Gender Disparity in the Use of Drug-Eluting Stents During Percutaneous Coronary Intervention for Acute Myocardial Infarction

Adeyemi Iyanoye, MD, Abel E. Moreyra, MD, Joel N. Swerdel, MS, MPH, Sampada K. Gandhi, MD, PhD, Javier Cabrera, PhD, Nora M. Cosgrove, RN, and John B. Kostis, MD, for the MIDAS 23 Study Group

Objective: We examined gender disparity in the use of drug-eluting stents (DES) versus bare metal stents (BMS) during percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI), and gender disparity in all-cause mortality after coronary stent implantation for AMI. Background: Gender disparities in AMI managements have been well documented, but it is unclear whether these disparities are seen in the type of coronary stent implantation for AMI and outcomes. Methods: Hospital discharge data from January 1, 2003 through December 31, 2010 in New Jersey from the Myocardial Infarction Data Acquisition System were used to identify 40,215 patients (12,878 women and 27,337 men) with coronary stent implantation for AMI. The in-hospital, short term (30 days) and long term (1 and 5 year) all-cause mortality rates, unadjusted and adjusted for demographics and comorbidities, were determined. Results: Women were older than men and had a higher prevalence of co-morbidities. Men had higher prevalence of prior coronary revascularizations. After adjustment for co-morbidities, there was no significant gender difference in the use of DES versus BMS for AMI, except in 2003 and 2006 where women were found to be more likely to receive a DES versus a BMS. After adjustment, women had higher odds of in-hospital deaths but no difference in short and long-term all-cause mortality rates. Conclusions: There was no significant gender difference in the proportion of DES implantation versus BMS for AMI in contemporary years. Women treated with either BMS or DES for AMI had higher in-hospital death than men. © 2015 Wiley Periodicals, Inc.

Key words: gender; drug-eluting stents; acute myocardial infarction; mortality; sex; differences; management

INTRODUCTION

Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy for patients with ST-elevation myocardial infarction (STEMI) [1]. Early invasive strategy is also recommended for unstable patients with unstable angina and non-ST-elevation myocardial infarction (NSTEMI) [2]. Gender disparities in acute myocardial infarction (AMI) managements have been well documented. Women are less likely than men to have cardiac catheterization and PCI for AMI [3,4]. Women have been reported to have a higher morbidity and mortality after PCI; however, when the data are adjusted for comorbidities and age, this difference in mortality between genders vanishes [5,6].

There have been conflicting reports of higher mortality rate in patients with drug-eluting stents (DES) [7,8] and increased late stent thrombosis over bare metal stents (BMS) [7,9]. Moreover, there are reports of more adverse outcomes after the use of DES in women, [10,11] giving rise to the possibility of gender disparity in the usage of one type of stent over another.

*Correspondence to: Abel E. Moreyra, MD, The Cardiovascular Institute at Rutgers Robert Wood Johnson Medical School, 125 Paterson Street 5th Floor, New Brunswick, NJ 08901. E-mail: moreyrae@rwjms.rutgers.edu

Received 29 July 2014; Revision accepted 10 January 2015

DOI: 10.1002/ccd.25837
Published online 19 March 2015 in Wiley Online Library (wileyonlinelibrary.com)
The aim of this study was to evaluate, in a statewide AMI database, whether there were gender disparities in the use of DES versus BMS for AMI in contemporary PCI practice and gender differences in outcomes according to used type of stent.

METHODS

Data Sources

The study was conducted with information from the Myocardial Infarction Data Acquisition System (MIDAS), New Jersey (NJ) statewide database [3,12,13], utilizing patient discharge data from January 1, 2003 through December 31, 2010. The database contains hospital discharge information from all nonfederal acute care hospitals in NJ and includes all records with a primary diagnosis of AMI (International Classification of Diseases, 9th Revision [ICD-9] codes 410.0 to 410.9). Information from the database was previously validated using a random sample of the medical charts [3,13]. Out-of-hospital death information was obtained by matching the MIDAS records to the NJ death registration files, using a record linking and consolidation software (The Link King) [14]. The algorithm for the record linkage has been shown to have high sensitivity and positive predictive value [15].

