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ORIGINAL ARTICLE

Sex and age differences of major cardiovascular events in patients after percutaneous coronary intervention

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Abstract

Background: Women usually have higher risk after receiving percutaneous coronary interventions (PCIs) than men with coronary artery disease (CAD). The aim of this study was to investigate the association of sex differences with future outcomes in CAD patients undergoing PCI, to assess the role of age, and to extend observed endpoints to stroke and congestive heart failure.

Methods: Six thousand six hundred forty-seven patients with CAD who received successful PCIs. The associations between clinic outcomes and sex were analyzed. The primary outcome was major cardiovascular events (MACE), including cardiac death, nonfatal myocardial infraction, and nonfatal stroke. The secondary outcome was MACE and hospitalization for heart failure (total CV events).

Results: During a mean of 52.7 months of follow-up, 4833 men and 1614 women received PCI. Univariate and multivariate analyses showed that women were independently associated with an increased risk of cardiac death (HR, 1.78; 95% CI, 1.32-2.41), hospitalization for heart failure (HR, 1.53; 95% CI, 1.23-1.89), MACE (HR, 1.34; 95% CI, 1.10-1.63), and total CV events (HR, 1.39; 95% CI, 1.20-1.62). In the subgroup analysis, women aged under 60 years had higher cardiovascular risks than men of the same age category.

Conclusion: Women with CAD after successful PCI had poorer cardiovascular outcomes than men. Additionally, younger women (aged <60 years) were especially associated with a higher risk of developing future adverse cardiovascular outcomes.

Keywords: Coronary artery disease; Percutaneous coronary intervention; Sex

1. INTRODUCTION

It is generally accepted that women have fewer cardiovascular diseases (CVDs) than men.[1] According to a literature review, women have less occurrence of fatal coronary heart disease (<1% vs 3.6%) and nonfatal MI (18.3% vs 37.5%) than men.[2] This could be caused by gender differences in the pathogenesis of coronary artery diseases (CADs), including the pathological plaque mechanism,[3] vascular anatomy, hormonal profiles, coagulation,[4] vascular risk factors, lifestyle factors, and socioeconomic status. However, not all clinical observations support that females have favorable clinical outcomes, and the situation is quite different when women already have a preexisting cardiovascular disease.[5–9]

Recent studies found that women with a history of CVD had poorer clinical outcomes than men.[10–13] For example, women had higher 30-day mortality rates after ST-segment elevation myocardial infarction (STEMI),[10] as well as a higher risk of developing future acute limb ischemia when suffering from symptomatic peripheral artery disease (PAOD).[11] Furthermore, after stroke, women have a higher risk of mortality,[14] stroke-related disability, and poorer quality of life than men.[15] All of this evidence shows that if women have CVD, the long-term outcome is unfavorable.

Recently, advances in percutaneous coronary intervention (PCI) and intracoronary imaging have greatly improved clinical outcomes. However, there is limited information about the long-term outcome in different sexes after coronary intervention. Kosmidou et al[13] reported that women have a higher risk of major adverse cardiovascular events (MACE) and target lesion failure than men at 5 years after PCI. In that study, women had a higher risk of cardiac death, myocardial infarction (MI), and ischemia-driven revascularization following PCI. Women who received PCI usually exhibit more comorbidities than a man

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such as older, hypertensive, and/or diabetic that may cause an adverse outcomes.[16] However, there is little information on other important outcomes, such as congestive heart failure and stroke in women.

In addition, women aged <55 years old seem to have higher risk. Another study reported a higher risk in women aged <60 years old after acute myocardial infraction, but not in women aged >60 years old.[10] This suggests that relatively young women with CAD have worse outcomes. Therefore, this study investigates the impact of sex differences in long-term outcomes following PCI among various age groups and extends observed endpoints to stroke and congestive heart failure.

2. METHODS

2.1. Baseline data collection

The design and results from our larger, retrospective, single-center observational study has been published previously.[17,18] Briefly, our study examined patients with symptomatic CAD who were successfully treated with PCI. The diagnosis of CAD included (1) positive evidence of ischemic changes such as treadmill test and nuclear stress test results, (2) a history of angina with an ischemic change in ECG recordings, and (3) MI attack or angina symptoms with a significant stenosis lesion in coronary computed tomography angiography. Between July 2006 and December 2015, there were 6447 eligible subjects received PCI with either coronary stenting or balloon angioplasty at Taipei Veteran General Hospital, Taiwan.

