# • FULL-LENGTH ARTICLES •

# Gender Disparities in Puerto Ricans Hospitalized with an Initial Acute Myocardial Infarction: A Population-based Perspective

Juan Carlos Zevallos, MD*; Jorge Yarzebski, MD, MPH†; Héctor Banchs, MD*;
Juan A. González-Sánchez, MD*; Hernando Mattei, PhD*; Robert J. Goldberg, PhD†;
María del Carmen González, MPH*; Juan Quevedo, MD*; Gruschenka Mojica, BS*;
Luis R. Pericchi, PhD‡; Mario R. García-Palmieri, MD*

**Objective: The published literature suggests differences in presenting symptoms for acute myocardial infarction (AMI), management, and outcomes according to gender and age. However, limited information exists on this topic among Hispanics.**

**Methods: In Puerto Rican patients hospitalized with an initial AMI, we examined differences in presenting symptoms, effective cardiac therapies, and in-hospital mortality as a function of gender and age groups. We reviewed the medical records of patients hospitalized with a validated AMI in 12 greater San Juan, Puerto Rico hospitals during 2007.**

**Results: The average age of 1,415 patients hospitalized with a first AMI was 66 years and 45 % were women. Chest pain (81%) was the most prevalent acute presenting symptom with significant differences in its frequency between women (77%) and men (85%)(p<0.001). Right arm pain, shortness-of-breath/dyspnea, and sweating/diaphoresis were most prevalent in patients 55-64 years old (45%), compared with patients 75 years and older (29%)(p<0.005). Relative to men and patients < 55 years old, coronary angiography/thrombolytic therapy and percutaneous coronary interventions were used less frequently in women and older patients (>75 years old). During hospitalization for AMI the in-hospital death rate was higher in women (8.6%) than men (6.0%), and increased with advancing age (p<0.05).**

**Conclusion: These findings suggest significant gender and age differences in presenting symptoms, management, and early mortality in Puerto Ricans hospitalized with an initial AMI. It remains of considerable importance that health care personnel become aware of these gender and age differences to improve the management and outcomes of these patients. [*P R Health Sci J 2012;4:192-198*]**

*Key words: Gender, Health care disparity, Myocardial infarction, Secondary prevention, Population surveillance*

Age-adjusted death rates from coronary heart disease (CHD) have declined steadily in Puerto Rico between 1999 and 2009. Data from the National Center for Health Statistics suggest that CHD mortality rates (per 100,000 population) declined from 95 to 64 for women and from 149 to 107 for men in Puerto Rico over this period (1, 2). Multiple factors likely have contributed to this decline, including greater control of CHD predisposing factors and use of effective therapeutic approaches. Despite these encouraging trends, CHD remains the single leading cause of death among Puerto Rican adults. In 2009, 1,495 women and 1,926 men died with CHD in Puerto Rico.

The results of several studies suggest that CHD occurs several years later in women than in men (3, 4). However, the death rates are higher in women than in men after they develop an acute myocardial infarction (AMI) (3, 5, 6). Numerous studies (7-12) suggest that chest pain is the most common symptom associated with AMI and that differences exist in the location, frequency, and quality of symptoms of AMI in women and men of different ages. In addition, women have been shown to receive less aggressive in-hospital therapy for AMI than men (13).

*University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico; †Department of Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, Massachusetts, United States of America; ‡University of Puerto Rico Río Piedras Campus, San Juan, Puerto Rico

Address correspondence to: Juan Carlos Zevallos, MD, Endowed Health Services Research Center, PO Box 3605067, San Juan, PR 00936-5067. Email: juan.zevallos@upr.edu

Despite the significant medical, socio-economic, and health consequences associated with CHD in Puerto Rico, contemporary information on the epidemiology, clinical profile, presenting symptoms, management practices, and outcomes of patients hospitalized with AMI in this predominantly Hispanic population is limited.