Study Patients

During the study period, 40,215 patients were discharged after their first admission with a primary diagnosis of AMI and received stents within 30 days of the AMI. Patients who were admitted to federal hospitals or nursing homes (<3% of all patients) or who sustained the infarction during an admission for another diagnosis or procedure were excluded.

Study Variables

Men and women were classified according to the type of coronary stent implantation [BMS (36.06) vs. DES (36.07)] they received for AMI. The coronary stent implantations for AMI were stratified by placement periods: within 1 (at index), 2, and 30 days from AMI admission. The 2 days allowed the capture of the MIDAS records to the NJ death registration files, using a record linking and consolidation software (The Link King) [14]. The algorithm for the record linkage has been shown to have high sensitivity and positive predictive value [15].

Mortality rates were examined by stratification into in-hospital deaths, short term (within 30 days after discharge), and long term (within 1 and 5 year deaths). Covariates included, with ICD-9 codes, were infarction site and type [STEMI—categorized as non-subendocardial (410.0–410.6) and NSTEMI—categorized as subendocardial (410.7), diabetes mellitus (250), hypertension (401, 402, 403, 404, 405)], arrhythmia (427), conduction disorders (426), congestive heart failure (428), chronic obstructive pulmonary disease (490–496), chronic liver disease (571), chronic kidney disease/renal disease (580–586), anemia (280–286), stroke (430, 431, 433.01–433.91, 434.01–434.91, 435, 436, 437.6), other cerebrovascular disease besides stroke (430–438), and cancer (140–239).

Statistical Analysis

Multivariate logistic regression was used to explore differences between BMS and DES use by gender after adjusting for age, race, medical insurance, site of AMI, pre- or -post discharge stent implantation, comorbidities, and vascular complications. In addition, the adjusted odds ratios (OR) for the association among gender, type of stent used, and in-hospital and 30 day all-cause mortality were determined. Cox proportional-hazard models comparing the risk of death associated with BMS versus DES with respect to gender were used for 1 and 5-year all-cause mortality. Statistical analyses were performed using Statistical Analysis Systems (SAS), version 9.3 (SAS Institute Cary, North Carolina). The State of New Jersey Department of Health and Senior Services and the Rutgers Robert Wood Johnson Medical School institutional review boards approved this study.

RESULTS

Clinical Characteristics

The baseline clinical characteristics of the patients are listed in Table I. From the 40,215 patients identified with first AMI, 68% were men and 32% were women. Women were 7 years older than men on average. The predominant race was white in both genders. Commercial insurance was the most frequent insurance for men while government insurance (Medicare or Medicaid) was for women. Men had a higher frequency of STEMI, and women had a higher frequency of NSTEMI. Women were more likely than men to have a history of hypertension, diabetes, renal disease, heart failure, stroke, other cerebrovascular disease, arrhythmia, COPD, cancer, conduction disorders, anemia and to develop vascular complications. Men were more likely than women to have PCI and coronary artery bypass graft surgery (CABG) prior to their first AMI.

Coronary Stent Implantations

Coronary stent implantations for AMI over the 8-year period of the study are shown in Table II and Fig. 1. Stents placed at the index to within 30 days of AMI admission are reported: total patients with stents within...
1 day (at index) of AMI were 19,552, within 2 days 29,813, and within 30 days 40,215. There was more than a three-fold increase in the use of DES at the index AMI between 2003 and 2004 for both genders. The highest proportion of use of DES for both genders was in 2005, peaking at \( \frac{88-89}{C24} \) within 30 days of AMI admission. In general, the ratio of DES/BMS used was similar between the genders through the years. However, after adjusting for demographics, covariates, and comorbidities, there were significant differences in the implantation of DES between women and men in 2003 (within 2 and 30 days of index AMI admission) and in 2006 (within 30 days of index AMI admission), as shown in Table II and Fig. 1. The unadjusted differences were also significant in 2003 for increase use of DES in women within 2 days [OR: 1.20 CI (1.01, 1.43), \( P = 0.04 \)] and 30 days of AMI [OR: 1.16 CI (1.02, 1.32), \( P = 0.03 \)]. In contrast, in 2006, the unadjusted difference was not significant within 30 days of AMI [OR: 1.03 CI (0.87, 1.22), \( P = 0.72 \)].

