Gender Differences in Hospital Mortality and Use of Percutaneous Coronary Intervention in Acute Myocardial Infarction

Microsimulation Analysis of the 1999 Nationwide French Hospitals Database

Carine Milcent, PhD*; Brigitte Dormont, PhD*; Isabelle Durand-Zaleski, MD; Philippe Gabriel Steg, MD

Background—Women with acute myocardial infarction have a higher hospital mortality rate than men. This difference has been ascribed to their older age, more frequent comorbidities, and less frequent use of revascularization. The aim of this study is to assess these factors in relation to excess mortality in women.

Methods and Results—All hospital admissions in France with a discharge diagnosis of acute myocardial infarction were extracted from the national payment database. Logistic regression on mortality was performed for age, comorbidities, and coronary interventions. Nonparametric microsimulation models estimated the percutaneous coronary intervention and mortality rates that women would experience if they were “treated like men.” Data were analyzed from 74,389 patients hospitalized with acute myocardial infarction, 30.0% of whom were women. Women were older (75 versus 63 years of age; \( P < 0.001 \)) and had a higher rate of hospital mortality (14.8% versus 6.1%; \( P < 0.0001 \)) than men. Percutaneous coronary interventions were more frequent in men (7.4% versus 4.8%; 24.4% versus 14.2% with stent; \( P < 0.001 \)). Mortality adjusted for age and comorbidities was higher in women \( (P < 0.001) \), with an excess adjusted absolute mortality of 1.95%. Simulation models related 0.46% of this excess to reduced use of procedures. Survival benefit related to percutaneous coronary intervention was lower among women.

Conclusions—The difference in mortality rate between men and women with acute myocardial infarction is due largely to the different age structure of these populations. However, age-adjusted hospital mortality was higher for women and was associated with a lower rate of percutaneous coronary intervention. Simulations suggest that women would derive benefit from more frequent use of percutaneous coronary intervention, although these procedures appear less protective in women than in men. (Circulation. 2007;115:833-839.)

Key Words: angioplasty ■ epidemiology ■ mortality ■ myocardial infarction ■ revascularization ■ sex ■ women

Previous studies have shown higher crude hospital mortality rates for acute myocardial infarction in women than in men. Part of the difference is accounted for by the older age of and higher prevalence of comorbidities in women.1 Less frequent use of revascularization procedures in women also may account for some of the excess mortality. Indeed, findings from large database studies2–11 have indicated that women with acute myocardial infarction tend to undergo less aggressive hospital management than men. However, the relation of lower rates of revascularization is debated: Some studies have found that the excess mortality in women was explained by older age and higher baseline risk12–17 or that it was restricted to a subgroup of female patients, whereas others have suggested that undertreatment in women had no effect on early mortality from acute myocardial infarction.18,19

Thus, although it is agreed that the age-adjusted mortality rate after acute myocardial infarction is higher in women than in men, uncertainty remains about whether this finding is related to differences in baseline risk or in management (particularly the use of revascularization) and whether the latter is related to gender bias (the Yentl syndrome20) or to differences in eligibility for aggressive therapies or patient preferences.21

The aims of the present study were to compare age-adjusted, gender-specific hospital mortality rates for patients hospitalized for acute myocardial infarction and to determine whether mortality variations could be explained by gender

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The online-only Data Supplement, consisting of expanded Methods, is available with this article at http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.106.664979/DC1.

