Sex Differences in the Treatment and Outcome of Patients with Acute Coronary Syndrome After Percutaneous Coronary Intervention: A Population-Based Study

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Abstract

Background: This study was performed to assess the influence of sex on drug therapy and long-term outcomes in acute coronary syndrome (ACS) patients who underwent percutaneous coronary intervention (PCI).

Methods: This is a retrospective cohort study of ACS patients who underwent PCI [women ($n=8,884$) and men ($n=23,937$)] between January 1, 2006, and December 31, 2007, with at least a 1-year follow-up, based on the National Health Insurance Research Database in Taiwan. Propensity score was used to identify a 1:1 matched cohort ($n=17,768$) for multivariable adjustment. The influence of sex on drug therapy and outcomes was examined by multivariate logistic regression and multivariable Cox proportional hazards regression.

Results: Female patients had an 18% and 12% lower likelihood of receiving aspirin (adjusted odds ratio [OR_{adj}]=0.82, 95% confidence interval [CI]=0.77–0.88) and clopidogrel (OR_{adj}=0.88, 95% CI=0.81–0.95), respectively, than male patients but had a 17% and 22% higher likelihood of receiving beta-blockers (OR_{adj}=1.17, 95% CI=1.10–1.24) and statins (OR_{adj}=1.22, 95% CI=1.14–1.29), respectively, than male patients in the matched cohort. The adjusted hazard ratio (HR_{adj}) of rehospitalization for revascularization in women was 0.84 (95% CI=0.79–0.90) compared with men after at least a 1-year follow-up in the matched cohort.

Conclusions: Female patients with ACS who underwent PCI were less likely to receive aspirin and clopidogrel but were more likely to receive beta-blockers and statins than male patients. Male sex was associated with a higher risk of rehospitalization for revascularization than female sex.

Introduction

CORONARY HEART DISEASE is the leading cause of mortality and morbidity in the United States. The term acute coronary syndrome (ACS) is a diagnosis that captures the full spectrum of disease severity of coronary atherosclerosis from unstable angina to non-ST-segment elevation myocardial infarction and ST-segment elevation myocardial infarction. ACS is the major cause of emergency department visits and hospitalizations in the United States.^{1,2} The benefits of drug therapy (such as aspirin, beta-blockers, angiotensin-converting enzyme inhibitors [ACEIs] or angiotensin receptor blockers [ARBs], statins, and clopidogrel) in reducing the risks of morbidity and mortality in ACS patients are supported by many clinical trials.^{3–7} Previous studies have revealed that female patients were associated with underutilization of drugs such as aspirin, beta-

blockers, ACEIs, statins, or clopidogrel for ACS patients as compared with male patients.^{8–12} Several studies have demonstrated that the gender differences in drug therapy in ACS patients may be related to patient demographic variables such as age, comorbidities such as heart failure, diabetes, and physician's perception of risk.^{13–16} Sex differences in the treatment of ACS patients have been reported and indicate that women are less likely than men to receive interventional therapies such as percutaneous coronary intervention (PCI) with/without a stent and coronary artery bypass graft (CABG).^{9,10,12,17–19}

Little is known if sex differences in drug therapies persist within selected ACS patients who have undergone PCI. There have been inconsistent results regarding the influence of sex on the long-term outcomes of this patient population.^{20–22} This is the first study that used a national insurance database and propensity score matching method to assess the influence

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of sex on drug therapy and outcome in ACS patients who underwent PCI.

Materials and Methods

This is a nationwide, retrospective, population-based cohort study of patients hospitalized for ACS between January 1, 2006, and December 31, 2007. The data were obtained from the 2005–2008 Taiwan National Health Insurance Research Database (NHIRD). The NHIRD includes all claims data of outpatient and inpatient visits from the National Health Insurance (NHI) program in Taiwan, which covers over 99% of the entire Taiwanese population (23.7 million people). Because the NHIRD is converted to de-identified dataset before being released to the public for research purposes, the study was exempt from full review by our Institutional Review Board.