Patients included in the analysis were categorized according to sex and age categories. They were subdivided into three groups: those with aged <60 years; those aged 60–74 years; and those aged >75 years according to definitions of elderly people.[19] A well-trained nurse research staff gathered baseline characteristics and risk factors from electronic medical records, including age, sex, smoking habit, family history of premature CAD, history of hypertension, diabetes, hyperlipidemia, and cerebral vascular disease. The baseline urine acid levels, lipid profiles, sugar measurements, and medications after PCI were collected in this study.

2.2. Ethics approval and consent to participate

All procedures were conducted in accordance with the Declaration of Helsinki and were approved by the Ethics Committee and Independent Review Board of Taipei Veterans General Hospital as well as the Joint IRB Ethics Committee Review Board in Taiwan. All patients should give their written informed consent before enrollment.

2.3. Clinical follow-up for adverse cardiovascular events

The primary outcome was MACE (a composite of cardiovascular death, nonfatal MI, and nonfatal stroke). The secondary outcome was the total major cardiovascular events, which was a composite of MACE plus hospitalization for congestive heart failure (MACE + CHF). Heart failure was diagnosed in our registry according medical record and ICD-10. MI was confirmed in patients presenting with ischemic symptoms with elevated serum cardiac enzyme levels and/or characteristic ECG changes. Ischemic stroke was confirmed as an obstruction within a brain blood vessel with imaging evidence by either MRI or CT scan and a new neurological deficit lasting for at least 24 hours. The protocol for follow-up of cardiovascular (CV) events was similar to previous reports.[17,18]

2.4. Statistics

Continuous variables were expressed as the mean and standard deviation in the presence of a normal distribution. Categorical variables were presented as both absolute frequencies (number of patients) and relative frequencies (percentage). The categorical variables were analyzed by a one-way analysis of variance (ANOVA), while subgroup comparisons of categorical variables were assessed by a χ^2 test or Fisher's exact test.

The primary and secondary outcomes were presented as overall percentages and expressed as proportions with a 95% confidence interval (CI). The event-free survival rate between different groups was calculated using the Kaplan–Meier method with significance evaluation using log rank tests. Hazard ratios (HRs) from a Cox regression model were used to analyze the outcome. *P* values of <0.05 were considered significant.

In addition to crude HRs, adjusted HRs were estimated after adjustment for potential confounding factors, including hypertension, diabetes, smoking habit, and revascularization. Statistical analysis was performed using SPSS software (Version 22.0, SPSS Inc., Chicago, IL, USA) and R version 3.2.3 (http://www.R-project.org/; R Foundation for Statistical Computing, Vienna, Austria). In all of the tests, the two-tailed alpha level for significance was 0.05.

3. RESULTS

From 2005 to 2015, a total of 6447 CAD patients, including 4833 males and 1614 females who underwent successful coronary intervention, were respectively enrolled in this study. The baseline characteristics of the participants are presented in Table 1. The median age of the male patients was 68 years, and that of the female was 70 years. Males had more acute coronary syndromes at enrollment (40.6% vs 36.1%, $p = 0.001$) and smokers (40.8% vs 6.6%, $p < 0.0001$). Females had more comorbidities than males, including hypertension (89.1% vs 85.7%, $p = 0.001$), diabetes (51.1% vs 35.1%, $p < 0.0001$), PAOD (7.3% vs 4.4%, $p < 0.0001$), and hyperlipidemia (45.5% vs 41.6%, $p = 0.007$).

In addition, males had a higher percentage of triple vessel disease (39.67% vs 36.9%). Both sexes had similar numbers of stent implantations, but slightly more female use drug-applied stents than male. Females also took more medicines than males at baseline, including ACEI/ARB (angiotensin-converting enzyme inhibitors/angiotensin receptor blockers), beta-blockers, and calcium channel blockers.

Table 2 shows the baseline characteristics of study subjects according to age group. Young patients seemed to have higher BMI, more hyperlipidemia disease, and more frequent smoking habits. Females tended to have worse lipid profiles compared with males in the same age categories. Younger patients of both sexes had less multivessel disease and a higher rate of taking medications except for thiazide diuretics. Both males and females had well-controlled lipid profiles and blood sugar.

