ORIGINAL ARTICLE

Short-Term Outcomes of Isolated and Combined Coronary Artery Bypass Graft Surgery in Women

Resultados a corto plazo de la cirugía coronaria aislada o combinada en mujeres

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ABSTRACT

Background: The outcome and treatment of cardiovascular disease in women differ among international studies.
Objective: The aim of this study was to compare in-hospital and 60-day mortality and complications following isolated or combined coronary artery bypass graft surgery between women and men.
Methods: The outcomes during hospitalization and at 60 days following isolated or combined coronary artery bypass graft surgery procedures performed between 2011 and 2017 were retrospectively analyzed. Perioperative variables, expected all-cause mortality estimated by EuroSCORE II and observed all-cause mortality were compared. A propensity score analysis was performed to match female and male populations.
Results: Among 1,670 isolated or combined coronary artery bypass graft procedures, 27.4% (n = 457) were performed in women, as well as 185 (14.2%) of 1,305 isolated surgeries. Mortality in women at 30 and 60 days was 2.7% and 4.3%. respectively, vs. 2.1% (RR: 1.26; 95% CI, 0.49-3.26; p = 0.632) and 2.3% (RR: 1.86; 95% CI, 0.86-4.05, p = 0.113, power 53%), respectively, in men. After analyzing the propensity score of patients undergoing isolated revascularization procedures, 60-day mortality in women was 4.0% vs. 2.3% in men (RR: 1.75; 95% CI; 0.52-5.87, p = 0.359).
Conclusions: Compared with men, women undergoing isolated or combined coronary artery bypass graft surgery were older, had higher expected risk calculated by EuroSCORE II and worse kidney function. Mortality after isolated or combined coronary artery bypass graft surgery was higher in women than in men at 60 days, and this difference remained even after adjusting for confounders.

Key words: Myocardial Revascularization - Women - Mortality

RESUMEN

Introducción: En relación con la cirugía coronaria, existen discrepancias respecto del pronóstico y tratamiento de la enfermedad cardiovascular en la mujer entre distintos estudios internacionales.
Objetivo: Analizar los resultados de mortalidad y complicaciones hospitalarias y a 60 días luego de la cirugía de revascularización miocárdica aislada o combinada, en forma comparativa entre mujeres y varones.
Material y métodos: Se analizaron en forma retrospectiva los resultados hospitalarios y a 60 días de la cirugía de revascularización coronaria aislada o combinada de acuerdo con el sexo, operados entre 2011 y 2017. Se compararon las variables perioperatorias, la mortalidad esperada con el EuroSCORE II y la mortalidad observada por toda causa. Se realizó un análisis de propensión para equiparar las poblaciones de mujeres y varones.
Resultados: De 1670 cirugías de revascularización coronaria aisladas o combinadas, el 27,4% (n: 457) eran mujeres; y, de 1305 cirugías aisladas, el 14,2% (n: 185) eran mujeres. La mortalidad en las mujeres a 30 y 60 días fue del 2,7% y del 4,3% vs. el 2,1% (RR = 1,26 IC95% 0,49-3,26, p = 0,632) y el 2,3% (RR = 1,86 IC95% 0,86-4,05, p = 0,113, potencia 53%) en los varones. Tras el análisis de propensión de los pacientes sometidos a cirugía coronaria asilada, la mortalidad a 60 días en las mujeres fue del 4,0% vs. 2,3% en los varones (RR = 1,75 IC95% 0,52-5,87, p = 0,359).
Conclusiones: En comparación con los varones, las mujeres sometidas a cirugía de revascularización coronaria tuvieron más edad y mayor riesgo esperado por el EuroSCORE II, peor función renal tanto para la cirugía coronaria combinada como aislada. La mortalidad luego de la cirugía de revascularización coronaria aislada o combinada fue mayor en mujeres que en hombres a 60 días e, incluso, esta diferencia se mantuvo después de ajustar por confundidores.