At the index AMI, there was no difference between women and men in the use of DES for AMI in either adjusted or unadjusted analyses. Within 2 days of AMI, during years 2004–2010, there was no difference between the genders in use of DES for AMI in either adjusted or unadjusted analyses. In 2008, within 30 days of AMI, the unadjusted difference was significant [OR: 0.88 CI (0.78, 0.99), \( P = 0.04 \)] for decreased DES use in women, however, this difference was absent after adjustment [OR: 1.02 CI (0.89, 1.16), \( P = 0.83 \)]. Besides the differences in 2003, 2006, and 2008 as stated above, there were no differences in the implantation of DES for AMI between the genders in the rest of the years for either adjusted or unadjusted analyses.
Mortality

Table III shows that women had significantly higher unadjusted mortality rates than men after receipt of stents for AMI. After adjustment for covariates and comorbidities, the difference remained for in-hospital deaths only, except for non-STEMI DES patients where it did not reach statistical significance. The gender difference in hospital mortality persisted after adjustment for the type of stent (DES vs. BMS). The adjusted short and long term mortality rates were not different between the genders (Fig. 2). There was no evidence of effect measure modification between stents and gender (Table III).

DISCUSSION

In this study, we found that, after adjustment for baseline characteristics, there was no significant gender difference in the use of DES versus BMS in AMI during contemporary years. There was a small increase in the proportion of women receiving DES compared to men in 2003 and 2006. These differences appeared within 2 days of the index AMI admission and remained at the 30 day of the AMI admission. The differences between men and women in these 2 years may be due to random variation, but it is possible that they could be related to the recent introduction of DES in the US in 2003, and concerns about increased rate of late stent thrombosis with DES first reported in 2006 [7,9,16,17].

Our findings are in contrast with the report by D’Ascenzo et al. suggesting than women are less likely to receive DES, and the paper on left main PCI by Sheiban et al. indicating a lower rate of DES in women [18,19]. The single center study by Jibran et al., and the NCDR paper by Anderson and associates reporting on 426,996 coronary stent patients, found no marked gender differences in the proportion of DES during PCI [20,21]. Some of the differences among the studies may be explained by different sample sizes, duration and timing of the studies, and most importantly, adjustment for different covariates in their study. In spite of the reported disparities [3,4] in the use of cardiac catheterization and PCI for AMI in women, in our study we found no disparity in the receipt of DES during PCI for AMI in contemporary years.

Mortality

Women had higher in-hospital mortality after receipt of DES or BMS during PCI for AMI than men after adjustment for comorbidities. This may be due, as reported by others, to women receiving less use of antiplatelet medication and β-blockers, smaller coronary vessels, delay in treatment and other unknown confounders [20,22]. All-cause mortality rate differences between women and men were absent in the long term follow up. Published data show conflicting results in the role of gender and outcomes in PCI [10,18]. In studies of PCI for acute coronary syndrome (ACS) women receiving DES tend to have worse outcomes compared to men [10,11,23], while studies of PCI that included stable coronary artery disease have not shown mortality differences with either DES [24–26] or BMS [24]. This apparent lack of difference in mortality between men and women may have been related to a “dilution” of results from the inclusion of women with stable coronary disease who are at lower risk.

As observed in De Luca et al. [27], Wijnbergen et al. [28], and in our study, differences in unadjusted mortality rates were absent after adjustment in the short and long term follow up. Our finding of
increased adjusted in-hospital deaths in women over men is consistent with the findings of Anderson et al. using the National Cardiovascular Data Registry (NCDR) CathPCI [21]. Women were found to have increased in-hospital death after coronary stenting, however, had better long term survival than men. The

![Fig. 2. Five year survival curves, female versus males with BMS and DES.](image)

