
Gender Differences in Clinical Outcome after Coronary Stenting

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Objective. The purpose of this study was to determine the effect of gender differences in the clinical outcome of women and men submitted to coronary stenting at our institution.

Background. Studies regarding gender differences in outcome after invasive coronary interventions have revealed conflicting data regarding risk for complications. Some studies have pointed to female gender as a predictor of mortality and complications after those procedures. To our knowledge no such evaluation has been performed in our country.

Methods. We reviewed the medical records, cardiac catheterization and procedural data of 205 men and 122 women referred to our section that underwent coronary stenting at the Cardiovascular Center of Puerto Rico and the Caribbean from July 1, 1998 to March 30, 1999. The clinical and procedural characteristics and the immediate procedure-related complications were analyzed. Clinical events during the six-month period after the procedure were evaluated in patients that returned for follow-up to the section. Student's t-test or Mann-Whitney-Wilcoxon, when appropriate, was used to compare

continuous data. The chi-square test or Fisher's exact test, was employed to compare categorical data.

Results. The initial procedural success and the frequency of early complications were comparable to those informed in the medical literature and not statistically significant between genders. The only statistically significant gender differences in outcome occurred in men who had higher re-hospitalization and re-intervention rates in the six-month period after the procedure. A lower mean ejection fraction and higher previous history of myocardial infarction and cigarette smoking in this group could have been related to the higher complication rate.

Conclusion. Although the sample examined is small, its findings point to the need of a larger prospective study to further explore the possibility that the previously reported differences in outcome in men and women submitted to interventional procedures would have a stronger relation to clinical factors than to the direct effect of gender.

Key words: Coronary stenting, Gender differences, Clinical outcomes, Puerto Rico

Coronary artery disease is the leading cause of morbidity and mortality in men and women in this part of the world (1). However, there are established gender differences in the clinical presentation and course of coronary artery disease and its response to revascularization procedures (2,3). It has been consistently reported that women usually develop coronary artery

disease later in life than men, and that they exhibit a comparatively worse prognosis once they have a myocardial infarction (MI) (4, 5). Various studies have also demonstrated that women usually have greater prevalence of cardiac risk factors and older age at the time of hospitalization for acute MI (6,7). Several analyses on the use of invasive procedures in patients with coronary artery disease have shown that women are submitted to such procedures less frequently than men (8-11). Studies regarding the effect of gender differences in outcome after percutaneous transluminal coronary angioplasty (PTCA) have revealed conflicting data concerning risk for complications. Earlier studies reported that PTCA in women is associated with less favorable acute outcome, higher mortality, and lower initial success rate when

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compared with men (12,13). More recent data have shown comparable rates of success, restenosis, survival and mortality between both genders, particularly in the long-term outcome of those that survive the initial procedure (14-19). Female gender has also been considered an independent predictor of vascular complications after PTCA and for prolonged hospital stay after coronary stenting (20). Complications like hypotension, need for blood transfusions and vascular repair have been found to be more frequent in women after invasive coronary interventions when compared to men (21). The purpose of this study was to determine whether there are gender differences in clinical outcome in women and men undergoing coronary stenting at our institution. Specific study endpoints were the following: (1) the determination of the incidence of in-hospital death after the procedure, (2) the in-hospital post-procedural occurrence of myocardial infarction, (3) the need for re-hospitalization for cardiac related problems (unstable angina pectoris, myocardial infarction, vascular complications) in the six-month period after the procedure, (4) the need for subsequent coronary artery bypass graft (CABG) or coronary re-intervention in the six-month period after the procedure.

Methods

Study population. We reviewed the medical records and the cardiac catheterization database of 327 patients referred to our section and that consecutively underwent coronary stenting at the Cardiovascular Center of Puerto Rico and the Caribbean from July 1, 1998 to March 30, 1999. A data form was designed to abstract information from the medical records including the following baseline clinical characteristics: age, gender, underlying diseases, current medications, prior MI, prior PTCA, prior CABG, ejection fraction and coronary vessels affected. Procedure characteristics (vessel intervened, type of stent, number of stents placed) were also recorded. Immediate procedure related complications were defined as complications occurring during the period of hospitalization for the initial intervention including death, myocardial infarction, life-threatening cardiac arrhythmias, need for CABG or coronary re-intervention, need for blood transfusions and vascular complications or hematomas. In addition, any clinical event in the six-month period after procedure (death, myocardial infarction, re-hospitalization for cardiac related problems (unstable angina pectoris, myocardial infarction, vascular complications) and need for CABG or coronary re-intervention were recorded in those patients that returned for follow-up to our section. A written permission for

medical record review was requested and granted by the Ethical and Research Committee of the Cardiovascular Center of Puerto Rico and the Caribbean.