Using as a model the well-established methodologies of the Worcester Heart Attack Study (WHAS) (14, 15), the University of Puerto Rico, in collaboration with assistance from the University of Massachusetts Medical School, established a surveillance program of AMI among Hispanics residing on the island: the Puerto Rico Heart Attack Study (PRHAS). The objectives of this article were to describe gender and age differences in the presenting symptoms of AMI, use of secondary prevention management practices, and in-hospital death rates in patients hospitalized with an initial AMI.

## Methods

### Study Population and Case Validation Approach

We reviewed the medical records of Hispanic residents of the greater San Juan, Puerto Rico area, which consists of the municipalities of Bayamón, Canóvanas, Carolina, Cataño, Guaynabo, Loíza, Río Grande, San Juan, and Trujillo Alto (2000 census estimate = 866,000) hospitalized for possible AMI at 12 academic and/or non-teaching medical, and non-military centers with emergency room capability located in the greater San Juan area. A complete listing with information on all hospital discharges from January 1 to December 31 of 2007 with International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 410 in the principal and/or secondary diagnosis position, and related acute and chronic coronary disease ICD-9 rubrics (i.e., 412 –old MI, 413 –angina pectoris, 414 – other forms of chronic CHD, and 786.5 –chest pain), was obtained from each of the participating hospitals.

Once the computerized discharge diagnosis printouts were obtained from each participating hospital, the appropriate ICD-9-CM codes for CHD were reviewed for purposes of case validation. The list of selected medical records to be reviewed was given to medical record department personnel at each participating hospital.

Trained nurse and physician abstractors reviewed the medical records of all identified patients meeting the pre-defined geographic inclusion criteria (e.g., resident of greater San Juan) and clinical criteria for AMI developed by the World Health Organization, which includes a clinical history suggestive of AMI, serum enzyme elevations, and serial ECG findings during hospitalization. Since this study was focused on patients with an initial (incident) AMI, records of previous hospitalizations for CHD were reviewed if the hospital chart indicated that the present hospitalization was not the first for CHD. Patients with ECG changes indicative of prior MI (old Q-waves on ECG) or prior documented MI (confirmed by medical records corresponding to prior hospitalizations) were excluded. Patients who developed AMI secondary to an interventional procedure or surgery, other than for the treatment of an acute coronary event, were excluded. Autopsy confirmation of recent onset MI satisfied the study inclusion criteria, irrespective of the other diagnostic criteria. Patients who were initially admitted to the emergency department and stabilized in one hospital, and transferred thereafter to another hospital, were only counted once.

### Data Collection

We utilized a standardized data collection form developed in the Worcester Heart Attack Study (14), which was adapted for use in Puerto Rico. Study abstractors created an online electronic database that included patient's demographic characteristics (i.e., age, gender, municipality of residence); acute presenting symptoms (i.e., chest pressure/discomfort, arm/hand numbness, indigestion/abdominal, back, chest, jaw, left/right arm and shoulder pain, cough, shortness of breath/dyspnea, fever, palpitation/rapid heart rate, sweating/diaphoresis, vomiting); coronary risk factors and comorbidities (i.e., diabetes, hypertension, hyperlipidemia, smoking, angina, stroke, heart failure); physiologic parameters (i.e., heart rate, blood pressure, lipid profile, serum creatinine or glucose findings); AMI type (i.e., ST-elevation AMI (STEMI) or non-ST-elevation AMI (NSTEMI)); use of invasive coronary procedures (i.e., cardiac catheterization/thrombolysis, percutaneous coronary interventions (PCI), and coronary bypass surgery (CABG)); and hospital survival status. We defined the use of effective cardiac treatment as the proportion of patients who received aspirin within 24 hours of admission or at the time of hospital discharge, and the receipt of beta-blockers, ACE inhibitors or ARBs, or lipid-lowering agents at discharge; we also examined the provision of smoking cessation counseling for current smokers at the time of hospital discharge.