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### TABLE 1. Distribution of Hospital Admissions for Acute Myocardial Infarction by Age and Gender and Comorbidities of Patients With Acute Myocardial Infarction

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>All Men</th>
<th>All Women</th>
<th>Male Gender Difference</th>
<th>OR (95% CI)</th>
<th>Male Gender Difference</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of coronary artery disease</td>
<td>24.2</td>
<td>24.8</td>
<td>0.98 (0.95–1.01)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valvular disease</td>
<td>7.5</td>
<td>6.4</td>
<td>1.16 (1.04–1.29)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conduction disease</td>
<td>19.4</td>
<td>17.6</td>
<td>1.08 (0.97–1.20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>27.7</td>
<td>24.5</td>
<td>1.13 (1.03–1.24)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>14.3</td>
<td>11.3</td>
<td>1.26 (1.13–1.41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>3.0</td>
<td>2.7</td>
<td>1.11 (0.93–1.33)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>6.4</td>
<td>6.8</td>
<td>0.95 (0.83–1.09)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other vascular disease</td>
<td>0.7</td>
<td>0.5</td>
<td>1.43 (0.95–2.14)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>14.6</td>
<td>13.1</td>
<td>1.12 (1.01–1.25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>3.9</td>
<td>3.7</td>
<td>1.04 (0.89–1.22)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P<0.001 for all comparisons between men and women.

1differences in epidemiology, in patterns of use of percutaneous coronary intervention (PCI), or in the benefit of PCI.

### Methods

#### Patients

All hospital admissions in France during 1999 with an International Classification of Diseases, ninth revision (ICD-9), discharge diagnosis of acute myocardial infarction were extracted from a national database. This database, used for hospital payment, provides medical records for all patients discharged from both private and public hospitals. The database contains all discharges nationwide, and French hospitals are financed by a single payer. Each admission is characterized by discharge diagnoses and procedure codes that determine the diagnosis-related group and reimbursement. In France, a patient classification system was implemented in 1983 because French hospitals are financed by a single payer. Each admission is characterized by discharge diagnoses and procedure codes that determine the diagnosis-related group and reimbursement. In France, a patient classification system was implemented in 1983 that is based on the all-patient diagnosis-related group model that was developed in the United States.

#### Statistical Methods

Categorical data are presented as percentages with absolute numbers. Logistic regressions were performed to test for gender differences in mortality and use of coronary interventions in each age group. Odds ratios are reported, and Wald tests and 95% confidence intervals (CIs) are provided to check for the significance of differences between proportions. Multivariable logistic regressions were performed to adjust for differences in age, comorbidities, and intervention rates.

A series of microsimulation models were developed in the spirit of the Oaxaca decomposition, creating a hypothetical set of events (procedures and outcomes) for the population. The first simulation predicted the probability of PCI and death, depending on gender, comorbidities, and use of PCI, and the death rate of women if they were “treated like men.” This simulation assessed gender differences resulting from variation in treatment while controlling for gender differences in age and comorbidities (see the Appendix in the online Data Supplement). We hypothesized that the only difference between men and women was the decision to use invasive procedures, and we computed the probability of death of women if they were treated like men of the same age with similar comorbidities. Each woman was attributed the age- and comorbidity-specific probability of PCI plus stent obtained from the male population. We then computed whether this “men-like” procedure rate resulted in reduced mortality in women. The second simulation tested the hypothesis that the outcome of PCI would differ according to gender, resulting in a higher death rate. The model was built for PCI plus stent. All tests were 2 sided, and values of P<0.05 were considered statistically significant. All analyses were performed with the StataSE 8 software and SAS statistical package (SAS version 8.2, SAS Inc, Cary, NC).