Palabras clave: Revascularización miocárdica - Mujeres - Mortalidad

Abbreviations

CABGS	Coronary artery bypass graft surgery	**SD**	Standard deviation

Rev Argent Cardiol 2020;88:432-436. http://dx.doi.org/10.7775/rac.v88.i5.18806

SEE RELATED ARTICLE: Rev Argent Cardiol 2019:87:403-404. http://dx.doi.org/10.7775/rac.v88.i5.19084

Received: 05/22/2020 – *Accepted:* 07/24/2020

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INTRODUCTION

Coronary artery disease is the leading cause of death due to non-communicable diseases worldwide. One in three deaths among women are from coronary artery disease which is also the leading cause of death in women in Argentina, followed by breast cancer (33% and 18%, respectively). (1) The outcome and treatment of cardiovascular disease in women vary among different international studies. (2-6) Some studies demonstrated that in patients with acute coronary syndromes undergoing surgery, women had higher in-hospital mortality, while men had higher long-term mortality, with a similar rate of complications between both sexes. (7) In some randomized studies, there has been an imbalance in the number of women who are selected for surgery instead of for percutaneous coronary intervention. (8) In the EXCEL trial, perioperative myocardial infarction was more common with percutaneous coronary intervention in women and with surgery in men. (9)

In Argentina, there is no information about mortality by sex after coronary artery bypass graft surgery (CABGS), despite the information provided by the two largest registries to date (ESMUCICA [10] and CONAREC XVI [11]) and other more recent individual studies (12, 13). The aim of this study was to compare in-hospital and 60-day mortality and complications following isolated or combined CABGS between women and men.

METHODS

The outcomes during hospitalization and at 60 days following isolated or combined CABGS procedures performed between 2011 and 2017 at Hospital de Clínicas, University of Buenos Aires, and its affiliated institutions, were retrospectively analyzed by sex. Perioperative variables and outcomes during follow-up were retrieved from a prospective database which included information since 2010. Combined procedures were those associated with heart valve replacement or repair or procedures on the ascending aorta. Perioperative variables, expected all-cause mortality estimated by EuroSCORE II and observed all-cause mortality were compared.

Statistical analysis

Continuous variables with normal distribution were expressed as mean ± standard deviation (SD) assuming normal distributions (Kolmogorov-Smirnov test). Categorical variables were compared using the chi-square test with Yates correction. Mortality by groups was also expressed as relative risk (RR) and 95% confidence interval (95% CI). Continuous variables were compared using Student's t test. Propensity score matching analysis was used to balance the female and male populations. Statistical analysis was performed using SPSS 23.0 statistical package (SPSS, IBM Corporation, Armonk, New York). A two-tailed p value < 0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved by the institutional review boards. Patient informed consent was not considered necessary as the study was based on retrospective data retrieved from medical records.

RESULTS

Among 1,670 isolated or combined CABGS procedures, 27.4% (n = 457) were performed in women. Table 1 shows baseline population characteristics according to sex. Age, left ventricular ejection fraction (LVEF), EuroSCORE II, atrial fibrillation, heart failure, and history of previous surgery were significantly more common in women than in men, while creatinine clearance, dyslipidemia, diabetes, current smoking, peripheral artery disease, previous myocardial infarction and unstable angina were more common in men. In women, in-hospital, 30- and 60-day mortality was 3.7%, 4.2% and 5.23%, respectively, vs. 2.3% (RR: 1.61; 95% CI, 0.89-2.92, p = 0.112), 2.4% (RR:1.74, 95% CI, 0.99-3.07, p = 0.054) and 2.5% (RR: 2.12, 95% CI, 1.26-3.59, p = 0.004) respectively, in men. The proportion of aortic valve and mitral valve surgeries in the combined procedures was similar among men and women.

A total of 1,305 patients underwent isolated CABGS, 14.2% (n = 185) of which were performed in women. Age, LVEF and EuroSCORE II were higher in women vs. men (68.4 [SD 9.0] vs. 64.2 [SD 9.8] years, $p < 0.001$, 57.5% [SD 10.0] vs. 55.6% [SD 11.6] p = 0.053 and 2.4% [SD 2,0] vs. 1.5% [SD 1.6], $p < 0.001$, respectively) and creatinine clearance was lower (67.5 [SD 22.0] vs. 87.9 [SD 30.1] mL/min, $p < 0.001$). The mean number of grafts was 2.3 in women (SD 0.7) vs. 2.5 (DS 0.4) in men (p = 0.003) and off-pump procedures were slightly less common in women (18.3% vs. 22.2%, p = 0.238). Mortality in women at 30 and 60 days was 2.7% and 4.3%, respectively, vs. 2.1% (RR: 1.26; 95% CI, 0.49-3.26; p = 0.632) and 2.3% (RR: 1.86; 95% CI, 0.86-4.05, p = 0.113, power 53%), respectively, in men. Table 1 summarizes in-hospital complications of isolated CABGS in women and men.

