prescriptions for benzodiazepines.

Sensitivity analysis

Table 3 shows analysis of propensity score matched-pairs for in-hospital outcome and procedures. The analysis included 2108 matched pairs. The method generated two similar groups with respect to the distribution of most confounding variables. Consistently with the main analyses, following matching, women underwent less angiographies, coronary percutaneous interventions and treatment with IIb/IIIa glycoprotein inhibitors.

Table 3. Propensity score-matched population. In-hospital outcome and procedure analyses.

Matching variables	Women (n=2108)	Men (n=2108)	p value
Age, mean (SD)	66.2 (13.1)	66.0 (13.0)	ns
Hypertension, n (%)	1481 (70.3)	1474 (69.9)	ns
Dyslipidemia, n (%)	968 (45.9)	1003 (47.6)	ns
Diabetes, n (%)	514 (24.4)	526 (25.0)	ns
Current smoking, n (%)	409 (19,4)	380 (18.0)	ns
Previous infarction, n (%)	302 (14.3)	299 (14.2)	ns
Previous percutaneous coronary intervention, n (%)	249 (11.8)	243 (11.5)	ns
Previous CABG, n (%)	115 (5.5)	126 (6.0)	ns
Previous CHF, n (%)	106 (5.0)	107 (5.1)	ns
Previous chronic angina, n (%)	244 (11.6)	239 (11.3)	ns
Systolic BP, mean (DE)	136.0 (28.2)	135.0 (26.4)	ns
HR, median (IQR)	75.0 (63.0 to 85.0)	75.0 (60.0 to 84.0)	ns
Clinical condition, n (%)			
AMI	661 (31.4)	660 (31.3)	ns
NSTE-ACS	1447 (68.6)	1448 (68.7)	ns
Type of change*, n (%)	743 (51.3)	768 (63.0)	ns
T wave	458 (61.6)	449 (58.5)	
ST	285 (38.4)	319 (41.5)	
Elevated enzymes*, n (%)	446 (30.8)	482 (33.3)	ns
Elevated enzymes and ECG*, n (%)	311 (21.5)	350 (24.2)	ns
Absence of differences in matching parameters indicates an adequate configuration of groups for analysis.			
Comparative in-hospital outcome and procedure analyses			
Recurrent/refractory angina*, n (%)	127 (8.8)	125 (8.6)	ns
Coronary angiography, n (%)	1132 (53.7)	1253 (59.4)	<0.001
Percutaneous coronary intervention, n (%)	668 (31.7)	822 (39.0)	<0.001
Reperfusion**, n (%)	423 (64.0)	419 (63.5)	ns
Primary percutaneous coronary intervention†	258 (61.1)	258 (61.7)	ns
Thrombolytics†	164 (38.9)	160 (38.3)	
IIb/IIIa inhibitors, n (%)	53 (2.5)	89 (4.2)	0,003
Percutaneous coronary intervention with IIb/IIIa††	50 (7.5)	86 (10.5)	<0.001
Mortality, n (%)	68 (3.2)	75 (3.6)	ns
NSTE-ACS	15 (1,0)	29 (2.0)	0.052
AMI	53 (8.0)	46 (7.0)	ns

SD: Standard deviation. CABG= coronary artery bypass grafting. CHF= chronic heart failure. BP= blood pressure. HR= heart rate. IQR: Interquartile range. AMI: Acute myocardial infarction. NSTE-ACS: Non ST-segment elevation acute coronary syndrome. ECG: Electrocardiogram. ns: not significant.
*Calculated among 1447 women and 1448 men with non ST-segment elevation acute coronary syndrome.
**Calculated among 661 women and 660 men with acute myocardial infarction.
†Calculated among 422 women and 418 men who underwent reperfusion therapy and were informed about the procedure used.
††Calculated among 668 women 822 men who underwent percutaneous coronary intervention.

Table 4 shows analysis of propensity score matched-pairs for treatments prescribed at discharge. One thousand eight hundred and thirty-two pairs were selected for this analysis. Results suggest that the method allowed case and control selection with similar distribution of known confounding variables. The analysis of treatments prescribed at discharge confirmed the results of logistic regression models regarding statins and beta-blockers; however, the association between genders disappeared for benzodiazepine prescription.