### TABLE 2. Use of Coronary Intervention According to Age Group

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>Men</th>
<th>Women</th>
<th>Men</th>
<th>Women</th>
<th>Observed Gender Difference</th>
<th>PCI+Stent, Women Relative to Men, OR (95% CI)</th>
<th>PCI/Coronary Angioplasty, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤55</td>
<td>24.6</td>
<td>28.4</td>
<td>9.1</td>
<td>8.3</td>
<td>6.1</td>
<td>0.74 (0.66–0.82)</td>
<td>62.1</td>
</tr>
<tr>
<td>56–65</td>
<td>24.9</td>
<td>26.6</td>
<td>7.9</td>
<td>6.7</td>
<td>28.1</td>
<td>23.4</td>
<td>59.1</td>
</tr>
<tr>
<td>66–75</td>
<td>24.9</td>
<td>24.3</td>
<td>7.3</td>
<td>6.6</td>
<td>22.1</td>
<td>19.9</td>
<td>51.4</td>
</tr>
<tr>
<td>76–85</td>
<td>16.7</td>
<td>12.2</td>
<td>5.0</td>
<td>4.2</td>
<td>15.1</td>
<td>11.2</td>
<td>54.6</td>
</tr>
<tr>
<td>&gt;85</td>
<td>4.3</td>
<td>1.9</td>
<td>1.6</td>
<td>1.0</td>
<td>5.0</td>
<td>2.5</td>
<td>60.6</td>
</tr>
<tr>
<td>Overall</td>
<td>22.6</td>
<td>16.2</td>
<td>7.4</td>
<td>4.8</td>
<td>24.4</td>
<td>14.2</td>
<td>58.5</td>
</tr>
</tbody>
</table>

P<0.001 for all comparisons.
The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

### Results

The database included 74,389 admissions for acute myocardial infarction, of which women represented 30.0%. The mean age of women was 75 years, compared with 63 years for men \( (P < 0.001) \). The age structure of the population by gender is illustrated in Table 1. Given the older age of women, comorbidities were more frequent in women than in men \( (P < 0.001) \) (Table 1).

### Use of Interventional Procedures

During the index admission, men were more likely to undergo coronary angiography and intervention than were women; this observation was consistent across all age groups \( (P < 0.001) \) (Table 2). Overall, the ratio of interventions to total coronary angiography was higher in men than in women, although this difference was heterogeneous with respect to age; in patients <75 years of age, angiography more frequently led to PCI in men than in women, whereas the converse was true in patients >75 years of age (Table 2).

### Hospital Mortality

The crude hospital mortality rate was higher for women than for men \( (14.8\% \text{ versus } 6.1\%; \ P < 0.0001) \). The odds ratio for crude mortality rates was 2.65 (95% CI, 2.52 to 2.79). This 8.64% difference was due mainly to gender differences in the age distribution. After adjustment for age (using the age distribution of women as reference), the absolute gender difference in mortality was 1.95%. Across age categories, crude mortality and mortality adjusted for comorbidities were consistently higher among women (Table 3).

The use of coronary interventions was associated with a lower mortality rate after adjustment for age and comorbidities \( (P < 0.01) \) (Figure 1). After adjustment for comorbidities and the use of interventions, the mortality rate remained consistently and significantly higher for women than for men in each age category except patients >85 years of age \( (P = 0.08) \) (Figure 2). The type of hospital to which patients were admitted and the volume of acute myocardial infarctions treated per hospital had no impact on gender differences in mortality (data not shown).

### Simulations

The 1.95% age-adjusted gender difference in mortality rate was explored further by simulations to determine its relation to gender differences in the use of coronary interventions, outcome of procedures, and impact of comorbidities.

### Simulated Rates of PCI Plus Stent

In the first simulation, an expected rate of PCI plus stenting for women was computed by using the probability of men with the same age and comorbidities (Table 5). The expected simulated rate of PCI plus stenting in women was 17.5% compared with observed rates of 14.2% in women and 24.4% in men. Therefore, approximately one third of the observed difference in the use of PCI plus stenting appeared to be related to gender disparity, and two thirds appeared to be related to age and comorbidities.

### Simulated Rates of Mortality

The relationship of reduced provision of PCI to the 1.95% gender gap in mortality \( (14.78\% \text{ in women versus } 12.83\% \text{ in men}) \) was explored further by simulations to determine its relation to gender differences in the use of coronary interventions, outcome of procedures, and impact of comorbidities.
age adjusted in men; Table 5) was explored in the second simulation, which computed “expected” mortality rates in women with 2 models (Table 4). Model 1 computed the expected probability of death of women if they had experienced the hospital rates of PCI plus stent of men of a similar age. Overall, this expected mortality rate would be 14.32%, thus accounting for 0.46% (relative percentage, 23.6%) of the age-adjusted 1.95% gender gap. Model 2 allowed for possible gender differences in the impact of comorbidities and PCI plus stent on mortality rate by computing the expected probability of death of women if they had similar rates of coronary interventions but also a similar response to PCI and comorbidities to that of men. The expected mortality rate in women calculated by this method would be 12.55% instead of 14.78%, accounting for 1.77% (relative percentage, 90.8%) of the 1.95% gender gap.