After analyzing the propensity score of patients undergoing isolated revascularization procedures (Table 2) 60-day mortality in women was 4.0% (n = 7) vs. 2.3% (n = 4) in men (RR: 1.75; 95% CI; 0.52-5.87, p = 0.359).

DISCUSSION

Our study demonstrated that mortality after isolated or combined CABGS was higher in women than in men in up to 60 months of follow-up. This difference persisted after adjustment for confounders using propensity score matching analysis. Even though these differences did not reach statistical significance, this could probably be due to the low power of the sample. Nevertheless, with 1,305 patients undergoing isolated CABGS and 365 undergoing combined procedures, this is one of the largest studies in Argentina presenting overall mortality and complications of heart surgery, and unlike the other studies, (10-13) it is the only one comparing mortality and morbidity according to sex.

Several previous studies with mid-term and long-term follow-up have reported that mortality is greater

Table 1. Baseline population characteristics according to sex for all the population undergoing surgery

Variables	Women N = 457 n (%)	Men N = 1,213 n (%)	*p* value
Age, years (mean ± SD)	69.8 (10.7)	65.2 (10.7)	<0.001
Hypertension	256 (56.0)	722 (59.5)	0.195
Dyslipidemia	125 (27.4)	498 (41.0)	<0.001
Diabetes	146 (31.8)	656 (54.1)	<0.001
Current smoking	31 (6.7)	171 (14.1)	<0.001
COPD	28 (6.1)	58 (4.8)	0.267
Chronic atrial fibrillation	32 (7.1)	44 (3.6)	0.003
Stroke	13 (2.8)	22 (1.8)	0.190
Peripheral vascular disease	10 (2.2)	53 (4.3)	0.037
Heart failure	19 (4.3)	9 (0.7)	<0.001
Myocardial infarction	23 (5.1)	141 (11.7)	<0.001
Unstable angina	8 (1.8)	57 (4.7)	0.005
Chronic kidney failure	6 (1.2)	17 (1.4)	0.890
Creatinine clearance, mL/min (mean ± SD)	67.5 (30.0)	85.7 (29.7)	<0.001
EuroSCORE II, % (mean ± SD)	4.1 (6.6)	2.9 (5.6)	0.002
LVEF, % (mean ± SD)	58.9 (9.5)	56.1 (11.8)	<0.001
Emergency surgery	15 (3.2)	22 (1.8)	0.069
Previous cardiac surgery	13 (2.8)	3 (0.2)	<0.001
Isolated CABGS	185 (40.5)	1,120 (92.3)	<0.001
CBP time, min (mean ± SD)	57.4 (10.9)	58.2 (9.2)	0.430
Aortic cross-clamp time, min (mean ± SD)	28.2 (6.3)	28.9 (6.0)	0.277

SD: Standard deviation. COPD: Chronic obstructive pulmonary disease. LVEF: Left ventricular ejection fraction. CABGS: Coronary artery bypass graft surgery. CBP: Cardiopulmonary bypass.

Table 2. In-hospital complications after isolated coronary artery bypass graft procedures in women vs. men

Complications	Women (n = 108)	Men (n = 1,120)	*p*
Postoperative infarction	3 (1.62%)	13 (1.16%)	0.486
Stroke	1 (0.54%)	5 (0.45%)	0.601
De novo dialysis	1 (0.54%)	9 (0.80%)	1.000
Prolonged MV/peneumonia	4 (2.16%)	11 (0.98%)	0.251
Reoperation for bleeding	3 (1.62%)	16 (1.43%)	0.743
Mediastinitis	1 (0.54%)	15 (1.34%)	0.715
Overall complication rate	13 (7.03%)	69 (6.16%)	0.653

MV: Mechanical ventilation. Values are expressed as n (%)

in women compared with men. (14-16) A Brazilian registry of myocardial revascularization surgeries performed between 2005 and 2007 on 63,272 patients from 191 centers reported higher mortality in women than in men after surgery (8.3% vs. 5.2%, $p < 0.001$). (17) Another registry which included 121 hospitals in the United States, with 10,708 women and 29,669 men undergoing isolated CABGS during 2003-2004 also showed similar results to our study. Mortality at 30 days in women was significantly higher than in men (4.6% vs. 5.2%, $p < 0.001$). (18) As in our study, women were older and had better LVEF and worse kidney function.