Allergies or contraindications to the receipt of effective medical therapies, including aspirin, beta-blockers, ACE inhibitors or ARBs, and lipid-lowering agents were not documented in the medical records that were reviewed. Data were captured electronically utilizing the REDCap™ web application exclusively designed for research studies that allows secure online management of surveys and databases (16).

### Data Analysis

Gender-specific means and frequency distributions of patient's demographic and clinical characteristics were calculated in a standard fashion. Differences in the distribution of five age groups (<55, 55-64, 65-74, 75-84, >85 years), demographic and clinical characteristics, presenting symptoms, and hospital

management practices between men and women were examined by using chi-square tests of statistical significance for discrete variables and t tests for continuous variables. In-hospital case-fatality rates were calculated in a standard manner. STATA® version 11.0 (17) was used for analysis. This study was approved by the Institutional Review Board of all participating hospitals and by the University of Puerto Rico School of Medicine.

## Results

### Patient Characteristics

The mean age of 1,415 Hispanic Puerto Rican patients (45% women) hospitalized with a validated initial AMI in the greater San Juan, Puerto Rico area was 66 years. On average, women were 5 years older than men (69 vs. 64 years, respectively).

A history of diabetes was present in approximately half of all patients and eight out of every ten patients had a history of hypertension. Women were significantly more likely than men to have a history of diabetes, hypertension, stroke, and heart failure, but were less likely to be current smokers (p<0.001). At the time of hospital admission, one out of every three patients was obese; the prevalence of obesity was similar in men and in women. On admission to the hospital, women presented with higher average serum HDL-cholesterol levels than men. However, men presented with higher average serum LDL-cholesterol, serum creatinine and hemoglobin levels than women p<0.005). Women were significantly less likely than men to present with a STEMI (24.4% vs. 35.2%; p<0.05) (Table 1).

### Acute Presenting Symptoms

Overall, chest pain was the most commonly reported acute symptom (81%) described upon arrival in the emergency department of participating study hospitals; women (77%) were less likely to complain of chest pain than men (85%)(p<0.001). (Figure 1) Approximately one out of every 4 women and one out of every 7 men presented without chest pain. (Figure 2) Compared with men, women were more likely to present with back pain, indigestion/abdominal pain, or fever (p<0.05) (Table 2).

Chest pain was more frequently reported by younger patients (<55 years old and 55-64 years old) (23.6% and 28.8%, respectively) as compared with older patients (75-84 years old and > 85 years old) (17.7% and 6.0%, respectively) (p<0.001).