After a mean period of 52.7 months of follow-up, 614 MACE cases were recorded, including 308 MIs, 120 ischemic strokes, and 224 cardiac deaths. In addition, 510 heart-failure hospitalizations and 1023 total CV events were identified (Table 3). Fig. 1 shows the Kaplan–Meier analysis survival results. Females were significantly associated with a higher risk of cardiac death (Fig. 1B), heart-failure hospitalization (Fig. 1D), MACE (Fig. 1E), and total CV events (Fig. 1F). After adjusting for comorbidities and revascularization procedures, women were associated with a significantly increased risk of cardiac death (HR, 1.78; 95% CI, 1.32-2.41; $p < 0.001$), Hospitalization for congestive heart failure (HR, 1.53; 95% CI, 1.23-1.89; $p < 0.001$), MACE (HR, 1.34; 95% CI, 1.10-1.63; $p = 0.003$), and total CV events (HR, 1.39; 95% CI, 1.20-1.62; $p < 0.001$) (Table 3).

Fig. 2 demonstrates the impact of sex differences in different endpoints according to age group. Females aged <60 years following PCI were especially associated with a significantly

Table 1

Baseline characteristics of the study population by sex (n = 6447)

	Male (n = 4833)	Female (n = 1614)	*p*
Age, y	68.19 ± 13.73	70.83 ± 10.63	<0.0001
Body mass index, kg/m^2	25.57 ± 4.16	25.38 ± 4.48	0.167
Systolic blood pressure, mmHg	129.43 ± 19.7	134.14 ± 21.4	<0.0001
Diastolic blood pressure, mmHg	73.86 ± 12.11	72.37 ± 12.3	<0.0001
Chronic disease			
Hypertension, n (%)	4140 (85.66%)	1438 (89.10%)	0.001
Diabetes mellitus, n (%)	1697 (35.11%)	824 (51.05%)	<0.0001
Acute coronary syndrome, n (%)	1964 (40.64%)	582 (36.06%)	0.001
Stroke, n (%)	262 (5.42%)	107 (6.63%)	0.070
PAOD, n (%)	211 (4.37%)	118 (7.31%)	<0.0001
Hyperlipidemia, n (%)	2011 (41.61%)	734 (45.48%)	0.007
Smoking, n (%)	1970 (40.76%)	107 (6.63%)	<0.0001
Uric acid, mg/dL	6.55 ± 1.85	6.21 ± 2.02	<0.0001
Total cholesterol, mg/dL	169.6 ± 39.45	180.6 ± 44.98	<0.0001
Triglyceride, mg/dL	133.73 ± 85.24	147.78 ± 87.08	<0.0001
HDL-C, mg/dL	41.57 ± 11.27	45.65 ± 13.6	<0.0001
LDL-C, mg/dL	105.24 ± 33.85	106.64 ± 37.15	0.207
Glucose, mg/dL	118.78 ± 39.8	132.75 ± 49.9	<0.0001
HbA1C,%	6.93 ± 1.36	7.29 ± 1.43	<0.001
Serum creatinine, mg/dL	1.52 ± 1.6	1.72 ± 1.99	<0.0001
eGFR, mL/min/1.73m^2	64.87 ± 25.95	55.07 ± 30.36	<0.0001
CAD severity			
SVD, n (%)	1373 (28.43%)	509 (32.01%)	0.02
DVD, n (%)	1541 (31.90%)	494 (31.07%)	
TVD, n (%)	1916 (39.67%)	587 (36.92%)	
Stent characteristics			
DES stent, n (%)	2569 (53.16%)	995 (61.65%)	<0.0001
BMS stent, n (%)	1634 (33.81%)	458 (28.38%)	<0.0001
Medications			
ACEI, n (%)	1033 (21.37%)	227 (14.06%)	<0.0001
ARB, n (%)	1583 (32.75%)	639 (39.59%)	<0.0001
Beta blocker, n (%)	2092 (43.29%)	778 (48.20%)	0.001
Calcium channel blocker, n (%)	1463 (30.27%)	619 (38.35%)	<0.0001
Statins, n (%)	2559 (52.95%)	865 (53.59%)	0.653
Diuretics Thiazide, n (%)	444 (9.19%)	187 (11.59%)	0.005