Thus, of the 8.64-point crude excess mortality in women with acute myocardial infarction, 6.69 is explained by the age structure of the population, 0.46 by the difference in procedure rates, and 1.77 by gender differences in the outcome of procedures and the impact of comorbidities (Table 5). The residual (−0.28) is related to differences in other characteristics (including unobservable characteristics). Thus, one quarter of the gender gap appears to be related to differential use of PCI plus stent between men and women.

The potential impact of increasing intervention rates in women (by following the same decision rules as for men) is illustrated in Figure 3, which displays the distributions of the observed age-adjusted mortality and the expected mortality in women. Age-adjusted mortality rate would be reduced (shifted to the left) across the entire risk distribution if rates of interventions were the same in women and men.

Discussion

The present analysis confirms the higher age-adjusted mortality rate from acute myocardial infarction in women relative to men, the so-called “gender gap” reported in previous studies.1–19 This gender gap was associated with strong gender differences in the provision of PCI during the index admission. We explored the possibility of gender disparities in the provision of health care for acute myocardial infarction patients but could not ascertain from the database whether such differences in revascularization could be explained by variation in eligibility, exclusion criteria, or patient preferences. The results of our study show that, after adjustment for age and comorbid conditions, there was a persistent mortality difference between men and women. Simulations of the expected mortality in women, if they had been referred for PCI as frequently as men with similar characteristics, suggest that gender disparities in the provision of PCI as frequently as men with similar characteristics, suggest that gender disparities in the provision of reperfusion accounted for approximately one quarter of the modifiable excess mortality. We explored the possibility that this gender difference could result from a predominance of treatments for acute myocardial infarction provided to women in potentially “lower-quality” institutions (eg, community hospitals or low-volume facilities) and found no difference between men and

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**TABLE 4. Use of Coronary Intervention and Simulated Rates of PCI Plus Stenting and Simulated Mortality Rates in Women**

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>PCI+Stent, %</th>
<th>Expected PCI + Stenting Rate, Women, %</th>
<th>Expected vs Observed Difference in Women, %</th>
<th>Simulation 1: Expected Mortality in Women (Procedure Rates of Men), %</th>
<th>Simulation 2: Expected Mortality in Women (Procedure Rates, Response to Procedures, and Comorbidities of Men), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤55</td>
<td>31.3</td>
<td>31.6</td>
<td>6.4</td>
<td>1.8</td>
<td>1.4</td>
</tr>
<tr>
<td>56–65</td>
<td>28.1</td>
<td>27.7</td>
<td>4.3</td>
<td>3.5</td>
<td>2.8</td>
</tr>
<tr>
<td>66–75</td>
<td>22.1</td>
<td>22.1</td>
<td>2.2</td>
<td>7.5</td>
<td>5.7</td>
</tr>
<tr>
<td>76–85</td>
<td>15.0</td>
<td>15.0</td>
<td>3.8</td>
<td>17.1</td>
<td>14.1</td>
</tr>
<tr>
<td>&gt;85</td>
<td>5.0</td>
<td>4.5</td>
<td>2.0</td>
<td>29.5</td>
<td>28.0</td>
</tr>
<tr>
<td>Overall</td>
<td>24.4</td>
<td>17.5</td>
<td>3.4</td>
<td>14.3</td>
<td>12.6</td>
</tr>
</tbody>
</table>

*P<0.001 for all comparisons.*
women (data not shown). The French healthcare system provides identical coverage and access to health care for men and women regardless of employment or social status. We therefore conclude that our results strongly support the hypothesis of gender disparity.

