Comparison of Hospital Versus Out of Hospital Coronary Death Rates in Women and Men

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Young women hospitalized with acute myocardial infarction (MI) have greater in-hospital mortality than young men. However, the reasons for this difference have not been well characterized. We analyzed the data from 423,067 patients (247,701 men and 175,366 women) who were discharged with the diagnosis of MI from nonfederal hospitals in New Jersey and 355,569 coronary heart disease (CHD) deaths in New Jersey from 1990 to 2004 in 4 age strata: 35 to 54, 55 to 64, 65 to 74 and ≥75 years. Of the patients hospitalized for MI, young (35 to 54 years) women had greater in-hospital mortality than young men (5.2% vs 2.5%, adjusted odds ratio 1.64, 95% confidence interval 1.48 to 1.81, p <0.0001). However, in a community-wide analysis, when the total out-of-hospital CHD deaths in New Jersey were examined, young women had a lower out-of-hospital death rate than young men (11 vs 55/100,000). Statewide, young women were 4 times less likely to be hospitalized for MI (78 vs 297/100,000, relative risk 0.26), but they were only 1/2 as likely to die from MI in the hospital (7 vs 17/100,000, relative risk 0.41). Thus, women had a greater odds ratio for in-hospital mortality but a lower odds ratio for out-of-hospital CHD death than men. In conclusion, the greater in-hospital mortality of young women hospitalized for MI compared to young men could be explained in part by the finding that young men were more likely to have out-of-hospital CHD death. **© 2010 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2010;106:26–30)**

Coronary heart disease (CHD) is a common cause of death of both women and men in the United States.[1,2] Although women, on average, develop their first acute myocardial infarction (MI) about 10 years later than men[2] and, overall, are less likely to develop MI than are men, several studies have shown that young women have greater in-hospital mortality than young men.[3,4] The reasons for this difference are not well known. Women are more likely to have atypical symptoms, are more likely to wait longer than men before going to the hospital, and are less likely to be diagnosed with MI on admission.[5] In addition, altered pain perceptions in women might result in improper management and a missed diagnosis.[6] It has been speculated that the worse outcome of MI in young women could be explained, in part, by the death of more men than women before hospitalization[6] and that the rate of death of young women during hospitalization is balanced by a greater rate of death before hospitalization among men.[7,8] The present study examined, in a statewide database, whether the greater mortality of young women hospitalized for MI could be explained by more young men dying from CHD outside the hospital.

Methods

The present study was conducted using a statewide MI hospitalization database and CHD deaths in New Jersey from 1990 to 2004.

Hospitalization data were obtained from the Myocardial Infarction Data Acquisition System (MIDAS). MIDAS contains hospital discharge abstracts submitted by nonfederal acute care hospitals in New Jersey (n = 91) and includes all records with a primary diagnosis of MI (*International Classification of Diseases, Ninth Revision* [ICD-9] codes 410.0 to 410.9). From 1990 to 2004, 423,067 patients (247,701 men and 175,366 women) were discharged with a primary diagnosis of MI. For these patients, information was obtained on the following variables: age, gender, race, comorbidity (i.e., hypertension, renal disease, diabetes, chronic obstructive pulmonary disease, liver disease, anemia, cerebrovascular disease, and cancer), and complications (i.e., left ventricular dysfunction and arrhythmia), as described in a previous publication.[9] MIDAS also includes all hospitalization records with any invasive cardiac procedure, including cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass grafting. Patients who were <35 years old were excluded from the present study. The information from the database, including the diagnosis of MI, was validated using a random sample of the medical charts.[10]

The vital status of the hospitalized patients with MI was determined by linkage of the MIDAS records with the New Jersey death registration, using the AutoMatch-Generalized Record Linkage System, version 3.0.[11] The method of de-

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Table 1
Clinical characteristics of patients with acute myocardial infarction (MI) by age and gender in New Jersey