Statistical analysis. Student's t-test or Mann-Whitney-Wilcoxon, when appropriate, was used to compare continuous data. The chi-square test, or Fisher's exact test, was employed to compare categorical data. Data were entered using Epi-Info 6.04c (22) and analyzed using SAS version 6.12 (23).

Results

The baseline clinical characteristics of the study population are shown in Table 1. This consisted of 205 men (62.7%) and 122 women (37.3%) that were consecutively submitted to stenting. Women tended to be slightly older than men (66.1 (10.3) vs. 64.1 (10.3), respectively), and this difference was marginally significant ($p=.08$). Men had a significant lower mean ejection fraction (49.7% (12.7%) when compared to women (53.9% (12.7%) ($p=0.005$). In terms of cardiac risk factors the only statistically significant difference was that of cigarette smoking history; 55 men (26.8%) and 20 women (16.4%) had such habit ($p=0.03$). Regarding pre-existing cardiovascular disease there was also a statistically significant difference between the two groups; one hundred men (48.8%) and 44 women (36.1%) had previous history of myocardial infarction ($p=0.03$). No significant gender differences were found regarding comorbid conditions, medication use or prior coronary interventions.

Table 2 shows the procedural characteristics. No statistically significant differences were found between the two groups. The most commonly diseased coronary artery in both groups was the left anterior descending. This was also the most commonly intervened artery. The majority of patients, 143 men (69.8%) and 93 women (76.2%), had only one stent implanted during the procedure and no significant difference was found in the mean number of stents implanted in the two groups. The most commonly used stent in both groups was the ACS Multi Link (data not shown).

Table 3 shows the procedure-related complications. Eighteen patients (10.4%) showed complications during the first 24 hours after the procedure. Thirteen men (6.3%) and 5 women (4.1%) had procedure-related complications, but this was not statistically significant ($p=0.59$). Only two patients died and both were men. A trend was observed for a higher hematoma formation at the catheter insertion site in women (3 women vs. 0 men; $p=0.05$).

Fifty-three men (25.9%) and 21 women (17.2%) returned to the section due to clinical events in the six-

Table 1. Baseline clinical characteristics of 205 men and 122 women who underwent stenting

Characteristic	Men n (%)	Women n (%)	P value
Mean age (SD) in years	64.1 (10.3)	66.1 (10.3)	0.08
Mean ejection fraction (SD) (%)	49.7 (12.7)	53.9 (12.7)	0.005
Median length of stay in days	1.00	1.00	0.49
Cardiac risk factors			
Systemic hypertension	158 (77.1)	102 (83.6)	0.16
Diabetes mellitus	81 (39.5)	57 (46.7)	0.20
Hyperlipidemia	92 (44.9)	66 (54.1)	0.11
Smoking history	55 (26.8)	20 (16.4)	0.03
Pre-existing cardiovascular disease			
Previous myocardial infarction	100 (48.8)	44 (36.1)	0.03
Congestive heart failure	12 (5.9)	4 (3.3)	0.30
Peripherovascular disease	7 (3.4)	6 (4.9)	0.50
Cerebrovascular disease	1 (0.5)	1 (0.8)	1.00
Cardiac valvulopathy	2 (1.0)	2 (1.6)	0.63
Atrial fibrillation	3 (1.5)	2 (1.6)	0.90
Sick sinus syndrome	6 (2.9)	2 (1.6)	0.71
Comorbid conditions			
Chronic obstructive pulmonary disease	5 (2.4)	6 (4.9)	0.34
Thyroid disease	6 (2.9)	8 (6.6)	0.12
Renal insufficiency	5 (2.4)	3 (2.5)	1.00
Malignancy	6 (2.9)	1 (0.8)	0.26
Medications			
Beta blockers	101 (49.3)	49 (40.2)	0.11
Alpha blockers	14 (6.8)	8 (6.6)	0.92
Nitrates	125 (61.0)	77 (63.1)	0.70
Aspirin	150 (73.2)	83 (68.0)	0.32
Antiplatelets	96 (46.8)	57 (46.7)	0.98
ACE inhibitors	81 (39.5)	42 (34.4)	0.36
Calcium channel blockers	62 (30.2)	46 (37.7)	0.17
Statins	73 (35.6)	40 (32.8)	0.60
Diuretics	25 (12.2)	20 (16.4)	0.29
Angiotensin II receptor blockers	6 (2.9)	6 (4.9)	0.37
Digitalis	20 (9.8)	11 (9.0)	0.83
Prior coronary interventions			
Prior coronary angioplasty	28 (13.7)	17 (14.0)	0.92
Prior coronary bypass	39 (19.0)	21 (17.2)	0.68