Among the variables explaining higher mortality in women than in men after CABGS, some studies have reported that female sex is an independent risk factor, that mortality is higher only in older patients, (19) or, on the contrary, that mortality is higher in younger patients. (20)

Smaller body mass index and the absence of internal thoracic artery grafting have been also associated with increased risk of death in women. (21) In another series with well-matched patients there were no differences in mortality between women and men. (20) Another study reported that the greater perioperative mortality in women is due to prevalence of cardiovascular risk factors and not sex per se. (22)

The differences in the outcomes between women and men are not limited to myocardial revascularization surgery, since other studies have shown that the rate of coronary angiography and percutaneous coronary interventions is lower in women than in men. (23-25) It has also been suggested that women receive revascularization at a more advanced stage of coro-

Variables	Women n (%)	Men n (%)	*p* value
Age, years (mean ± SD)	68.4 (8.8)	67.4 (8.6)	0.272
Hypertension	104 (59.4)	113 (64.6)	0.322
Dyslipidemia	65 (37.1)	81 (46.3)	0.083
Diabetes	51 (29.1)	49 (28.0)	0.813
Current smoking	19 (10.9)	23 (13.1)	0.511
COPD	8 (4.6)	7 (4.0)	0.792
Chronic atrial fibrillation	5 (2.9)	9 (5.1)	0.275
Stroke	6 (3.4)	5 (2.9)	0.759
Peripheral vascular disease	7 (4.0)	13 (7.4)	0.197
Heart failure	2 (1.1)	2 (1.1)	1.000
Chronic dialysis	1 (0.6)	0 (0.0)	0.177
LVEF, % (mean ± SD)	57.7 (9.9)	56.2 (10.8)	0.175

SD: Standard deviation. COPD: Chronic obstructive pulmonary disease. LVEF: Left ventricular ejection fraction

Table 3. Distribution of baseline preoperative variables according to sex after propensity score matching analysis (N = 175 by group)

nary heart disease. (26)

The question is whether these disparate results are only due to the study design or merely secondary to a cultural issue. When compared with men, the proportion of women included in randomized clinical trials is lower than the incidence of cardiovascular risk factors (diabetes, hypercholesterolemia or hypertension), coronary artery disease, heart failure, or mortality from these diseases.

A woman herself may consider that she is less likely than a man to suffer a heart attack or even cannot recognize that she is experiencing a myocardial infarction, and therefore delay seeking medical care. A study performed in Spain in 2017 showed that only 39% of women who were experiencing a myocardial infarction recognized their symptoms as due to a heart attack, compared with 57% of men. This also led to a delay in emergency room visits: 237 minutes for women vs. 98 minutes for men. (27)

Cardiovascular mortality in women and men has decreased in Argentina over the past 36 years. In 1980, cardiovascular mortality was 342 per 100,000 population in women and 285 per 100,000 population in men and decreased to similar levels of 250 and 252, respectively, in 2003, reaching 165 and 169 per 100,000 population, respectively, in 2016. (28) In the United States, mortality due to ischemic heart disease decreased by 40% (across all races, all ages, women, and men) from 1999 (190/100,000) to 2017 (112/100,000). (29) When the results are analyzed separately, mortality per 100,000 population is lower in women (96 vs. 132), but clearly much lower than cardiovascular mortality in Argentina, so we still have a long way to go to reduce cardiovascular mortality.

This study has some limitations. Firstly, it is a retrospective analysis from a few centers in Buenos Aires. Secondly, some confounders could not have been considered despite propensity score matching analysis. Finally, the sample size did not have enough power to demonstrate statistical differences in mortality between women and men.

CONCLUSIONS

In this comparative study of CABGS outcomes, women undergoing isolated or combined procedures were older and had higher expected risk calculated by EuroSCORE II and worse kidney function. Mortality after isolated or combined CABGS was higher in women than in men at 60 days, and this difference remained even after adjusting for confounders. These results may express that cardiovascular disease in women is overlooked, and therefore they may be considered for surgery later, or with more advanced vascular disease.

Conflicts of interest

Raúl A. Borracci is Director of the Argentine Journal of Cardiology. The other authors do not have any conflicts of interest to declare. (See authors' conflicts of interest forms on the website/Supplementary material).

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