This finding provides a rationale for implementing measures to ensure optimal provision of coronary interventions in women experiencing myocardial infarction. In addition, the simulations indicate that more liberal use of PCIs in women would likely result in consistent benefit across all risk strata. An additional finding from the simulations was that the use of PCI in women may be associated with a reduced benefit compared with that in men, possibly because of anatomic or biological differences.

Underuse of invasive procedures in women with acute myocardial infarction has been reported previously, although the independent relationship between gender and worse outcomes is still debated. There is recent evidence from the United States that, despite widespread debate about the gender gap, sex differences in the provision of therapies in acute myocardial infarction have remained unchanged. However, in that analysis, gender differences in the provision of therapeutic interventions and in outcomes were less marked than in the present study and were largely influenced by the appropriateness of procedures.

The issue of less aggressive treatment resulting in a higher mortality rate in women was raised as early as 1991 by Healy. The present simulations indicate that, even if women were treated just like men, some excess mortality would remain. The explanation for the reduced protective effect against death afforded by PCI in women is unclear. It may be related to generally poorer outcomes of PCI in women (less benefit and higher complication rates), possibly because of smaller target-vessel size, increased vessel tortuosity, and other biological differences. Indeed, previous analyses have found that women had an excess risk of death or myocardial infarction in the early post-PCI period as compared with men, particularly when interventions are attempted in an unstable setting (although these differences pertained mostly to women undergoing coronary artery bypass grafting), but that these differences appear to abate over time.

The impact of lower revascularization rates in women on mortality rate strengthens the case for better dissemination and implementation of guidelines for acute myocardial infarction treatment in women.

**Study Limitations**

This analysis is subject to several limitations. The database included all forms of acute myocardial infarction, regardless of delay to presentation, presence of ST-segment elevation, and eligibility for reperfusion therapy, because myocardial infarction was defined by ICD-9 coding. No data were collected on ethnicity because French law explicitly prohibits the collection of such variables and detailed information on medication use, including the use of fibrinolysis. In addition, our analysis pertains to all indications for PCI during the index admission but does not allow us to explore which procedures were done as primary PCI rather than elective PCI or to assess the appropriateness of the indications, a factor that has been linked to gender differences in use of procedures. In that respect, it is important to acknowledge that no information is available in our dataset on the angiographic features in men and women. Nevertheless, there may be important gender differences in vessel size, tortuosity, and general eligibility for PCI that may translate into differences in the use of PCI (such as women having smaller diseased

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**TABLE 5. Decomposition of Gender Differences in Average Death Rates**

<table>
<thead>
<tr>
<th>Description</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average death rate for men</td>
<td>6.1%</td>
</tr>
<tr>
<td>Average death rate for men adjusted for age distribution*</td>
<td>12.83%</td>
</tr>
<tr>
<td>Average death rate for women</td>
<td>14.78%</td>
</tr>
<tr>
<td>Average death rate for women adjusted for differences in procedure rates</td>
<td>14.32%</td>
</tr>
<tr>
<td>Difference (women vs men)</td>
<td>8.64%</td>
</tr>
<tr>
<td>Difference resulting from variations in age distribution</td>
<td>6.69%</td>
</tr>
<tr>
<td>Age-adjusted difference</td>
<td>1.95% (1.17–2.73)†</td>
</tr>
<tr>
<td>Of which</td>
<td></td>
</tr>
<tr>
<td>Difference resulting from gender variation in procedure rates</td>
<td>0.46% (0.13–0.76)†</td>
</tr>
<tr>
<td>Difference resulting from gender variation in reactions to secondary diagnoses and procedures</td>
<td>1.77% (1.01–2.53)†</td>
</tr>
<tr>
<td>Residual: difference resulting from gender variation in other characteristics (eg, secondary diagnoses and unobservable characteristics)</td>
<td>−0.28%</td>
</tr>
</tbody>
</table>

*Women’s age distribution was the reference.
†95% CI on differences was obtained by 50 bootstrap replications.