month period after the procedure, a trend towards a higher rate of clinical events among men ($p=0.07$). Forty-six men (22.4%) and 16 women (13.1%) required re-hospitalization at our institution due to clinical events after the procedure and this was statistically significant ($p=0.03$). There were no statistically significant differences between both groups in terms of myocardial infarction or

Table 2. Procedural characteristics of 205 men and 122 women who underwent stenting

Characteristic	Men n (%)	Women n (%)	P value
Diseased Coronary Vessels			
Right	138 (67.6)	81 (66.4)	0.82
Left anterior descending	170 (82.9)	97 (79.5)	0.99
Circumflex	121 (64.3)	64 (52.5)	0.23
Saphenous vein graft	19 (9.3)	7 (5.7)	0.23
Left internal mammary graft	2 (1.0)	1 (0.8)	1.00
Coronary vessels intervened			
Right	77 (37.7)	43 (35.2)	0.65
Left anterior descending	91 (44.4)	60 (49.2)	0.40
Left circumflex	43 (21.1)	30 (24.6)	0.46
Saphenous vein graft	11 (5.4)	2 (1.6)	0.14

CABG. Men, however, exhibited a higher trend for episodes of unstable angina ($p=0.07$). Forty-eight men (23.4%) required coronary re-intervention during the six-month period after the procedure, compared to 17 women (13.9%) reaching statistical significance ($p=0.04$). In this group, 17 men (8.3%) and only one woman (0.9%) required cardiac catheterization and PTCA to other than the original coronary lesion, and this was again statistically significant ($p=0.004$).

Table 3. Procedural-related complications of 205 men and 122 women who underwent stenting

Characteristic	Men n (%)	Women n (%)	P value
Overall complications in original hospitalization			
Severe hypotension	1 (0.5)	1 (0.8)	1.00
Vascular complications	6 (2.9)	0 (0.0)	0.30
Hematoma	0 (0.0)	3 (2.5)	0.05
Arrhythmias	1 (0.5)	1 (0.8)	1.00
Acute stent occlusion	3 (0.9)	0 (0.0)	0.53
Death	2 (1.0)	0 (0.0)	0.53
Clinical events after hospital discharge			
Overall events	53 (25.9)	21 (17.2)	0.07
Death	3 (1.5)	4 (3.3)	0.43
Myocardial infarction	6 (2.9)	3 (2.5)	1.00
Re-hospitalization	46 (22.4)	16 (13.1)	0.03
Unstable angina	15 (7.3)	8 (6.5)	0.07
CABG	6 (2.9)	3 (2.5)	1.00
Coronary re-intervention	48 (23.4)	17 (13.9)	0.04
Cardiac catheterization	16 (7.8)	7 (5.7)	0.48
Cardiac catheterization + target vessel revascularization	15 (7.3)	9 (7.4)	0.98
Cardiac catheterization + revascularization to other lesion	17 (8.3)	1 (0.9)	0.004

Discussion

As stated above several studies have shown important gender differences in clinical characteristics in the acute and long-term outcomes of patients submitted to coronary interventional procedures (18). It has been reported that women referred for PTCA are usually older than men and that are submitted to such procedures less frequently than men (8-11). Other studies have also documented a greater prevalence of cardiac risk factors in women and have even proposed that female gender is a predictor for higher short-term mortality after PTCA. However, the long-term results have been reported as similar in the two genders in the patients that survive the original intervention (13, 14). Gender differences regarding complications after coronary stenting have obtained less attention in the literature. In a report by Carrozza et al. of 250 patients submitted to stenting, including 70 women, female gender was not found to be a predictor of restenosis (19).