Variable	Age Group (years)			
	35–54		≥55	
	Women (n = 14,510)	Men (n = 52,909)	Women (n = 160,856)	Men (n = 194,792)
Race				
White	70.3%	78.2%	83.8%	84.9%
Black	18.9%	8.7%	8.2%	6.1%
Other	10.8%	13.1%	8.0%	9.0%
Co-morbidity				
Diabetes mellitus	30.1%	18.2%	31.5%	27.5%
Hypertension	44.3%	38.9%	51.6%	45.2%
Renal disease	4.9%	2.8%	8.9%	9.2%
Anemia	11.7%	5.4%	17.3%	12.4%
Cancer	1.4%	0.6%	3.5%	5.0%
Cerebrovascular disease	3%	1.5%	7.8%	6.2%
Complications				
Arrhythmia	13.4%	15.6%	16.7%	19.9%
Left ventricular dysfunction	13.1%	8.6%	27%	20.2%
Arrhythmia and left ventricular dysfunction	5.6%	4.6%	20.2%	17.9%
Procedure				
Cardiac catheterization	45.2%	49.3%	26.1%	34.8%
Percutaneous coronary intervention	22.8%	29.3%	11.3%	15.7%
Coronary artery bypass grafting	5.9%	8.0%	5.7%	9.3%
Site of myocardial infarction				
Anterior, interior, lateral	52.2%	62.9%	38.9%	43.8%
Subendocardial	38.2%	30.2%	48.2%	44.8%
Other	9.7%	6.9%	12.9%	11.4%

Differences between women and men were statistically significant ($p < 0.001$) for all variables in both age strata.

Table 2
Case fatality and multivariate-adjusted odds ratios (ORs) of dying during acute myocardial infarction (MI) hospitalization and within 28 days stratified by gender

Age Group (yrs)	Women		Men		Women Versus Men	
	Admissions (n)	Deaths (n)	Admissions (n)	Deaths	Adjusted OR*	95% CI
In-hospital						
35–54	14,510	758 (5.2%)	52,909	1,313 (2.5%)	1.64	1.48–1.81
55–64	23,427	1,871 (8%)	54,230	2,737 (5%)	1.59	1.49–1.70
65–74	44,120	5,469 (12.4%)	65,302	6,750 (10.3%)	1.35	1.29–1.41
≥75	93,309	19,358 (20.7%)	75,260	15,329 (20.4%)	1.06	1.04–1.09
28 Days						
35–54	14,510	764 (5.3%)	52,909	1,526 (2.9%)	1.39	1.26–1.54
55–64	23,427	1,932 (8.2%)	54,230	3,010 (5.6%)	1.44	1.35–1.53
65–74	44,120	5,622 (12.7%)	65,302	7,186 (11%)	1.25	1.21–1.31
≥75	93,309	20,939 (22.4%)	75,260	16,571 (22%)	1.02	1.00–1.05

Logistic regression analysis adjusted for age, gender, race, diabetes, hypertension, renal disease, anemia, cancer, cerebrovascular disease, complication, year of admission, and infarction site.
CI = confidence interval.

termining the sensitivity and specificity of this probabilistic record linkage procedure has been described in a previous report and was found to be 98% and 99%, respectively.[12] The in-hospital and 28-day case-fatality after hospitalization for MI were computed separately for men and women.

Multivariate logistic regression analysis was used to estimate the odds ratios (ORs) for the association between gender and mortality in 4 age strata: 35 to 54, 55 to 64, 65 to 74, and ≥75 years. The association between gender and mortality was stratified by age and was adjusted within each age group for age, gender, race, diabetes, hypertension, renal disease, anemia, cancer, cerebrovascular disease, complications, year of admission, and site of MI, as coded at discharge (anterio**r,** ICD-9 code 410.0, 410.1; inferior, 410.2, 410.3, 410.4, 410.6; lateral, 410.5; subendocardial, 410.7; and other, 410.8, 410.9).