DISCUSSION

Our results indicate the presence of gender differences in in-hospital management and discharge prescriptions of evidence-based treatments. The analyses of the Epi-Cardio database, representing a wide range of practice in Argentina suggest that, in the presence of a similar clinical profile, women were less likely to receive invasive treatment strategies and statin and beta-blocker prescriptions after presenting an ACS.

As is classically acknowledged, women present with coronary disease at a later age than men, which is associated with a different distribution of multiple demographic factors (risk factors and comorbidities) that might influence therapeutic decision making in ACS and determine outcome differences. For this reason we have applied different rigorous methods of statistical adjustment, using both multivariate analysis and propensity score matching to rank the differences observed. Some of these differences disappear with the adjustments, but others clearly persist.

Female gender was associated with a lower probability of invasive strategy in the NSTE-ACS group, lower percutaneous coronary intervention rate and less use of IIb / IIIa inhibitors. These results are consistent with observational studies from other countries in which women had a lower probability of being studied with coronary angiography (4, 6) Likewise, works that included large populations found higher rates of invasive strategy and medical treatment in men, and lower use of revascularization in women, which persisted after controlling for angiographic findings and other predictors. (3, 9, 10, 14, 17)

There has been an attempt to explain the difference observed in revascularization strategies from biological differences between both genders, such as smaller diameter of the coronary vessels seen in women, higher prevalence of obstructive coronary disease and more incidence of smooth muscle cell dysfunction. (17, 18) However, the differences in the use of revascularization persist after stratification adjustments according to angiographic findings, suggesting that other factors influence these decisions. Other studies have not confirmed these findings, indicating a similar use of revascularization between genders in patients studied with coronary angiography and presenting similar rate of long term events. (11, 12) These inconsistencies could be related to differences in the populations included, in the available data, analytical methods, institutions or regions in which they were performed and the time window considered.

Our results also suggest that women are associated with lower probability of receiving beta-blocker and statin prescriptions, and higher probability of being prescribed benzodiazepines at hospital discharge. These results are consistent with other observational studies that reported lower use of evidence-based treatments at discharge from ACS among women. (7, 8, 19-21)

Regarding the greater probability of benzodiazepine prescription among women, it might be related to different distribution of anxiety symptoms (22) between genders (confounders). (confounders). This phenomenon has also been described in patients with chronic ischemic heart disease. (23) In the ACS context this information should be confirmed by other studies, as well as the reasons for these prescriptions. Due to lack of data regarding contraindications for evidence-based treatments, this finding is particularly relevant in our study, since women were less likely to receive statins in the groups with or without benzodiazepines, although both drugs have similar contraindications.

The largest proportion of gender bias in coronary heart disease comes from observational studies, which allow exposing the problem but are not designed to explain the reasons. It is difficult to understand the reasons for the observed gender differences in ACS treatment, (24) considering that the clinical decisions that are adopted for each patient also involve multiple aspects aside from evidence. (25) From this viewpoint, an aspect to consider might be the absence of a gender perspective among health professionals. (26) If professionals do not understand the differences they can hardly identify the specificities (27), which would lead to inequities or gender biases. Another aspect to consider, related to the first, is the preference of male/female patients, particularly in relation to invasive treatment strategies. The gaps in the implementation of recommendations and guidelines could be reduced through educational strategies.

Study limitations

The main limitation of our study is its observational nature. Although we have detected possible gender bias in the therapeutic approach to SCA, as the analysis was based on discharge summaries from databases, there are variables that might explain the findings and were not considered, such as the preference of male/female patients or factors that increase the procedure or drug risks (body mass index, renal function, pulmonary disease, blood pressure and heart rate at discharge). The consistency of our findings with previous studies that evaluated the therapeutic opportunity by adjusting for these confounding variables, suggests that the results cannot be explained by these unmeasured factors

Table 4. Propensity score-matched population for analysis of treatments prescribed at discharge.