**Table 1**. Distribution of Selected Characteristics by Gender of Patients with Initial Acute Myocardial Infarction

| Characteristic | Female (n=637) % | Male (n=778) % | p-value |
|---|---|---|---|
| *Demographics* | | | |
| Age, years (mean +/- SD) | 68.6 +/- 13.3 | 63.2 +/- 13.7 | p<0.001 |
| Age groups % (n) | | | |
| <55 | 15.4 | 26.1 | p<0.001 |
| 55-64 | 24.5 | 28.8 | |
| 65-74 | 24.2 | 22.8 | |
| 75-84 | 23.4 | 15.8 | |
| ≥85 | 12.6 | 6.6 | |
| *Risk factors and Comorbidities* | | | |
| Angina | 3.6 | 3.6 | p=0.98 |
| Body Mass Index > 30 kg/m2 | 30.7 | 29.2 | p=0.64 |
| Current smoker | 10.2 | 22.2 | p<0.001 |
| Diabetes | 54.0 | 40.7 | p<0.001 |
| Heart failure | 10.8 | 4.4 | p<0.001 |
| Hypertension | 80.5 | 64.7 | p<0.001 |
| Hyperlipidemia | 23.5 | 20.8 | p=0.27 |
| Stroke | 6.4 | 2.5 | p=0.002 |
| *Physiological Parameters mean, (+/- SD) at hospital presentation)* | | | |
| Initial heart rate, beats/minute | 85.8 (+/- 23.2) | 81.9 (+/- 20.2) | p=0.99 |
| Systolic blood pressure, mmHg | 144.8 (+/- 35.8) | 141.7 (+/- 31.6) | p=0.95 |
| Diastolic blood pressure, mmHg | 78.4 (+/- 18.4) | 80.8 (+/- 17.2) | p<0.05 |
| Initial cholesterol, mg/dL | 179 (+/- 52.8) | 167 (+/- 47.4) | p=1.0 |
| Initial HDL-cholesterol, mg/dL | 49.8 (+/- 22.0) | 36.9 (+/- 18.4) | p=0.001 |
| Initial LDL-cholesterol, mg/dL | 86.3 (+/- 54.7) | 96.0 (+/- 57.9) | p=0.001 |
| Creatinine, mg/dL | 33.3 (+/- 25.0) | 37.1 (+/- 22.9) | p=0.005 |
| Glucose, mg/dL | 127.2 (+/- 104.2) | 118.0 (+/- 107.2) | p=0.94 |
| Hemoglobin, g/dL | 12.5 (+/- 1.8) | 14.3 (+/- 7.6) | p<0.001 |
| *Use of Medication and Secondary Prevention Practices* | | | |
| Aspirin within 24 hours of admission | 76.2 | 83.3 | p<0.001 |
| ACE inhibitor / Angiotensin receptor blockers (ARB) at discharge | 54.9 | 64.8 | p=0.58 |
| Lipid-lowering agent at discharge | 53.3 | 57.3 | p=0.72 |
| Use of β blocker at discharge | 51.3 | 51.2 | p=0.99 |
| Aspirin at discharge | 57.8 | 66.5 | p<0.005 |
| Smoking cessation counseling among current smokers | 29.2 | 27.5 | p=0.82 |
| Overall beneficial therapy | 49.8 | 55.0 | p<0.05 |
| *Procedure (%)* | | | |
| Cardiac catheterization/ Thrombolysis | 57.5 | 68.2 | p<0.001 |
| Percutaneous coronary intervention | 37.6 | 51.6 | p<0.05 |
| Coronary Stent Placed | 19.8 | 26.7 | p<0.05 |
| Coronary Artery Bypass Surgery | 5.9 | 7.1 | p=0.4 |
| *Acute Myocardial Infarction Characteristics* | | | |
| ST-segment elevation | 24.4 | 35.2 | p<0.05 |

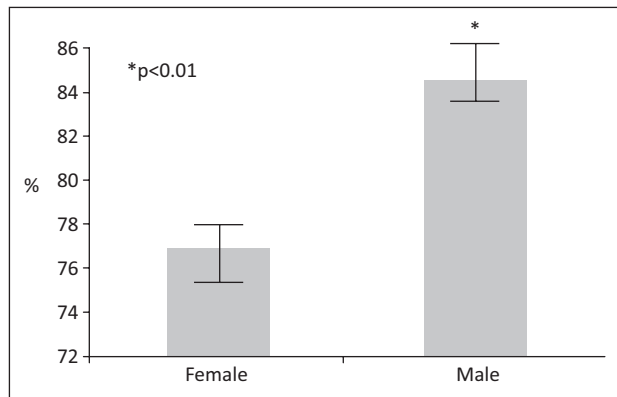Note: Percentages are rounded and may not add up to 100%

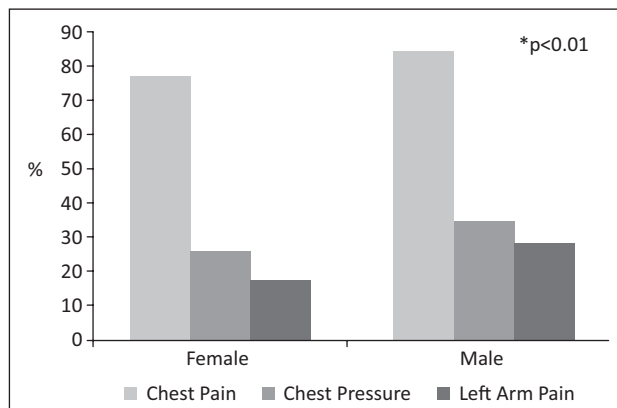Figure 1. Gender Differences in Chest Pain Associated with Acute Myocardial Infarction