Study population

We identified patients who had their first hospitalization for ACS between January 1, 2006, and December 31, 2007, ($n=111,347$) from the NHIRD. Patients with ACS were defined as those who had primary discharge diagnosis codes of 410.xx, 411.xx, or 414.xx based on the *International Classification of Diseases, Ninth Revision* (ICD-9-CM codes).²³ Excluding the patients who were previously admitted to hospitals because of ACS in 2005, were less than 18 years old, or had an unknown discharge date for the first ACS event, 87,321 ACS patients were included. PCI was identified by ICD-9-CM procedure codes of 3601, 3605, or 3606. A total of 32,821 ACS patients who underwent PCI were categorized into women ($n=8884$) and men ($n=23,937$) (Fig. 1). The use of drug therapy, including aspirin, beta-blockers, ACEI or ARB, statins,

FIG. 1. Flowchart of patient enrollment.

and clopidogrel, was defined as having at least one prescription within 365 days after the first ACS event.

A propensity score-matching approach was used to create subgroups for further adjustment of potential confounders between female and male groups by balancing covariates.^{24,25,26} A propensity score regarding the probability of being female group was calculated for each patient by a logistic regression model with covariates of age, ischemic heart disease, cerebrovascular disease, heart failure, hypertension, diabetes mellitus, renal disease, hyperlipidemia, peripheral vascular disease, liver disease, peptic ulcer, and gastroesophageal reflux disease (GERD). The propensity score was then used to match patients in the male group with patients in the female group at a 1:1 ratio via propensity score nearest-neighbor matching. The randomly selected patients in the male group were matched to the patients in the female group with the closest propensity score within the width of the propensity score of 0.01. This process was repeated until 8,884 patients matched by propensity score from the male group were found.^{24,27} Patients were excluded from the matched cohort analysis if no match was found. A male group of 8,884 patients was selected from 23,937 persons. Therefore, a matched cohort of 17,768 persons was included (Fig. 1).

Clinical outcomes

The outcomes were rehospitalization for PCI with stent, PCI without stent, coronary artery bypass graft surgery (CABG), or revascularization (PCI or CABG surgery) after the discharge date for the index ACS event. Patients who underwent PCI were defined as those having a code of 3601 or 3605 or having a stent with a code of 3606. Patients who had CABG surgery were defined as those having a code of 3611-3616 based on the ICD-9-OP codes. All patients were followed-up for at least 1 year, starting from the discharge date of the index ACS event until the last study date (December 31, 2008) or the occurrence of outcomes, whichever came first.

Statistical analyses

Differences in baseline characteristics between female and male patients were compared by chi-square tests and *t*-tests. Multivariate logistic regression models were constructed to

examine the relationships between the sex and the use of drug therapy. Multivariate logistic regression models were adjusted for patient demographics and prior medical histories (hypertension, hyperlipidemia, diabetes, cerebrovascular disease, renal disease, heart failure, peripheral vascular disease, ischemic heart disease, peptic ulcer, and GERD). The effect of sex on rehospitalization for revascularization was analyzed by a multivariable Cox proportional hazards regression model. Patient demographics, prior medical histories (hypertension, hyperlipidemia, diabetes, cerebrovascular disease, renal disease, heart failure, peripheral vascular disease, ischemic heart disease, liver disease, peptic ulcer, and GERD), and medications (aspirin, beta-blocker, ACEI, ARB, statin, and clopidogrel) received within 365 days after the first ACS event were adjusted in the multivariable Cox proportional hazards regression model. All tests were two-sided, and an alpha level of 0.05 was considered as statistically significant. All analyses were performed using SPSS software version 16.0 (SPSS Inc.) or SAS software version 9.2 (SAS Institute).

Results

The ACS cohort consisted of 87,321 patients, among which 32,821 underwent PCI, of whom 8884 were women and 23,937 were men. In the original ACS patients after PCI cohort, women were older [69.6 ± 10.2 (mean $\pm$ SD) years for women and 63.7 ± 12.3 years for men, $p < 0.001$] and had a higher rate of hypertension, diabetes, cerebrovascular disease, renal disease, and heart failure. The two groups were balanced in the matched cohort in terms of age [69.6 ± 10.2 years for women vs. 69.6 ± 10.6 years for men], rate of hypertension, cerebrovascular disease, renal disease, heart failure, and other baseline characteristics except diabetes (Table 1).