Table 3
Population rates (per 100,000) and relative risk of acute myocardial infarction (MI) hospitalization, in-hospital death, and out-of-hospital coronary heart disease (CHD) death in women and men in New Jersey, stratified by age

Age (yrs)	Acute MI Hospitalization			In-Hospital Deaths			Out-of-hospital CHD deaths		
	Women	Men	Relative Risk	Women	Men	Relative Risk	Women	Men	Relative Risk
35–54	78	297	0.26	7	17	0.41	11	55	0.20
55–64	402	1,029	0.39	67	144	0.47	81	276	0.29
65–74	891	1,686	0.53	259	495	0.52	260	621	0.42
≥75	1,910	2,793	0.68	1,211	1,648	0.73	1,741	1,896	0.92

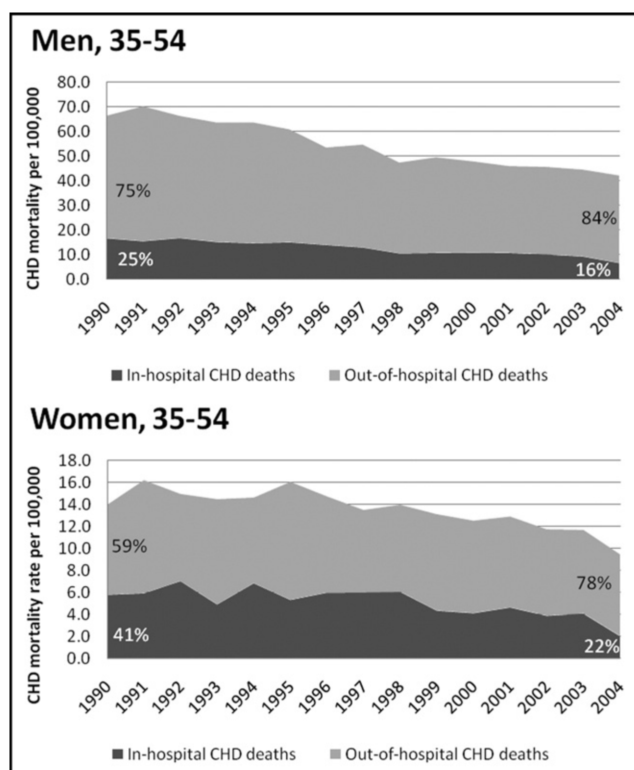

Figure 1. Decreases in CHD mortality (per 100,000) partitioned to out-of-hospital *(light gray)* and in-hospital *(dark gray)* CHD deaths among men and women 35 to 54 years old in New Jersey from 1990 to 2004.

We used ICD-9 codes 410 to 414 and 429 and ICD-10 codes I20 to I25 to identify 355,569 CHD deaths, 173,671 in men and 181,898 in women, in New Jersey, from 1990 to 2004. We categorized a death as an out-of-hospital death using the variable location of death in the death registry. Trends in gender- and age-specific population CHD mortality were estimated. The age-specific population estimates by calendar year for men and women were obtained from the New Jersey Department of Health and Senior Services Vital Statistics.

Statistical analysis was performed using Statistical Analysis Systems, version 9.0 (SAS Institute, Cary, North Carolina). The State of New Jersey Department of Health and Senior Services and the Robert Wood Johnson Medical School institutional review boards approved the present study.

Results

In the 35 to 54-year age group, 21% of the patients hospitalized for MI were women compared to 45% of the patients in the ≥55-year age group. Young (age 35 to 54 years) women were more likely to have co-morbid conditions than were young men, including diabetes mellitus, hypertension, renal disease, anemia, and cerebrovascular disease during hospitalization (Table 1). Also, young women were more likely to have left ventricular dysfunction, and young men were more likely to have arrhythmias associated with MI. The MI of young men was more likely to be coded at discharge as anterior, inferior or lateral. In young women, it was more likely to be coded as subendocardial. Young women were less likely to undergo invasive cardiovascular procedures, including cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass grafting than young men.

Table 2 lists the in-hospital and 28-day case-fatality of the men and women hospitalized for MI. In-hospital case-fatality increased with age in both genders, and women had greater in-hospital case-fatality than men in all age groups. The OR for in-hospital mortality for women versus men attenuated with age (Table 2). The OR (women vs men) for in-hospital mortality, adjusted for age, co-morbidities, complications, year of diagnosis, and MI type, was 1.64 (95% confidence interval 1.48 to 1.81) in the young age group and decreased to 1.06 (95% confidence interval 1.04 to 1.09) for the oldest (≥75 years) age group. The adjusted OR (women vs men) for mortality at 28 days was 1.39 (95% confidence interval 1.26 to 1.54) for women aged 35 to 54 years compared to men in the same age group, decreased with increasing age, and was of borderline significance in the oldest age group (Table 2).