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Figure 3. Probability density of age-adjusted mortality and simulated mortality (based on simulation 2) using revascularization decision rules used for men.
vessels, which could account for the lower ratio of PCI to angiography in women than in men (54% versus 58%).

This analysis pertains to a dataset that is 7 years old, and some changes in practice have taken place over this period that are related mainly to more frequent use of primary PCI. However, it is uncertain whether these changes have been unbalanced across gender. This analysis relied on a discharge database to document comorbidities; therefore, only a limited amount of information was available, and potential confounder variables may have been missed. Although the prospective payment system creates an incentive to record exhaustively secondary diagnoses and procedures, its use to finance French hospitals has so far been limited, resulting in potential underreporting. Because comorbid conditions affect women more frequently than men (particularly with regard to peripheral arterial disease, which tends to be underdiagnosed in women), underreporting of comorbidities may result in an artificial underestimation of the gender gap. The simulations used to estimate expected rates of reperfusion or hospital mortality in women if they were treated like men are subject to caution because medical organizational factors such as delayed diagnosis are not accounted for. Finally, outcomes were assessed at discharge, and previous analyses31 have suggested that gender differences in early outcomes may become attenuated over a longer follow-up. Overall, this type of simulation may simplify a series of complex variables involved in patient care; thus, the estimates of the effect of each therapy may be imprecise.

The strength of our findings lies in the size of the population and the use of microsimulation analyses. The latter have been introduced in econometric models that compare salaries in men and women and were recently extended to other economic fields such as health-econometric studies. To the best of our knowledge, they have not been used yet in the analysis of healthcare delivery.

Acknowledgments

The database was provided by PMSI, the Ministry for Health and Solidarity, DHOS-DREES, France. The authors are indebted to the Direction de la Recherche des Études, des Études, de l’Evaluation et des Statistiques (DREES) for providing access to the database. Dr Sophie Rushon-Smith, who was funded by Association Naturalia et Biologia, provided editorial assistance in the preparation of this manuscript.

Disclosures

Dr Durand-Zaleski has been a consultant and a speaker for Sanofi-Aventis, Merck Sharp & Dohme, Medtronic, Novo Nordisk, Smith & Nephew, and Boston Scientific. Dr Steg has been a consultant or speaker for Janssen-Cilag, Sanofi-Aventis, Biologia, medac, Biotechne, and ZLB-Behring. The other authors report no conflicts.

References

CLINICAL PERSPECTIVE

Age-adjusted mortality after acute myocardial infarction is higher in women than in men, but it is uncertain whether this discrepancy is related to differences in baseline risk or in management (particularly the use of revascularization) and whether the latter is related to gender bias, differences in eligibility for aggressive therapies, or patient preferences. The present study used the national payment database to analyze all hospital admissions in France in 1999. Data were analyzed from 74,389 patients with a discharge diagnosis of acute myocardial infarction, 30.0% of whom were women. Women were older and had a higher rate of hospital mortality (14.8% vs 6.1%; \( P < 0.0001 \)) but underwent fewer procedures than men. Mortality rate adjusted for age and comorbidities was higher in women \( (P < 0.001) \), with an excess adjusted absolute mortality of 1.95%. Nonparametric microsimulation models estimated the percutaneous coronary intervention and mortality rates that women would experience if they were “treated like men.” Simulations related 0.46% absolute mortality (ie, a quarter of the excess age-adjusted mortality) to reduced use of procedures in women. In addition, the survival benefit related to percutaneous coronary intervention was lower among women. Thus, the age-adjusted hospital mortality rate was higher for women and was associated with a lower rate of percutaneous coronary intervention. Simulations suggest that women would derive benefit from more frequent use of percutaneous coronary intervention, although these procedures appear less protective in women than in men. The impact of undertreatment on women’s mortality rate strengthens the case for better dissemination and implementation of guidelines for treatment of acute myocardial infarction in women.
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