Figure 2. Prevalence of Symptoms Frequently Associated with Acute Myocardial Infarction

## Hospital Management Practices

At the time of hospital admission, approximately 4 out of every 5 patients were treated with aspirin. At hospital discharge, approximately 3 out of every 5 patients were prescribed aspirin or ACE inhibitors/ARBs whereas only one half of patients were prescribed lipid-lowering medications and beta-blockers. Women were significantly less likely to have received aspirin within 24 hours of admission and at discharge, and to have received each of the beneficial cardiac therapies than men (Table 1). Only one third of current smokers received smoking cessation counseling at the time of hospital discharge.

In examining the management of patients hospitalized with AMI according to type of AMI, women were less likely to have undergone cardiac catheterization/thrombolysis or a PCI than men (Table 1).

## Hospital Death Rates

One hundred and two patients died in the hospital after developing an initial AMI. The overall in-hospital death rate was significantly higher for women (8.6 %) than men (6.0 %) (p<0.05). The in-hospital death rate increased significantly with advancing age in both men and in women (3).

**Table 2**. Differences in Acute Myocardial Infarction Presenting Symptoms Stratified by Gender

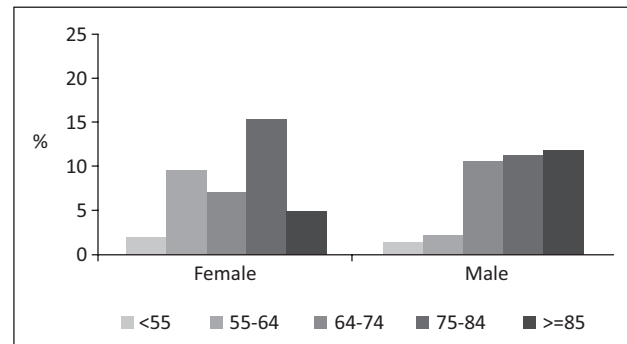| Symptom | Total (%) | Female (%) | Male (%) | p-value |
|---|---|---|---|---|
| Chest pain | 81.2 | 76.9 | 84.6 | p<0.01 |
| Chest pressure | 30.9 | 25.9 | 34.8 | p<0.05 |
| Left arm pain | 23.4 | 17.3 | 28.3 | p<0.001 |
| Back pain | 10.3 | 13.5 | 7.6 | p<0.001 |
| Abdominal pain | 7.6 | 9.8 | 5.7 | p<0.05 |
| Fever | 2.6 | 3.8 | 1.5 | p<0.05 |



Figure 3. Hospital Mortality by Gender and Age Group

## Discussion

The results of this population-based study of Puerto Rican men and women suggest marked differences in symptom presentation, hospital management and short-term outcomes during hospitalization for an initial AMI. In comparison with men, women were less likely to complain of chest pain, were older, experienced a larger number of comorbidities, were less likely to receive effective cardiac medications, and experienced a higher in-hospital death rate.

Data in Puerto Ricans suggest that, on average, women die eight years later than men (83 years old vs. 75 years old) (2). The decline in CHD mortality rates observed between 1999 and 2009 in Puerto Rico may be attributed to the same factors observed in a similar decline in the United States between 2006 and 2010 (18): an increasing number of people are living with CHD, and there have been continued improvements in CHD treatment and in risk factor reduction strategies (19).