Values are n (%) or mean ± SD.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; BMS = bare metal stent; CAD = coronary artery disease; DES = drug eluting stent; DVD = double vessel disease; HDL = high-density lipoprotein; LDL = low density lipoprotein; PAOD = peripheral arterial occlusive disease; SVD = single vessel disease; TVD = triple vessel disease.

higher risk of MI (HR, 1.99; 95% CI, 1.08-3.66; $p = 0.028$), cardiac death (HR, 3.19; 95% CI, 1.28-7.95; $p = 0.013$), HF (HR, 2.86; 95% CI, 1.18-5.99; $p = 0.018$), MACE (HR, 2.01; 95% CI, 1.24-3.27; $p = 0.005$), and total CV events (HR, 2.24; 95% CI, 1.46-3.42; $p < 0.001$). Table 4 shows the clinical outcome of study subjects according to sex and age categories. Females aged >75 years were significantly associated with a risk of hospitalization for heart failure (HR, 1.43; 95% CI, 1.08-1.89; $p = 0.012$) and total CV events (HR, 1.35; 95% CI, 1.10-1.65; $p = 0.005$), and younger females with CAD at age <60 years were especially associated with higher cardiovascular risk including nonfatal MI; cardiac death and hospitalization for congestive heart failure, even after adjusting for successful PCI and comorbidities. MACE (HR, 2.01; 95% CI, 1.24-3.27; $p = 0.005$).

4. DISCUSSION

The main finding of this retrospective cohort study is that after a successful intervention, women with CAD were associated with an increased risk of future adverse clinical outcomes than men, including CV death, MACE, and total CV events. This was still true after adjustment for baseline characteristics, comorbidities, medications, treatment procedures, and severity of the coronary disease. Younger women (aged <60 years) were especially associated with a higher risk of developing future adverse cardiovascular outcomes compared with men, and the association of sex differences declined gradually with age, but women still had worse outcomes than men after coronary intervention.

There is a myth that cardiovascular disease is a "male disease," which needs to be discussed. In Europe, 56% of deaths in women and 43% in men are because of coronary heart disease, stroke, and other cardiovascular diseases.[20] The prognosis of women with chronic and acute coronary syndromes is worse than that of men.[21] In one study,[22] women who had acute coronary syndrome, especially STEMI, had higher mortality (9.6%) than men (5.3%). Women also tend to have poorer clinical outcomes than men after multivariable risk adjustment (adjusted odds ratio, 1.06; 95% CI, 0.99-1.15) in acute coronary syndrome.

Cenko et al[10] revealed that women who suffered STEMI aged under 60 years had higher early mortality risk (odds ratio, 1.88; 95% CI, 1.04-3.26; $p = 0.02$) than men after adjustment for medications, primary PCI, and other coexisting comorbidities. Above all, women (especially young women) have a higher risk of cardiovascular mortality than men do. The current study confirmed the observation that younger women (aged <60 years) were associated with worse outcomes than men. It is interesting that the association between poor PCI outcome and women declined with increasing age, but there was still a significant association with total CV events and congestive heart failure, even among women aged >75 years. In addition, our study did not find an association with the endpoint of stroke.

The occurrence of worse outcomes in clinical observations of women is very interesting. Although men have a higher prevalence of CAD, women with CAD usually have more comorbidities.[5,8,10] Women who have coronary heart disease seem to have more comorbidities, such as hypertension and diabetes mellitus (all $p < 0.001$).[23] Elizabeth et al[24] reported that women are more strongly associated with MI. In women, systolic blood pressure (HR, 1.09; 95% CI, 1.02-1.16), smoking status (HR, 1.55; 95% CI, 1.32-1.83), and DM (HR, 1.47; 95% CI, 1.16-1.87) were associated with higher HRs for MI compared with men.

In women with CAD, our data demonstrated a higher prevalence of risk factors, including HTN and DM. Furthermore, younger women with CAD (aged <60 years) smoked more, had more hyperlipidemia than women aged >60 years, and had worse clinical outcomes. This suggests that smoking habit and LDL profiles may contribute to the poor outcome in younger women with CAD. In addition, nearly 50% of young women with CAD (aged <60 years) had diabetes and unsatisfactory HbA1c control (HbA1c: 7.5 ± 1.7), which may also contribute to the risk in younger women with CAD.