Matching variables	Women (n=1832)	Men (n=1832)	p value
Age, mean (SD)	66.0 (12.8)	65.8 (12.4)	ns
Hypertension, n (%)	1315 (71.8)	1318 (71.9)	ns
Dyslipidemia, n (%)	875 (47.8)	860 (46.9)	ns
Diabetes, n (%)	451 (24.6)	469 (25.6)	ns
Current smoking, n (%)	361 (19.7)	367 (20.0)	ns
Previous infarction, n (%)	269 (14.7)	258 (14.1)	ns
Previous percutaneous coronary intervention, n (%)	226 (12.3)	235 (12.8)	ns
Previous CABG, n (%)	102 (5.6)	118 (6.4)	ns
Previous CHF, n (%)	93 (5.1)	93 (5.1)	ns
Previous chronic angina, n (%)	215 (11.7)	219 (12.0)	ns
Systolic BP, mean (DE)	137.2 (27.7)	136.5 (25.7)	ns
HR, median (IQR)	75.0 (62.3 to 83.0)	75.0 (61.0 to 83.0)	ns
Clinical condition, n (%)			ns
AMI	534 (29.1)	507 (27.7)	
NSTE-ACS	1298 (70.9)	1325 (72.3)	
Type of change*, n (%)	667 (51.4)	713 (53.8)	ns
T wave	412 (61.8)	412 (57.8)	ns
ST	255 (38,2)	301 (42.2)	
Elevated enzymes*, n (%)	391 (30.1)	445 (33.6)	ns
Elevated enzymes and ECG*, n (%)	267 (20.6)	307 (23.2)	ns
Coronary angiography, n (%)	1005 (54.9)	1035 (56.5)	ns
Percutaneous coronary intervention, n (%)	585 (31.9)	580 (31.7)	ns
Reperfusion**, n (%)	344 (64.4)	297 (58.6)	ns
Primary percutaneous coronary intervention†	211 (61.5)	183 (61.6)	
Thrombolytics†	132 (38.5)	114 (38.4)	
IIb/IIIa inhibitors, n (%)	47 (2.6)	46 (2.5)	ns
Percutaneous coronary intervention with IIb/IIIa††	44 (7.5)	45 (7.8)	ns
Absence of differences in matching parameters indicates an adequate configuration of groups for analysis.			
Treatments at discharge			
Aspirin	1732 (94.5)	1725 (94.2)	ns
Statins	1556 (84.9)	1598 (87.2)	0.046
Beta-blockers	1497 (81.7)	1557 (85.0)	0.008
ACEI	1103 (60.2)	1133 (61.8)	ns
ARB	180 (9.8)	140 (7.6)	0.021
ACEI / ARB	1277 (69.7)	1269 (69.3)	ns
Thienopyridines	1192 (65.1)	1237 (67.5)	ns
Clopidogrel	1179 (64.4)	1219 (66.5)	ns
Calcium blockers	267 (14.6)	287 (15.7)	ns
Nitrates	225 (12.3)	263 (14.4)	ns
Benzodiazepines	318 (17.4)	299 (16.3)	ns

SD: Standard deviation. CABG= coronary artery bypass grafting. CHF= chronic heart failure. BP= blood pressure. HR= heart rate. IQR: Interquartile range. AMI: Acute myocardial infarction. NSTE-ACS: Non ST-segment elevation acute coronary syndrome. ECG: Electrocardiogram. ns: not significant.
*Calculated among 1447 women and 1448 men with non ST-segment elevation acute coronary syndrome.
**Calculated among 661 women and 660 men with acute myocardial infarction.
†Calculated among 422 women and 418 men who underwent reperfusion therapy and were informed about the procedure used.
††Calculated among 668 women 822 men who underwent percutaneous coronary intervention.

The use of benzodiazepines in the community is more common in women than in men (28, 29) which may have influenced its greater indication. However, we lack information in our cohort of previous use of non-cardiac drugs.

Our results on the treatments prescribed at discharge do not evaluate treatment intensity (dose), so the differences in treatment that may appear should be considered as conservative estimates, since there are probably quantitative differences in the use of these drugs. (30)

CONCLUSIONS AND FINAL COMMENT

Our results, obtained from a large cohort of ACS patients representative of a wide range of cardiology practices in Argentina, suggest that gender bias exists in relation to the management of acute ischemic heart disease, including less aggressiveness both in acute management as well as in evidence-based treatments at discharge.

While these results are not definitive, and there might be unmeasured confounders that explain the observed differences, the magnitude of the topic justifies adopting an educational strategy to try to generalize the instructions and guidelines, and see whether it helps to correct bias and improve female outcomes. The first step is recognizing the problem, for which this cohort provides solid and unprecedented data in our country.