Information on the prevalence of CHD and the distribution of risk factors for CHD in Puerto Rico is limited to data from the Behavioral Risk Factor Surveillance System (20). The prevalence of Puerto Ricans reporting having been told they had a heart attack has remained unchanged between 2005 (4.0%) and 2010 (4.2%). Similarly, the proportion of Puerto Ricans reporting having ever been told they had angina or CHD has also remained unchanged between 2005 (8.5%) and 2010 (8.2%) (20). Improvements in the management of patients with CHD are difficult to document in Puerto Rico, and the major risk factors for CHD (e.g., obesity, diabetes, and

cholesterol), hypertension awareness and current smoking have remained relatively stable during this period in women and in men (20). Thus, it is likely that other unmeasured, or inadequately measured factors likely explain gender differences in the age at death, along with the decline in CHD mortality rates in Puerto Ricans.

In our study, Puerto Rican women were five years older than men at the time of hospitalization for AMI, and were more likely to have a medical history of diabetes, hypertension, stroke, and heart failure. Similar patterns suggesting a later manifestation of CHD and a higher prevalence of CHD comorbidities in women have been published (3, 4). In the Puerto Rico Heart Attack Study, women experienced a higher likelihood of dying during hospitalization for an initial AMI. These findings are consistent with the in-hospital or short-term post-discharge mortality rates reported in several other studies (21-24). Despite these differences, and considerable speculation, limited information is available to understand why women have worse outcomes after the occurrence of an AMI than men (25).

Our findings suggest that Puerto Rican women and patients > 75 years old present with less "typical" AMI symptoms than men and comparatively younger patients. Although chest pain was the most common symptom reported by both women and men at the time of hospital admission for AMI, several differences in acute symptom patterns were noted. For example, as shown in Figure 2 women reported chest pain less frequently than men. These findings are similar to those of other studies which indicate that women are more likely to present with more atypical symptoms such as back, jaw, and neck pain and nausea and/or vomiting, dyspnea, palpitations, indigestion, dizziness, fatigue, loss of appetite, and syncope but less likely to report chest pain than men (26). Further understanding that the acute presenting symptoms of CHD are different in women and in persons of different age strata will help developing more effective measures to improve their clinical outcome, as well as in the design of future investigations.

### Clinical Implications

Despite having an adverse clinical profile, coronary angiography and thrombolysis as well as PCI procedures and stent placement were used less frequently in Puerto Rican women. Data from CHD registries suggest that women are less likely than men to receive medically proven therapies for AMI (28). Women experience more vague symptoms, which may account for the underuse of effective therapies. In addition, they may gain less benefit from the use of thrombolytic therapy than men. Indeed, increased use of thrombolytic therapy has resulted in a continued decrease in cardiovascular deaths for men, but not for women (26). It is unclear if this disparity is a result of inequitable access to therapy or decreased efficacy of these agents in women.

Our findings suggest that overall, the use of aspirin at the time of hospitalization, as well as the prescription of aspirin, ACE inhibitors/ARBs, beta-blockers, lipid-lowering medications, and smoking cessation counseling at the time of hospital discharge were employed in six out of every 10 patients. Thus, efforts remain needed to enhance the use of evidence-based therapies, reduce possible gender disparities, and improve short-term prognosis in Puerto Rican Hispanics hospitalized with an initial AMI.

Findings from the WHAS suggest similar prescribing rates after excluding patients with contraindications to the use of cardiac medications (27). The proportion of patients receiving ACE inhibitors/ARBs at discharge in our study was lower in women than in men; these findings are consistent with those reported in the WHAS, which indicate that women were significantly less likely to receive aspirin and ACE inhibitors/ARBs as compared to men (28). Increasing age in both women and men was associated with a reduced likelihood of receiving effective cardiac therapies including aspirin, beta-blockers, lipid-lowering therapy and thrombolytic agents (29).

These data suggest that the reasons for the marked gender and age –related differences in the use of cardiac medications be more systematically explored specially from the more generalizable perspective of a population-based investigation and during recent years (30).