In high-income, middle-income, and low-income countries, women tend to receive less secondary prevention treatment than men, such as cardiac investigation and coronary revascularization.[25] Pagidipati et al[26] revealed that women less frequently received pharmacological and invasive therapy when they suffered acute coronary syndromes. Our study shows that women with CAD also received fewer PCI procedures than men during follow-up (20.22% vs 14.13%; $p < 0.001$), but women took more medicines. After adjusting for coronary intervention procedures during the follow-up period, women still had worse outcomes, especially young women aged <60 years. This indicates that young women with CAD are a high-risk group, and aggressive medical treatment should be provided even after a successful PCI.

Table 2

Baseline characteristics of the study population in the different sex and age categories

	Male			Female			*p*
	<60	60–75	>75	<60	60–75	>75	
	(n = 1490)	(n = 1359)	(n = 1984)	(n = 234)	(n = 778)	(n = 602)	
Body mass index, kg/m^2	27.1 ± 4.8	25.7 ± 3.6	24.3 ± 3.5	26.4 ± 5.5	25.5 ± 4.4	24.8 ± 4.1	<0.0001
Systolic blood pressure, mmHg	127.3 ± 18.6	129.1 ± 18.7	131.3 ± 21.0	130.9 ± 21.6	135.0 ± 20.8	134.2 ± 22.1	<0.0001
Diastolic blood pressure, mmHg	78.4 ± 11.8	74.6 ± 11.5	69.9 ± 11.4	77.1 ± 12.3	73.0 ± 11.39	69.6 ± 12.8	<0.0001
Chronic disease							
Hypertension, n (%)	1259 (84.5)	1169 (86.02)	1712 (86.29)	200 (85.47)	713 (91.65)	525 (87.21)	0.0003
Diabetes mellitus, n (%)	464 (31.14)	546 (40.18)	687 (34.63)	112 (47.86)	416 (53.47)	296 (49.17)	<0.0001
Acute coronary syndrome, n (%)	663 (44.5%)	512 (37.7)	789 (39.7)	88 (37.6)	234 (30.1)	260 (43.2)	<0.0001
Stroke, n (%)	37 (2.48)	68 (5)	157 (7.91)	11 (4.7)	44 (5.66)	52 (8.64)	<0.0001
PAOD, n (%)	23 (1.54)	56 (4.12)	132 (6.65)	11 (4.7)	43 (5.53)	64 (10.63)	<0.0001
Hyperlipidemia, n (%)	749 (50.27)	582 (42.83)	680 (34.27)	121 (51.71)	375 (48.2)	238 (39.53)	<0.0001
Smoking, n (%)	666 (44.7)	543 (39.96)	761 (38.36)	26 (11.11)47	43 (5.53)	38 (6.31)	<0.0001
Uric acid, mg/dL	6.5 ± 1.7	6.4 ± 1.8	6.7 ± 2.0	6.1 ± 2.0	6.1 ± 1.9	6.5 ± 2.2	<0.0001
Total cholesterol, mg/dL	178.4 ± 44.6	169.5 ± 38.8	163.2 ± 38.8	193.0 ± 49.0	182.3 ± 47.0	173.1 ± 38.7	<0.0001
Triglyceride, mg/dL	161.7 ± 98.0	134.7 ± 83.4	112.7 ± 69.0	167.1 ± 98.6	152.0 ± 89.2	134.1 ± 76.6	<0.0001
HDL-C, mg/dL	39.5 ± 10.1	41.3 ± 10.9	43.2 ± 12.1	46.1 ± 13.6	46.1 ± 13.5	44.9 ± 13.8	<0.0001
LDL-C, mg/dL	112.7 ± 36.9	104.0 ± 34.4	100.6 ± 30.0	116.3 ± 40.4	108.0 ± 38.3	100.8 ± 33.0	<0.0001
Glucose, mg/dL	120.9 ± 43.6	119.3 ± 39.4	117.1 ± 37.4	139.9 ± 60.3	132.0 ± 48.6	130.6 ± 46.4	<0.0001
eGFR, mL/min/1.73m^2	76.6 ± 25.2	65.3 ± 25.6	55.9 ± 23.1	69.7 ± 41.8	56.8 ± 28.8	47.1 ± 23.95	<0.0001
HbA1C, %	7.1 ± 1.5	6.9 ± 1.3	6.8 ± 1.2	7.5 ± 1.7	7.4 ± 1.5	7.0 ± 1.3	<0.0001
Serum creatinine, mg/dL	1.4 ± 1.6	1.6 ± 1.6	1.7 ± 1.3	1.7 ± 2.2	1.7 ± 1.9	1.8 ± 1.6	<0.0001
eGFR, mL/min/1.73m^2	76.6 ± 25.2	65.3 ± 25.6	55.9 ± 23.1	69.7 ± 41.8	56.8 ± 28.8	47.1 ± 23.95	<0.0001
CAD							
SVD, n (%)	532 (35.7)	368 (27.08)	473 (23.84)	93 (39.74)	253 (35.52)	163 (27.08)	<0.0001
DVD, n (%)	495 (33.22)	432 (31.79)	614 (30.95)	71 (30.34)	249 (32.01)	174 (28.9)	0.4826
TVD, n (%)	460 (30.87)	559 (41.1)	897 (45.21)	68 (29.06)	263 (33.8)	256 (42.52)	<0.0001
Stent characteristics							
DES Stent, n (%)	880 (59.06)	814 (59.9)	875 (44.1)	140 (59.83)	483 (62.08)	372 (61.79)	<0.0001
BMS Stent, n (%)	422 (28.32)	391 (28.77)	821 (41.38)	63 (26.92)	201 (25.84)A	194 (32.23)	<0.0001
Medications							
ACEI, n (%)	426 (28.59)	276 (20.31)	331 (16.68)	39 (16.67)	105 (13.5)	83 (13.79)	<0.0001
ARB, n (%)	431 (28.93)	483 (35.54)	669 (33.72)	85 (36.32)	315 (40.49)	239 (39.7)	<0.0001
Beta blocker, n (%)	773 (51.88)	604 (44.44)	715 (36.04)	135 (57.69)	379 (48.71)	264 (43.85)	<0.0001
Calcium channel blocker, n (%)	356 (23.89)	415 (30.54)	692 (34.88)	82 (35.04)	321 (41.26)	216 (35.88)	<0.0001
Statins, n (%)	987 (66.24)	736 (54.16)	836 (42.14)	140 (59.83)	424 (54.5)	301 (50)	<0.0001
Diuretics, n (%)	73 (4.9)	114 (8.39)	257 (12.95)	21 (8.97)	86 (11.05)	80 (13.29)	<0.0001