Within 365 days after PCI in ACS patients, use of aspirin or clopidogrel was less likely in women than in men in both the original and matched cohort. Whereas the use of beta-blockers or statins was more likely in women than in men in the matched cohort, there was no significant difference in the use of statins in the original cohort. The proportions of patients receiving aspirin, beta-blockers, ACEI or ARB, statins, and clopidogrel were 74.3%, 63.9%, 63.4%, 53.7%, and 82.4% in

TABLE 1. BASELINE CHARACTERISTICS OF THE ORIGINAL AND MATCHED COHORTS OF ACUTE CORONARY SYNDROME PATIENTS WHO UNDERWENT PERCUTANEOUS INTERVENTION

Characteristic	Original cohort			Matched cohort		
	Female (n=8,884)	Male (n=23,937)	p	Female (n=8,884)	Male (n=8,884)	p
Age [years; mean (SD)]	69.6 (10.2)	63.7 (12.3)	<0.001	69.6 (10.2)	69.6 (10.6)	0.692
Comorbidity [n (%)]						
Hypertension	5,593 (63.0)	12,840 (53.6)	<0.001	5,593 (63.0)	5,569 (62.7)	0.709
Hyperlipidemia	1,934 (21.8)	6,163 (25.7)	<0.001	1,934 (21.8)	1,971 (22.2)	0.503
Diabetes mellitus	3,921 (44.1)	7,085 (29.6)	<0.001	3,921 (44.1)	3,751 (42.2)	0.010
Cerebrovascular disease	178 (2.0)	367 (1.5)	0.03	178 (2.0)	170 (1.9)	0.665
Renal disease	563 (6.3)	938 (3.9)	<0.001	563 (6.3)	531 (6.0)	0.318
Heart failure	1,016 (11.4)	2,027 (8.5)	<0.001	1,016 (11.4)	960 (10.8)	0.181
Ischemic heart disease	3,838 (43.2)	11,803 (49.3)	<0.001	3,838 (43.2)	3,848 (43.3)	0.880
Liver disease	96 (1.1)	327 (1.4)	0.042	96 (1.1)	93 (1.0)	0.826
Peptic ulcer	305 (3.4)	722 (3.0)	0.054	305 (3.4)	312 (3.5)	0.774
Peripheral vascular disease	3 (0.0)	13 (0.1)	0.454	3 (0.0)	2 (0.0)	0.655
Gastroesophageal reflux disease	63 (0.7)	144 (0.6)	0.274	63 (0.7)	60 (0.7)	0.786

ACS, acute coronary syndrome; PCI, percutaneous intervention; SD, standard deviation.

TABLE 2. SEX DIFFERENCES IN THE DRUG THERAPY OF PATIENTS AFTER PCI IN THE ORIGINAL AND MATCHED COHORTS

Drug therapy [n (%)]	Original cohort			Matched cohort		
	Female (n=8,884)	Male (n=23,937)	p	Female (n=8,884)	Male (n=8,884)	p
Aspirin	6,597 (74.3)	19,013 (79.4)	<0.001	6,597 (74.3)	6,910 (77.8)	<0.001
Clopidogrel	7,321 (82.4)	20,328 (84.9)	<0.001	7,321 (82.4)	7,479 (84.2)	0.001
Beta-blocker	5,678 (63.9)	14,870 (62.1)	0.003	5,678 (63.9)	5,363 (60.4)	<0.001
ACEI or ARB	5,636 (63.4)	15,010 (62.7)	0.222	5,636 (63.4)	5,719 (64.4)	0.195
Statin	4,767 (53.7)	12,874 (53.8)	0.841	4,767 (53.7)	4,372 (49.2)	<0.001

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; Statin, HMG-CoA reductase blocker.

women and 77.8%, 60.4%, 64.4%, 49.2%, and 84.2% in men, respectively, in the matched cohort (Table 2).

Multivariable logistic regression analysis revealed that female sex was associated with an 18% and 12% lower likelihood of receiving aspirin (adjusted odds ratio [OR_{adj}] 0.82, 95% confidence interval [CI] 0.77–0.88) and clopidogrel (OR_{adj} 0.88, 95% CI 0.81–0.95), respectively, than male sex in the matched cohort (Table 3). Women had a 17% and 22% higher likelihood of receiving of beta-blockers (OR_{adj} 1.17, 95% CI 1.10–1.24) and statins (OR_{adj} 1.22, 95% CI 1.14–1.29), respectively, than men in the matched cohort (Table 3). There was no significant difference between the two sexes in the use of ACEI or ARB (OR_{adj} 0.95, 95% CI 0.89–1.01) (Table 3). The results of the impact of sex on drug therapy in ACS patients after PCI were similar in both the original and matched cohorts except for statin use (Table 3).