RESUMEN

Diferencias de género en el tratamiento de Síndromes Coronarios Agudos: resultados del Registro Epi-Cardio

Introducción

Existen evidencias controvertidas sobre la existencia de sesgo de género en la atención de pacientes con síndromes coronarios agudos (SCA), y resulta relevante conocer datos de nuestro país al respecto.

Objetivo

Evaluar diferencias de género en la atención de SCA en las unidades de cuidados cardiovasculares participantes del registro Epi-Cardio.

Material y métodos

Se incluyeron 8.997 registros de pacientes con diagnóstico de SCA. Se realizaron análisis ajustados y análisis de sensibilidad mediante puntaje de propensión.

Resultados

El género femenino estuvo asociado independientemente a menor indicación intrahospitalaria de cinecoronariografía (OR 0,73; IC95% 0,65-0,82), y menor uso de inhibidores IIb/IIIa en pacientes con SCA sin segmento ST elevado (SCASSTE).

Luego de análisis ajustados no hubo diferencia significativa en el uso de terapia de reperfusión en pacientes con infarto ni en mortalidad intrahospitalaria.

Al alta las mujeres tuvieron significativamente menor probabilidad de recibir prescripciones para beta-bloqueantes y estatinas, y mayor probabilidad de recibir prescripciones para benzodiacepinas, en comparación con los hombres.

Conclusiones

Estos hallazgos sugieren la existencia de sesgo de género en el manejo de pacientes con SCA, manifestado por la selección de estrategias más conservadoras y menor prescripción de fármacos recomendados en prevención secundaria a mujeres. Las diferencias en el abordaje de los SCA entre géneros deberían ser investigadas más profundamente, dado que la subutilización de terapias basadas en evidencias podría tener un impacto en la evolución clínica de las mujeres.

Palabras clave > Síndromes coronarios agudos- Género- Cardiopatía isquémica- Mujeres

Conflicts of interest

None declared.

REFERENCES

1. Ayanian JZ , Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. N Engl J Med 1991;325:221-5. http://doi.org/fjmjc2

2. Healy B. The Yentl syndrome. N Engl J Med 1991;325:274-5. http://doi.org/dd8kk6

3. Tavris D, Shoaibi A, Chen AY, Uchida T, Roe M, Chen J. Gender differences in the treatment of non-ST segment elevation myocardial infarction. Clin Cardiol 2010;33:99-103. http://doi.org/dcjkr6

4. Poon S, Goodman S, Yan R, Bugiardini R, Bierman A, Eagle K, et al. Bridging the gender gap: Insights from a contemporary analysis of sexrelated differences in the treatment and outcomes of patients with acute coronary syndromes. Am Heart J 2012;163:66-73. http://doi.org/fjqffz

5. Nguyen JT, Berger AK, Duval S, Luepker RV. Gender disparity in cardiac procedures and medication use for acute myocardial infarction. Am Heart J 2008;155:862-8. http://doi.org/bdtrms

6. 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. http://doi.org/bj4mdg

7. Jani SM, Montoye C, Mehta R, Riba A, DeFranco A, Parrish R, et al. Sex differences in the application of evidence-based therapies for the treatment of acute myocardial infarction. Arch Intern Med 2006;166:1164-70. http://doi.org/ct6hch

8. Greenland P, Gulati M. Improving outcomes for women with myocardial infarction. Arch Intern Med 2006;166:1162-3. http://doi.org/bzxnvx

9. Radovanovic D, Erne P, Urban P, Bertel O, Rickli H, Gaspoz JM. Gender differences in management and outcomes in patients with acute coronary syndromes: results on 20.290 patients from the AMIS Plus Registry. Heart 2007;93:1369-75. http://doi.org/b57kd3

10. 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

11. Roeters van Lennep JE, Zwinderman AH, Roeters van Lennep HWO, Westerveld HE, Plokker HWM, Voors AA, et al. Gender differences in diagnosis and treatment of coronary artery disease from 1981 to 1997. No evidence for the Yentl syndrome. Eur Heart J 2000;21:911-8. http://doi.org/bxz5s5

12. Alfredsson J, Lindbäck J, Wallentin L, Swahn E. Similar outcome with an invasive strategy in men and women with non-ST-elevation acute coronary syndromes: From the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART). Eur Heart J 2011;32:3128-36. http://doi.org/bgb8fw