Values are n (%) or mean ± SD.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; BMS = bare metal stent; CAD = coronary artery disease; DES = drug eluting stent; DVD = double vessel disease; HDL = high-density lipoprotein; LDL = low density lipoprotein; PAOD = peripheral arterial occlusive disease; SVD = single vessel disease; TVD = triple vessel disease.

Table 3

Clinical outcome in study population according to sex categories

	Male		Female		Model 1		Model 2		Model 3	
	n (%)	Event Rate /100 Pt-Yrs	n (%)	Event Rate /100 Pt-Yrs	HR 95%CI	*p*	HR 95%CI	*p*	HR 95%CI	*p*
MI	235 (4.86%)	1.12	73 (4.52%)	1.18	1.04 (0.80–1.35)	0.778	1.26 (0.95–1.68)	0.114	1.24 (0.93–1.65)	0.139
Stroke	92 (1.90%)	0.43	28 (1.73%)	0.44	1.04 (0.68–1.59)	0.847	1.06 (0.67–1.67)	0.798	1.05 (0.67–1.64)	0.845
Cardiac death	146 (3.02%)	0.68	78 (4.83%)	1.23	1.68 (1.28–2.21)	0.000	1.84 (1.36–2.48)	0.000	**1.78 (1.32–2.41)**	**<0.001**
HF	370 (7.66%)	1.79	140 (8.67%)	2.33	1.26 (1.04–1.54)	0.018	1.51 (1.22–1.88)	0.000	**1.53 (1.23–1.89)**	**<0.001**
Revascularization	977 (20.22%)	5.42	228 (14.13%)	4.03	0.73 (0.64-0.85)	<0.001	0.77 (0.66-0.90)	0.001	0.98 (0.84-1.15)	0.816
MACE	450 (9.31%)	2.17	164 (10.16%)	2.67	1.20 (1.00–1.43)	0.051	1.37 (1.13–1.67)	0.002	**1.34 (1.10–1.63)**	**0.003**
Total CV event	748 (15.48%)	3.75	275 (17.04%)	4.75	1.22 (1.07–1.41)	0.004	1.42 (1.22–1.65)	0.000	**1.39 (1.20–1.62)**	**<0.001**

MI = nonfatal myocardial infarction; Stroke = nonfatal stroke; HF = Hospitalization for congestive heart failure.