The adjusted hazard ratios (HRs) for rehospitalization for PCI and revascularization in female ACS patients who had received aspirin, beta-blockers, ACEIs or ARBs, statins, and clopidogrel were 0.82 (95% CI 0.74–0.91) and 0.81 (95% CI 0.73–0.90) when compared with female ACS patients who did not receive any of the above medications in the matched cohort. Similar results were found in the male ACS patients.

The adjusted HRs for rehospitalization for PCI, PCI with stent, CABG, and revascularization in women were 0.86 (95% CI 0.80–0.91), 0.88 (95% CI 0.80–0.95), 0.63 (95% CI 0.47–0.83), and 0.84 (95% CI 0.79–0.90), when compared with men in the matched cohort (Table 4). The sex differences in re-

hospitalization for PCI, PCI with stent or CABG were similar in both the original and matched cohorts (Table 4).

Discussion

This is the first study involving a large, nationally representative sample that uses a propensity score matching method to adjust for risk in exploring the influence of sex on the use of medication and outcome of patients with ACS after PCI. In the original cohort of our study, women were 6 years older than men and had a higher cardiovascular risk because of diabetes (10% higher than men) and hypertension (14% higher than men), among other comorbidities, which was similar to other studies.^{10,28–31} Using the propensity score matching method to adjust for risk, we demonstrated that even with national health insurance coverage, women were less likely to use aspirin and clopidogrel but not beta-blockers and statins among ACS patients who underwent PCI as compared with men.

Use of antiplatelets

Our result that women were 18% less likely to receive aspirin than men was similar to that of several studies conducted in ACS patients.^{9,19,32,33} Though aspirin has been associated with a significant reduction of serious cardiovascular events in both women and men,³⁴ there may be concern of increased incidence of bleeding among women.³³

Similar to previous studies, this study indicated that women were less likely to receive clopidogrel than men.^{9,32,33,35}

TABLE 3. ASSOCIATION BETWEEN SEX AND THE DRUG THERAPY IN ACS PATIENTS AFTER PCI IN ORIGINAL AND MATCHED COHORTS

Original cohort [n (%)]	Female (n=8,884)	Male (n=23,937)	Multivariate-adjusted OR (95% CI)
Aspirin	6,597 (74.3)	19,013 (79.4)	0.84 (0.79–0.90)*
Clopidogrel	7,321 (82.4)	20,328 (84.9)	0.90 (0.84–0.97)*
Beta-blocker	5,678 (63.9)	14,870 (62.1)	1.20 (1.13–1.26)*
ACEI or ARB	5,636 (63.4)	15,010 (62.7)	0.96 (0.91–1.01)
Statin	4,767 (53.7)	12,874 (53.8)	1.19 (1.13–1.26)*
Matched cohort [n (%)]	Female (n=8,884)	Male (n=8,884)	Multivariate-adjusted OR (95% CI)
Aspirin	6,597 (74.3)	6,910 (77.8)	0.82 (0.77–0.88)*
Clopidogrel	7,321 (82.4)	7,479 (84.2)	0.88 (0.81–0.95)*
Beta-blocker	5,678 (63.9)	5,363 (60.4)	1.17 (1.10–1.24)*
ACEI or ARB	5,636 (63.4)	5,719 (64.4)	0.95 (0.89–1.01)
Statin	4,767 (53.7)	4,372 (49.2)	1.22 (1.14–1.29)*

**p* < 0.05.

95% CI, 95% confidence interval; OR, odds ratio.

TABLE 4. ASSOCIATION BETWEEN SEX AND THE OUTCOMES IN ACS PATIENTS AFTER PCI IN ORIGINAL AND MATCHED COHORTS

Original cohort [n (%)]	Female (n=8,884)	Male (n=23,937)	Multivariate-adjusted HR (95% CI)
Revascularization	1,756 (19.8)	5,760 (24.1)	0.83 (0.79–0.88)*
PCI	1,687 (19.0)	5,478 (22.9)	0.84 (0.80–0.89)*
PCI with stent	967 (10.9)	3,130 (13.1)	0.85 (0.79–0.92)*
CABG	80 (0.9)	311 (1.3)	0.66 (0.51–0.85)*
Matched cohort [n (%)]	Female (n=8,884)	Male (n=8,884)	Multivariate-adjusted HR (95% CI)
Revascularization	1,756 (19.8)	2,084 (23.5)	0.84 (0.79–0.90)*
PCI	1,687 (19.0)	1,970 (22.2)	0.86 (0.80–0.91)*
PCI with stent	967 (10.9)	1,100 (12.4)	0.88 (0.80–0.95)*
CABG	80 (0.9)	126 (1.4)	0.63 (0.47–0.83)*

* $p < 0.05$.