<table>
<thead>
<tr>
<th>Year</th>
<th>Total patients</th>
<th>Female</th>
<th>Male</th>
<th>Female</th>
<th>Male</th>
<th>Adj. OR Female vs. Male (95% CI)</th>
<th>Adj. P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>1,902</td>
<td>110</td>
<td>257</td>
<td>108</td>
<td>1,108</td>
<td>1.24 (0.94, 1.64)</td>
<td>0.13</td>
</tr>
<tr>
<td>2004</td>
<td>2,134</td>
<td>417</td>
<td>1,029</td>
<td>500</td>
<td>327</td>
<td>1.18 (0.94, 1.47)</td>
<td>0.16</td>
</tr>
<tr>
<td>2005</td>
<td>2,367</td>
<td>587</td>
<td>1,406</td>
<td>268</td>
<td>160</td>
<td>1.19 (0.91, 1.55)</td>
<td>0.2</td>
</tr>
<tr>
<td>2006</td>
<td>2,577</td>
<td>631</td>
<td>1,554</td>
<td>277</td>
<td>151</td>
<td>1.26 (0.97, 1.63)</td>
<td>0.09</td>
</tr>
<tr>
<td>2007</td>
<td>2,570</td>
<td>453</td>
<td>1,037</td>
<td>746</td>
<td>418</td>
<td>1.09 (0.91, 1.31)</td>
<td>0.37</td>
</tr>
<tr>
<td>2008</td>
<td>2,559</td>
<td>415</td>
<td>1,091</td>
<td>732</td>
<td>40.2</td>
<td>1.08 (0.89, 1.30)</td>
<td>0.44</td>
</tr>
<tr>
<td>2009</td>
<td>2,629</td>
<td>452</td>
<td>1,266</td>
<td>659</td>
<td>34.1</td>
<td>1.18 (0.97, 1.44)</td>
<td>0.11</td>
</tr>
<tr>
<td>2010</td>
<td>2,814</td>
<td>546</td>
<td>1,373</td>
<td>685</td>
<td>31.5</td>
<td>1.19 (0.98, 1.44)</td>
<td>0.08</td>
</tr>
<tr>
<td>Total</td>
<td>19,552</td>
<td>3,611</td>
<td>9,013</td>
<td>4,915</td>
<td>35.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significant P value <0.05, Adj.—adjusted, AMI—acute myocardial infarction, BMS—bare metal stent, CI—confidence interval, DES—drug-eluting stent, OR—odds ratios.

Fig. 2. Five year survival curves, female versus males with BMS and DES.
NCDR results included both non-AMI and AMI patients, therefore it has similar limitations as discussed above.

In our study, women were older and had higher frequency of comorbidities than men. In contrast, men had higher prevalence of prior PCI and CABG before their first AMI. Similar results were found in studies investigating the role of gender differences in outcomes of AMI using post hoc analysis of clinical trials [6,10,23] or registry data [5]. The differences in baseline characteristics between men and women become an important feature when evaluating the benefits of medical therapies or interventions with respect to gender.

Limitations and Strengths

Our study has inherent limitations of a retrospective, non-randomized, and administrative database. The study does not include some important data such as coronary artery size or body surface area (BSA), complexity of coronary artery lesions, type of anticoagulation, details on access site complications, adherence to dual antiplatelet therapy and duration of treatment, and time to reperfusion (door-to-balloon time). Women have been reported to have smaller caliber coronary artery size than men [29]. This potentially predisposes women to higher restenosis after PCI and adverse outcomes. Despite extensive statistical modeling to adjust for confounders on the clinical outcomes may not be completely controlled in our study.

On the other hand, our study has several strengths. Unlike previous reports, this study includes all patients with AMI that received stents in NJ over 8 years, allowing for analysis of secular trends. The database is random chart-validated [3,13] statewide, and provides “real world” information. In addition, we report on long-term mortality comparing men to women who received DES or BMS after AMI. More importantly, this is the largest study, to our knowledge, pertaining to this subject.

CONCLUSION

Despite long history of gender disparity, with women receiving less catheterization and PCI than men after AMI, we did not find a difference between men and women in the use of DES for AMI in contemporary PCI practice. Our study confirms the importance of baseline characteristics associated with increased mortality rate in women over men presenting with their first AMI. Even after adjustment for comorbidities, women have higher in-hospital deaths than men but no difference in short and long term mortality rates after receipt of stents during PCI for AMI.
REFERENCES


8. FDA website Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf2/P020026a.pdf.


Gender and Stents in AMI 227

Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