In our study we could not find a statistically significant difference in terms of age between the two groups, but only a trend for older age in women. Although, the predominant distribution of men versus women in our study is in accordance to that observed in the series reviewed in the literature, it can not be established with certainty whether those numbers reflect the previously stated finding that women are submitted less frequently to interventional procedures or to a bias in the referral of patients to our tertiary center. In contrast to other studies showing a higher prevalence of coronary risk factors and short-term mortality in women submitted to coronary interventions (6,13), we found no significant gender difference in early mortality or coronary risk factors between both groups, aside from a higher history of cigarette smoking in men. The most statistically significant clinical differences between the two groups found in our review were a higher prevalence of previous myocardial infarction and lower baseline mean ejection fraction values in men. As those two findings have been consistently identified as strong predictors of outcome in patients with coronary artery disease, they could have possibly influenced the higher rate of overall clinical events and complications observed in men in the six-month period after the intervention. We did not find any significant differences in the two groups regarding medical therapy nor procedure characteristics.

The analysis of the clinical endpoints in the first 24 hours after the procedure showed no statistically significant difference related to gender, just a trend for higher hematoma formation at the catheter insertion site in women. In that way and in contrast to other reported studies (13,14,18), female gender was not associated in

our review with an unfavorable early post-procedural outcome. Moreover, upon examining the rate of overall events in a period of six months after the procedure, men experienced a less favorable outcome showing a statistically significant higher rate of re-hospitalizations and re-interventions.

Based on the sample of patients studied, it can be concluded that coronary stenting is a safe and effective procedure in our center, with a very low rate of complications. Furthermore, in contrast to previous reports, female gender did not appear to correlate with a higher occurrence of early or long-term complications. As interventional techniques represent very important tools for the management of women with coronary artery disease, the findings of the study are encouraging as they portray excellent early and long-term results and comparable to those obtained in men. Whereas, this was a retrospective study and only a relatively small sample of patients returned for follow-up, its findings should be confirmed in a larger prospective study. That could settle the issue of whether the reported differences in outcome in men and women submitted to interventional procedures bear a stronger relation to clinical factors or to a direct effect of gender.

Resumen

Varios estudios en la literatura médica han descrito un panorama conflictivo sobre la influencia del género en los resultados y las complicaciones de los procedimientos de intervención coronaria (angioplastia o implantación de *stents*). El objetivo de este estudio fue determinar si las diferencias en género de los pacientes sometidos a implantes de *stents*, tienen algún efecto sobre la morbilidad y la mortalidad relacionadas a dicha intervención. No tenemos conocimiento que ese análisis se haya efectuado en nuestro medio hospitalario anteriormente. Se analizaron los expedientes clínicos, los datos de cateterismo cardíaco y de esa intervención en 205 hombres y 122 mujeres referidos a la Sección de Cardiología del Centro Cardiovascular de Puerto Rico y del Caribe. Además, se recopilaron datos sobre la evolución clínica de los pacientes intervenidos que regresaron a seguimiento a nuestra sección. El éxito inicial de la intervención y la frecuencia de complicaciones iniciales fueron comparables a las informadas en la literatura, sin observarse diferencias estadísticamente significativas relacionadas al género. Sin embargo, contrario a estudios previos, hubo diferencias estadísticamente significativas relacionadas al género durante los 6 meses posteriores al procedimiento, con una frecuencia mayor de re-hospitalizaciones y re-

intervenciones en los hombres. Como la muestra de hombres mostró valores inferiores en la fracción de eyección promedio e historial previo mayor de infartos de miocardio y tabaquismo, esos factores pudieran tener relación con el número mayor de complicaciones. Aunque la muestra estudiada es reducida en tamaño, los datos obtenidos sugieren la necesidad de explorar en un estudio prospectivo más abarcador, si las diferencias anteriormente reportadas en los resultados de procedimientos invasivos en hombres y mujeres está más relacionada a diferencias en factores clínicos que al efecto directo del género.

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