95% CI, 95% confidence interval; OR, odds ratio; CABG, coronary artery bypass graft surgery.

Because of the Taiwan NHI reimbursement policy, clopidogrel was usually used in patients after ACS. Less than 3% of ACS patients used ticlopidine instead of clopidogrel. There are conflicting results concerning the benefit of clopidogrel single or combination therapy with aspirin in different sexes.^{34,36} In addition, clopidogrel has been associated with a higher risk of major bleeding in women than in men.³⁷ The associations of drug therapy and outcomes in ACS patients who underwent PCI with sex remained the same in both sexes after we included the gastrointestinal bleeding history in the analysis. However, we did not include other bleeding history in the analysis, which may also have influenced prescribing of aspirin or clopidogrel.

Use of beta-blockers and statins

Women in our study were 17% more likely to receive beta-blockers than were men. The result is different from that of a study conducted using the American College of Cardiology National Cardiovascular Data Registry, in which no significant sex difference was found in the use of beta-blocker in ACS patients who underwent PCI.³³

The result in our study that women were 22% more likely than men to receive statins may be explained by the fact that women have more cardiovascular risk factors and are more likely to meet Taiwan's NHI reimbursement policy for statins use than men. This is different from a previous study that indicated that women were 10% less likely to receive statins than men.³³ However, the baseline clinical characteristics were significantly different between women and men in that study, which was different from our matched cohort.³³

Benefits of drug therapy in different sexes

This study gives us a clue whether health care is given in an unbiased manner in both sexes. Only limited literature is available for sex-specific pathophysiology, drug therapy, interventional therapy, and outcomes in ACS patients. According to the currently available evidence, both sexes benefit equally from aspirin, beta-blockers, ACEI and statins, but contradictory data has been found for clopidogrel.^{34,37}

Outcome of patients with ACS after PCI in different sexes

Al-Fiadh et al.³¹ indicated that female sex was associated with a higher rate of major adverse cardiac events (MACE) (10.1% vs. 6.4%, $p < 0.001$) at 30 days than male sex. After 12 months, there was no significant difference in mortality, MACE, and revascularization (PCI with or without stent or CABG) between women and men. However, the clinical baseline characteristics such as age and comorbidities between female and male groups were significantly different.³¹

We have demonstrated that women were 14%, 12%, and 37% significantly less likely to be rehospitalized for PCI with or without stent and CABG, respectively, than men, after adjusting for demographic variables and comorbidities in ACS patients who underwent PCI in a matched cohort followed up for one to three years at a nationwide level. This result may be explained by the fact that women were less likely to present with ST-elevation myocardial infarction, which requires revascularization.³¹ In addition, among ACS patients who underwent PCI, women had less extensive atherosclerosis types, such as three-vessel or main stem disease, that always require revascularization.³⁸ In addition, this result may also be interpreted as women being less likely than men to receive interventional therapies such as PCI with/without a stent and CABG.^{9,10,12,17}

Interpretation of the results in this study

Limited studies have reported the association between female sex and drug therapy and outcomes in ACS patients who underwent PCI,^{13,39–41} but none of them are nationwide studies. The value of our study is the use of a national health insurance database with multivariable adjustment by a propensity score matching method. In our study, the associations of drug therapy and outcomes in ACS patients who underwent PCI with sex were similar in the original and propensity score matched cohort. Similar results were found in the subgroup analyses involving hospital levels and in the subgroup analysis involving different regions. Sex differences in the drug therapy and the outcome of patients with ACS after PCI were shown in the subgroup analysis by stratifying the cohort by different ICD codes 410, 411, or 414 (Appendix Table A1).