Considering the total population of New Jersey, rather than only those hospitalized for MI, women had lower population out-of-hospital CHD death rates (Table 3). Similar effects were observed when MI hospitalizations and in-hospital deaths were examined in a community-wide analysis when the total out-of-hospital CHD deaths in New Jersey were examined. Young women had a lower out-of-hospital death rate than young men (11 vs 55/100,000). Although young women were 4 times less likely (78 vs 297) to be hospitalized for MI, they were only 1/2 as likely (7 vs 17) to die from MI in the hospital. Thus, women had greater adjusted ORs for in-hospital mortality but lower ORs for out-of-hospital CHD death than men.

During the 15-year study period, a marked decrease in in-hospital death occurred for men (about 60%, from 16.7 to

6.7/100,000) and women (by 66%, from 5.8 to 2.0/100,000) in the 35 to 54-year age group. The decrease in out-of-hospital CHD death was more pronounced for men (28.4%, from 49.6 to 35.5/100,000) than for women (10%, from 8.2 to 7.4/100,000; Figure 1). For young men, the risk in-hospital death compared to out-of-hospital death decreased from 0.34 to 0.19 from 1990 to 2004, and the risk for young women decreased from 0.71 to 0.27. Thus, the gender difference with respect to in-hospital versus out-of-hospital death decreased with time. This resulted from the more pronounced decrease of in-hospital case fatality among young women and the decrease in out-of-hospital death among young men.

Discussion

The findings of the present population-based study highlight that young women (aged 35 to 54 years) hospitalized with acute MI were more likely to die in the hospital than were young men. The opposite was true when population community-wide CHD mortality, especially out-of-hospital CHD mortality, was considered. This apparent discrepancy could be explained by the greater out-of-hospital death rate among men. The findings of the present report have confirmed findings from previous studies[3,6,13–16] that indicated that young women hospitalized with acute MI have greater in-hospital mortality than young men.

The reasons for the worse outcomes of MI in young women are not well known. Some studies have suggested that hospitalized young women fare worse than young men because of more co-morbid conditions, including diabetes, metabolic syndrome, and heart failure.[5,9,17,18] Women also have had a more complicated hospital course, with greater rates of refractory pulmonary edema and cardiogenic shock after MI[16] and have been less likely to undergo invasive interventions and treatment than men.[10] However, these factors do not account entirely for women's worse mortality after admission.[19]

It is possible that the greater CHD mortality outside the hospital for young men, possibly reflecting more transmural MI, counterbalances the greater in-hospital case-fatality for young women. It is also possible that the different presentation of CHD in young women results in more women diagnosed with unstable angina pectoris, influencing the estimation of in-hospital case fatality by classifying only the more severe cases in women as MI. The difference between men and women is more pronounced at a younger age. This could have been because of the strong effect of age on both in-hospital MI case fatality and out-of-hospital mortality that renders the effect of gender relatively less important. The different pattern of CHD presentation in women, with more cases of unstable angina pectoris and fewer cases of ST-segment elevation MI, might have contributed to the observed differences in outcomes.[20,21] Young women admitted to the hospital but not meeting the definition of acute MI could influence in-hospital acute MI case fatality.[22]

In the past 15 years, the differences between young men and young women in out-of-hospital versus in-hospital CHD mortality have decreased, primarily because of a more pronounced decrease in in-hospital MI case fatality in young women and a more marked decrease in out-of-hospital death among young men. Overall, considering both genders, the pronounced decrease in in-hospital case fatality of MI was not paralleled by a similar decrease in out-of-hospital CHD death, where most CHD deaths occur. The decrease in CHD mortality in women has lagged behind that observed in men.[23,24] It has been hypothesized that the current focus on obstructive CHD might not benefit women, who are more likely to have nonobstructive disease.[25–27]

Overall, our data have indicated that the greater mortality of young women who were hospitalized for acute MI could have been because young men are more likely to die outside the hospital. In-hospital mortality improved more in young women than in young men, and out-of-hospital deaths decreased primarily in young men. These trends resulted in attenuation of the differences between young men and young women.

1. Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, Zheng ZJ, Flegal K, O'Donnell C, Kittner S, Lloyd-Jones D, Goff DC Jr, Hong Y, Adams R, Friday G, Furie K, Gorelick P, Kissela B, Marler J, Meigs J, Roger V, Sidney S, Sorlie P, Steinberger J, Wasserthiel-Smoller S, Wilson M, Wolf P. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2006;113:e85–e151.
2. Rogers WJ, Canto JG, Lambrew CT, Tiefenbrunn AJ, Kinkaid B, Shoultz DA, Frederick PD, Every N. Temporal trends in the treatment of over 1.5 million patients with myocardial infarction in the US from 1990 through 1999: the National Registry of Myocardial Infarction 1, 2 and 3. *J Am Coll Cardiol* 2000;36:2056–2063.
3. Peltonen M, Lundberg V, Huhtasaari F, Asplund K. Marked improvement in survival after acute myocardial infarction in middle-aged men but not in women: The Northern Sweden MONICA study 1985–94. *J Intern Med* 2000;247:579–587.
4. Nohria A, Vaccarino V, Krumholz HM. Gender differences in mortality after myocardial infarction: why women fare worse than men. *Cardiol Clin* 1998;16:45–57.
5. Vaccarino V, Parsons L, Every NR, Barron HV, Krumholz HM. Sex-based differences in early mortality after myocardial infarction: National Registry of Myocardial Infarction 2 participants. *N Engl J Med* 1999;341:217–225.
6. Andrikopoulos GK, Tzeis SE, Pipilis AG, Richter DJ, Kappos KG, Stefanadis CI, Toutouzas PK, Chimonas ET. Younger age potentiates post myocardial infarction survival disadvantage of women. *Int J Cardiol* 2006;108:320–325.
7. Tunstall-Pedoe H, Morrison C, Woodward M, Fitzpatrick B, Watt G. Sex differences in myocardial infarction and coronary deaths in the Scottish MONICA population of Glasgow 1985 to 1991: presentation, diagnosis, treatment, and 28-day case fatality of 3991 events in men and 1551 events in women. *Circulation* 1996;93:1981–1992.
8. Sonke GS, Beaglehole R, Stewart AW, Jackson R, Stewart FM. Sex differences in case fatality before and after admission to hospital after acute cardiac events: analysis of community based coronary heart disease register. *BMJ* 1996;313:853–855.
9. Zeller M, Steg PG, Ravisy J, Laurent Y, Janin-Manificat L, L'Huillier I, Beer JC, Oudot A, Rioufol G, Makki H, Farnier M, Rochette L, Verges B, Cottin Y. Prevalence and impact of metabolic syndrome on hospital outcomes in acute myocardial infarction. *Arch Intern Med* 2005;165:1192–1198.
10. Kostis JB, Wilson AC, O'Dowd K, Gregory P, Chelton S, Cosgrove NM, Chirala A, Cui T; MIDAS Study Group. Myocardial Infarction Data Acquisition System. Sex differences in the management and long-term outcome of acute myocardial infarction: a statewide study. *Circulation* 1994;90:1715–1730.
11. Jaro M. Advances in record-linkage methodology as applied to matching the 1985 census of Tampa, Florida. *J Am Stat Assoc* 1989;84:414–420.
12. Gregory P, Rhoads G, Wilson A, O'Dowd K, Kostis J. Impact of availability of hospital-based invasive cardiac services on racial differences in the use of these services. *Am Heart J* 1998;138:507–517.