MACE includes nonfatal MI, nonfatal stoke and cardiac death.

Total CV events includes MACE plus hospitalization for CHF.

The hazard ratio is for the female as compare with the male.

Model 1: Crude hazard ratio.

Model 2: adjusted with history of hypertension, diabetes, smoke.

Model 3: adjusted with history of hypertension, diabetes, smoke, and revascularization.

CHF = congestive heart failure; CV = cardiovascular; MI = nonfatal myocardial infarction; MACE = major cardiovascular events.

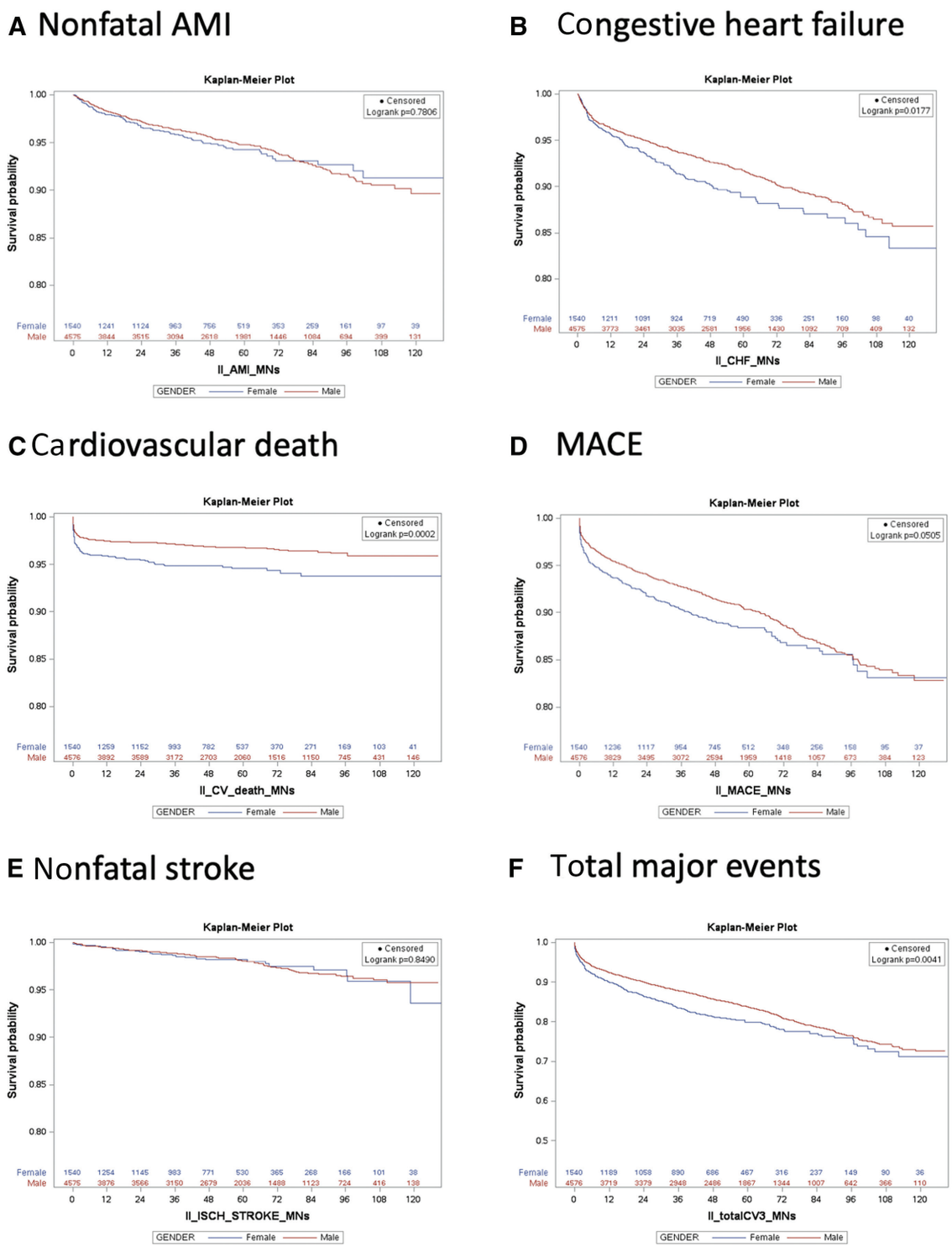

Fig. 1 Kaplan–Meier survival curve analysis showing (A) cardiovascular death, (B) nonfatal MI, (C) nonfatal stroke, (D) congestive heart failure, (E) MACE, and (F) total major events. MACE = major cardiovascular events; MI = myocardial infarction.