These results raise the question of the equality of drug therapy between women and men after their ACS events after adjusting for age and comorbidity. Although our study found that female sex was associated with decreased use of drug therapy such as aspirin and clopidogrel in ACS patients who underwent PCI, women had increased use of beta-blockers and statins. These results did not simply imply "inequality" therapy for several reasons. First, existing guidelines are mostly based on randomized controlled trials in ACS patients with a higher percentage of men. Second, women may be vulnerable to the adverse effects of the drug therapy, and the risks of the medications might outweigh their benefits. Furthermore, disease-specific guidelines often do not take into account sex differences in ACS patients. Additional research to develop sex-specific therapeutic strategy in ACS patients may be needed.

Our findings should be interpreted in the context of the following limitations. First, the identification of diagnoses of ACS, invasive procedures, and comorbid medical conditions was dependent on the ICD-9-CM codes. This was a limitation of our study compared with studies using a standardized diagnostic approach. However, the Bureau of NHI in Taiwan reviews charts from random samples of a certain percentage of medical claims from every hospital quarterly to verify the validity of disease diagnoses. Second, although we have adjusted for many potentially confounders related to rehospitalization of cardiovascular events, information such as smoking history, dietary habits, and body mass index that may be risk factors for cardiovascular disease were not available in NHIRD. Third, although the absolute differences of 1.0% to 3.5 % between drug therapy in male and female ACS patients who underwent PCI were significant, these might be small effects detected in large sample sizes. Fourth, the acute and planned rehospitalization for revascularization could not be differentiated by using NHIRD. Fifth, death records were not available in the NHIRD, but we identified rehospitalization for PCI with or without stent or CABG for ACS patients.

Conclusions

Female patients with ACS who underwent PCI were less likely to receive aspirin and clopidogrel but were more likely to receive beta-blockers and statins compared to male patients. Male sex was associated with a higher risk for rehospitalization for revascularization in ACS patients who underwent PCI than female sex. Further studies to understand the sex differences in the effectiveness of drug therapy and outcomes in ACS patients are warranted.

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Author Disclosure Statement

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Appendix

TABLE A1. ASSOCIATION BETWEEN SEX AND THE DRUG THERAPY AND THE OUTCOMES IN ACS PATIENTS AFTER PCI IN THE MATCHED COHORT STRATIFIED BY CODES

<i>Multivariate-adjusted hazard ratio (95% CI)</i>				
	<i>ICD 410, 411, or 414 (n=17,768)</i>	<i>ICD 410 (n=4,904)</i>	<i>ICD 411 (n=652)</i>	<i>ICD 414 (n=12,212)</i>
Drug therapy				
Aspirin	0.82 (0.77–0.88)*	0.70 (0.61–0.81)*	1.00 (0.67–1.49)	0.88 (0.81–0.95)*
Clopidogrel	0.88 (0.81–0.95)*	0.73 (0.63–0.85)*	0.95 (0.59–1.54)	0.95 (0.87–1.05)
Beta-blocker	1.77 (1.10–1.24)*	0.96 (0.86–1.09)	1.05 (0.75–1.47)	1.28 (1.19–1.38)*
ACEI or ARB	0.95 (0.89–1.01)	0.82 (0.72–0.93)*	1.26 (0.89–1.77)	1.02 (0.94–1.10)
Statin	1.22 (1.14–1.29)*	1.12 (1.00–1.27)*	1.26 (0.91–1.77)	1.26 (1.17–1.36)*
Outcomes				
Revascularization	0.84 (0.79–0.90)*	0.87 (0.78–0.98)*	0.70 (0.51–0.95)*	0.86 (0.79–0.93)*
PCI	0.86 (0.80–0.91)*	0.88 (0.78–0.99)*	0.72 (0.52–0.99)*	0.88 (0.81–0.95)*
PCI with stent	0.88 (0.80–0.95)*	0.87 (0.75–1.02)	0.73 (0.46–1.17)	0.91 (0.82–1.02)
CABG	0.63 (0.47–0.83)*	0.70 (0.43–1.12)	0.32 (0.06–1.63)	0.61 (0.43–0.87)*

*Statistically significant.

International Classification of Diseases (ICD) 410: Patients diagnosed with acute myocardial infarction; ICD 411: Patients diagnosed with unstable angina but not underwent catheterization; ICD414: Patients diagnosed with unstable angina after underwent catheterization.