13. Möllmann H, Liebetrau C, Nef H, Hamm C. The Swedish paradox: or is there really no gender difference in acute coronary syndromes? Eur Heart J 2011;32:3070-2. http://doi.org/b9pg86

14. Alfredsson J, Stenestrand U, Wallentin L, Swahn E. Gender dif-

ferences in management and outcome in non-ST-elevation acute coronary syndrome. Heart 2007;93:1357-62. http://doi.org/cj68v6
15. Gagliardi JA, de Abreu M, Mariani JA, Silberstein MA, de Sagastizábal DM, Salzberg S y cols. Motivos de ingreso, procedimientos, evolución y terapéuticas al alta de 54.000 pacientes ingresados a unidades de cuidados intensivos cardiovasculares en la Argentina. Seis años del Registro Epi-Cardio. Rev Argent Cardiol 2012;80:446-54.
16. Rosembaum PR, Rubin DB. The Central Role of the Propensity Score in Observational Studies for Causal Effects. Biometrika 1983;70(1):41-55. http://doi.org/dbstnf
17. Hvelplund A, Galatius S, Madsen M, Rasmussen J, Rasmussen S, Madsen JK, et al. Women with acute coronary syndrome are less invasively examined and subsequently less treated than men. Eur Heart J 2010;31:684-90. http://doi.org/fcqz47
18. Anderson DR, Pepine CJ. Gender differences in the treatment for acute myocardial infarction: bias or biology? Circulation 2007;115:823-6. http://doi.org/cn3r7b
19. Peterson ED, Shah BR, Parsons L, Pollack CV, French WJ, Canto JG, et al. Trends in quality of care for patients with acute myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J 2008;156:1045-55. http://doi.org/ck5drw
20. Kumbhani DJ, Fonarow GC, Cannon CP, Hernandez AF, Peterson ED, Peackok WF, et al. Predictors of adherence to performance measures in patients with acute myocardial infarction. Am J Med 2013;126:74.e1-9
21. 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 (ACCNCDR). Am Heart J 2009;157:141-8. http://doi.org/bb62hp
22. Januzzi J, Stern T, Pasternak R, DeSanctis R. The influence of anxiety and depression on outcomes of patients with coronary artery disease. Arch Intern Med 2000;160:1913-20. http://doi.org/dh62hs
23. Williams D, Bennett K, Feely J. Evidence for an age and gender bias in the secondary prevention of ischaemic heart disease in primary care. Br J Clin Pharmacol 2003;55:604-8. http://doi.org/b7hgtz
24. Alfredsson J, Swahn E. Management of acute coronary syndromes from a gender perspective. Fundam Clin Pharmacol 2010;24:719-28. http://doi.org/bg8k8t
25. Malterud K. The art and science of clinical knowledge: evidence beyond measures and numbers. Lancet 2001;358:397-400. http://doi.org/bqswdf
26. Risberg G, Hamberg K, Johansson E. Gender perspective in medicine: a vital part of medical scientific rationality. A useful model for comprehending structures and hierarchies within medical science. BMC Medicine 2006;4:20. http://doi.org/dwt8x8
27. Tajer D. Los imaginarios profesionales en la construcción del "coronario" y la "coronaria". Paidós Tramas Sociales. Heridos corazones. Vulnerabilidad coronaria en varones y mujeres. 1.ª ed. Buenos Aires; 2009. p. 201-57. ISBN 978-950-12-4557-8.
28. Rosman S, Le Vaillant M, Palletier-Fleury N. Gaining insight into benzodiazepine prescribing in general practice in France: a data-based study. BMC Family Practice 2011;12:28. http://doi.org/cps55d
29. Sonnenberg CM, Bierman E. Deeg D, Comis H, van Tilburg W, Beekman H. Ten-year trends in benzodiazepine use in the Dutch population. Soc Psychiatry Psychiatr Epidemiol 2011;47:293-301. http://doi.org/cb32x8
30. Sachdeva A, Cannon CP, Deedwania PC, Labresh KA, Smith SC Jr, Dai D, et al. Lipid levels in patients hospitalized with coronary artery disease: an analysis of 136,905 hospitalizations in Get With The Guidelines. Am Heart J 2009;57:111-7. http://doi.org/bqvtcs