### Conclusions

In summary, findings of this community-wide observational study suggest marked differences in the proportion of risk factors and comorbidities, acute presenting symptoms, therapeutic management, and in-hospital death rate between women and men and according to age in patients hospitalized with an initial AMI in the greater San Juan, Puerto Rico area during 2007. The strong cooperation and enthusiasm of hospital officials from all participating medical centers located in the largest metropolitan area of Puerto Rico sets the stage for developing long-term, island-wide surveillance for CHD. The Puerto Rico Heart Attack Study offers a unique opportunity to examine gender and age disparities, as well as to characterize the demographic, clinical characteristics, and in-hospital management strategies of Hispanics hospitalized with AMI on the island.

### Resumen

Objetivo: La literatura científica sugiere diferencias de sexo y edad en la presentación de síntomas, manejo y resultados de pacientes con infarto agudo del miocardio (IAM). Esta información es limitada en sujetos hispanos. Métodos: Los récords médicos de pacientes puertorriqueños hospitalizados con IAM inicial en 12 hospitales de San Juan, Puerto Rico durante 2007 fueron evaluados para examinar la presentación

de síntomas, terapia y mortalidad hospitalaria en relación a sexo y a grupos de edad. Resultados: La edad promedio de 1,415 pacientes (45% mujeres) hospitalizadas con IAM fue de 66 años. El dolor de pecho (81%) fue el síntoma más prevalente y mostró diferencias significativas en la frecuencia entre mujeres (77%) y hombres (85%) (p<0.001). Dolor en el brazo derecho, falta de aire/disnea y sudoración fueron más prevalentes en pacientes de 55-64 años (45%), en comparación con pacientes de 75 años y más (29%) (p=0.004). En relación a hombres y pacientes < 55 años, la coronariografía/trombolisis e intervenciones percutáneas coronarias se usaron menos frecuentemente en mujeres y en pacientes mayores de 75 años. La mortalidad hospitalaria después de un IAM fue significativamente mayor en mujeres (8.6%) en comparación a hombres (6%), y se incrementó con la edad (p<0.05). Conclusión: Estos hallazgos sugieren diferencias significativas en sexo y edad en la presentación de los síntomas, manejo y mortalidad temprana en puertorriqueños hospitalizados con IAM inicial. Es muy importante que el personal médico se percate de estas diferencias de sexo y edad para mejorar el manejo y los resultados de estos pacientes.

## Acknowledgments

## References

1. Murphy SL, Xu J, Kochanek KD. Deaths: Preliminary Data for 2010. National Vital Statistics Reports vol. 60 no 4. January 11, 2012.

2. Puerto Rico Department of Health: http://www.salud.gov.pr Accessed May 5, 2012.

3. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. Am Heart J 1986;111:383-390.

4. Centers for Disease Control and Prevention. Coronary heart disease incidence, by sex: United States, 1971–1987. MMWR Morb Mortal Wkly Rep 1992;41:526-529.

5. Wingard DL, Cohn BA, Kaplan GA, Cirillo PM, Cohen RD. Sex differentials in morbidity and mortality risks examined by age and cause in the same cohort. Am J Epidemiol 1989;130:601-610.

6. Keil JE, Gazes PC, Loadholt B, Tyroler HA, Sutherland S, Gross AJ, Knowles M, Rust PF. Coronary heart disease mortality and its predic-tors among women in Charleston, South Carolina. In: Eaker E, Packard B, Wenger NK, Clarkson TB, Tyroler HA, eds. Coronary Heart Disease in Women: Proceedings of an NIH Workshop. New York, NY: Haymarket Doyma; 1987:90-98.

7. Mujtaba SF, H Rizvi SN, Talpur A, Younis F, Minhas K, Farooqui Z. Gender based differences in symptoms of acute coronary syndrome. J Coll Physicians Surg Pak 2012;22:285-8.

8. Arslanian-Engoren C, Patel A, Fang J, Armstrong D, Kline-Rogers E, Duvernoy CS, Eagle KA. Symptoms of men and women presenting with acute coronary syndromes. Am J Cardiol 2006;98:1177-81.

9. Bell DM, Nappi J. Myocardial infarction in women: a critical appraisal of gender differences in outcomes. Pharmacotherapy. 2000;20:1034-44.