13. Simon T, Mary-Krause M, Cambou JP, Hanania G, Gueret P, Lablanche JM, Blanchard D, Genes N, Danchin N. Impact of age and gender on in-hospital and late mortality after acute myocardial infarction: increased early risk in younger women: results from the French nation-wide USIC registries. *Eur Heart J* 2006;27:1282–1288.
14. Malacrida R, Genoni M, Maggioni AP, Spataro V, Parish S, Palmer A, Collins R, Moccetti T. A comparison of the early outcome of acute myocardial infarction in women and men. The Third International Study of Infarct Survival Collaborative Group. *N Engl J Med* 1998; 338:8–14.
15. MacIntyre K, Stewart S, Capewell S, Chalmers JW, Pell JP, Boyd J, Finlayson A, Redpath A, Gilmour H, McMurray JJ. Gender and survival: a population-based study of 201,114 men and women following a first acute myocardial infarction. *J Am Coll Cardiol* 2001; 38:729–735.
16. Fabijanic D, Culic V, Bozic I, Miric D, Stipic SS, Radic M, Vucinovic Z. Gender differences in in-hospital mortality and mechanisms of death after the first acute myocardial infarction. *Ann Saudi Med* 2006; 26:455–460.
17. Rosengren A, Spetz CL, Koster M, Hammar N, Alfredsson L, Rosen M. Sex differences in survival after myocardial infarction in Sweden: data from the Swedish National Acute Myocardial Infarction Register. *Eur Heart J* 2001;22:314–322.
18. Turhan H, Yetkin E. Poor in-hospital outcome in young women with acute myocardial infarction: does metabolic syndrome play a role? *Int J Cardiol* 2006;112:257–258.
19. Gold LD, Krumholz HM. Gender differences in treatment of heart failure and acute myocardial infarction: a question of quality or epidemiology? *Cardiol Rev* 2006;14:180–186.
20. Blomkalns AL, Chen AY, Hochman JS, Peterson ED, Trynosky K, Diercks DB, Brogan GX Jr, Boden WE, Roe MT, Ohman EM, Gibler WB, Newby LK. Gender disparities in the diagnosis and treatment of non–ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) National Quality Improvement Initiative. *J Am Coll Cardiol* 2005;45:832–837.
21. Hellermann JP, Reeder GS, Jacobsen SJ, Weston SA, Killian JM, Roger VL. Longitudinal trends in the severity of acute myocardial infarction: a population study in Olmsted County, Minnesota. *Am J Epidemiol* 2002;156:246–253.
22. Chambless L, Keil U, Dobson A, Mahonen M, Kuulasmaa K, Rajakangas AM, Lowel H, Tunstall-Pedoe H. Population versus clinical view of case fatality from acute coronary heart disease: results from the WHO MONICA Project 1985–1990. Multinational MONItoring of Trends and Determinants in CArdiovascular Disease. *Circulation* 1997;96:3849–3859.
23. Heron MP, Hoyert DL, Xu J, Scott C, Tejada-Vera B. Deaths: preliminary data for 2006. *Natl Vital Stat Rep* 2008;561:1–52.
24. Ford ES, Capewell S. Coronary heart disease mortality among young adults in the U.S. from 1980 through 2002: concealed leveling of mortality rates. *J Am Coll Cardiol* 2007;50:2128–2132.
25. Bairey Merz CN, Shaw LJ, Reis SE. Ischemic heart disease in women: insights from the NLHBI-sponsored Women's Ischemia Syndrome Evaluation (WISE) study—part II: gender differences in presentation, diagnosis, and outcome with regard to sex-based pathophysiology of atherosclerosis, macro- and micro-vascular CAD. *J Am Coll Cardiol* 2006;47(Suppl):21s–29s.
26. Shaw LJ, Bairey Merz CN, Pepine CJ, Reis SE, Bittner V, Kelsey SF, Olson M, Johnson BD, Mankad S, Sharaf BL, Rogers WJ, Wessel TR, Arant CB, Pohost GM, Lerman A, Quyyumi AA, Sopko G; WISE Investigators. Insights from the NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE) study—part I: gender differences in traditional and novel risk factors, symptom evaluation, and gender-optimized diagnostic strategies. *J Am Coll Cardiol* 2006;47(Suppl): S4–S20.
27. Shaw LJ, Burgiardini R, Merz CNB. Women and ischemic heart disease: evolving knowledge. *J Am Coll Cardiol* 2009;54:1561–1575.