10. Shu W, Lei W, Peng S. Recent development of ischaemic heart disease in sex difference. Postgrad Med J 2007;83:240-3.

11. Goldberg RJ, Gorak EJ, Yarzebski J, Hosmer DW, Dalen P, Gore JM, Alpert JS, Dalen JE. A communitywide perspective of sex differences and temporal trends in the incidence and survival rates after acute myocardial infarction and out-of-hospital deaths caused by coronary heart disease. Circulation 1993;87:1947-1953.

12. McSweeney JC, Cody M, O'Sullivan P, et al. Women's Early Warning Symptoms of Acute Myocardial Infarction. American Heart Association. Circulation 2003;108:2619-2623.

13. 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.

14. Goldberg RJ, Gore JM, Alpert JS, et al. Recent changes in attack and survival rates of acute myocardial infarction (1975 through 1981). The Worcester Heart Attack Study. JAMA 1986;255:2774-2779.

15. Goldberg RJ, Samad, NA, Yarzebski J, et al. Temporal trends in cardiogenic shock complicating acute myocardial infarction. N Engl J Med 1999;340:1162-1168.

16. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377-81.

17. STATA Corp. Data Analysis and Statistical Software. Version 11, 2010. Available at http://www.stata.com

18. Fang J, Shaw KM, Keenan NL. Div for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion. Prevalence of Coronary Heart Disease. United States, MMWR 2006 – 2010. October 14, 2011 / 60/40;1377-1381.

19. Ford ES, Ajani UA, Croft JB, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. N Engl J Med 2007; 356:2388-98.

20. Centers for Disease Control and Prevention (CDC). Behavioral Risk Factor Surveillance System Survey Data. Atlanta, Georgia: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2006-2010. Available at http://apps.nccd.cdc.gov/BRFSS/display.asp?cat=HC&yr=2009&qkey=868&state=PR Accessed on May 5, 2012.

21. Henning R, Lundman T. The Swedish Cooperative Study, Part I: a description of the early stage. Acta Med Scand. 1975;586(suppl): 27-29.

22. Puletti M, Sunseri L, Curione M, Erba SM, Borgia C. Acute myocardial infarction: sex-related differences in prognosis. Am Heart J 1984;108:63-66.

23. Greenland P, Reicher-Reiss H, Goldbourt U, Behar S. In-hospital and 1-year mortality in 1,524 women after myocardial infarction: comparison with 4,315 men. Circulation 1991;83:484-491.

24. Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction: results from the Myocardial Infarction Triage and Intervention Registry. Arch Intern Med 1992;152:972-976.

25. Maggioni AP, Maseri A, Fresco C, Franzosi MG, Mauri F, Santoro E, Tognoni G. Age-related increase in mortality among patients with first myocardial infarctions treated with thrombolysis. N Engl J Med 1993;329:1442-1448.

26. Patel H, Rosengren A, Ekman I. Symptoms in acute coronary syndromes: does sex make a difference? Am Heart J 2004;148:27-33.

27. Fornasini M, Yarzebski J, Chiriboga D, et al. Contemporary trends in evidence-based treatment for acute myocardial infarction. Am J Med 2010;123:166-172.

28. Nguyen HL, Goldberg RJ, Gore JM, et al. Age and sex differences, and changing trends, in the use of evidence-based therapies in acute coronary syndromes: perspectives from a multinational registry. Coron Artery Dis 2010;21:336-344.

29. McCormick D, Gurwitz JH, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Use of aspirin, beta-blockers, and lipid-lowering medications before recurrent acute myocardial infarction: missed opportunities for prevention? Arch Intern Med 1999;159:561-567.

30. Shaw L J, Lewis J F, Hlatky M A. et al Women's Ischemic Syndrome Evaluation: current status and future research directions, report of the National Heart Lung Blood Institute (NHLBI) workshop, section 5: gender-related risk factors for ischemic heart disease, October 2-4, 2002. Circulation 2004.