This study has several limitations that should be mentioned. First, although we studied more than 5000 patients, this was still a single-center retrospective observational registry, which raises the potential for selection bias. Second, data were not collected on baseline cardiac function, angiographic characteristics, smoking duration, insulin dose, cancer type, and so on. Our results may not be applied to patients who had CAD but had contraindications or relative contraindications for PCI because of critical combined illnesses or unsuitable conditions.

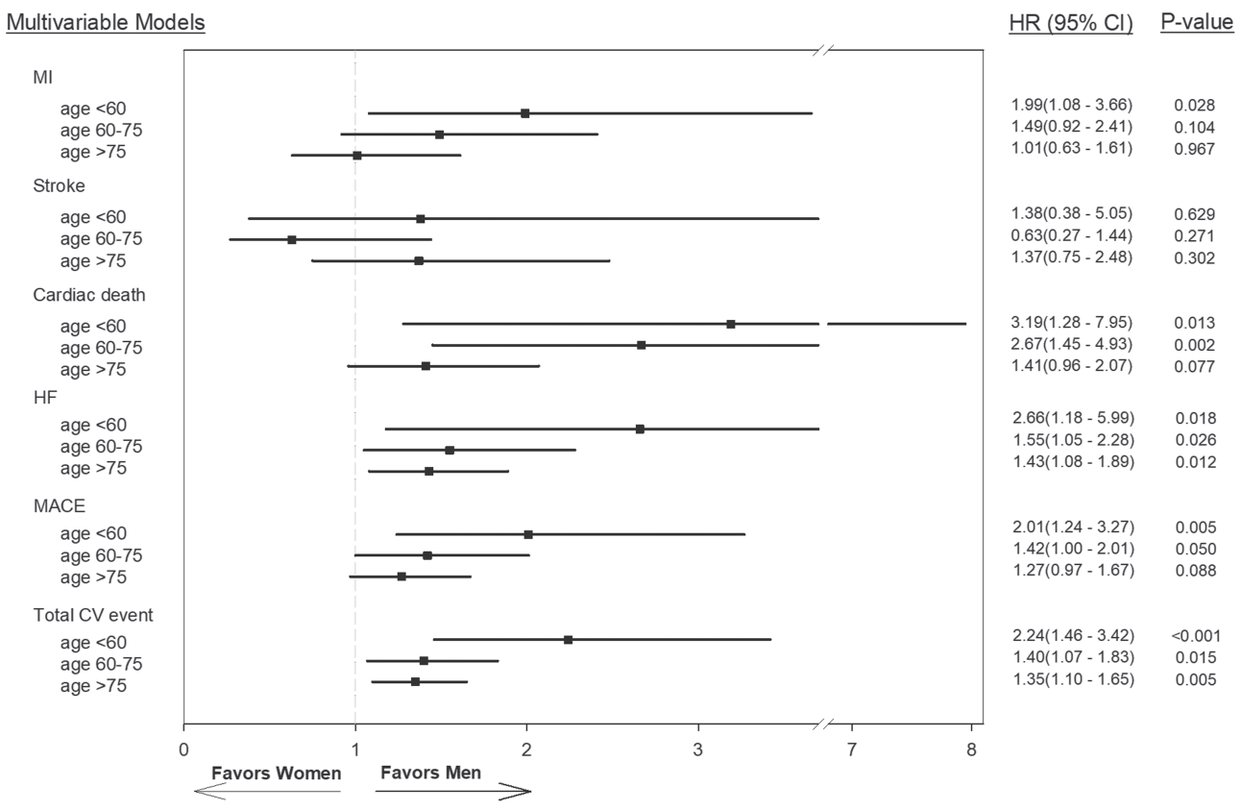

Fig. 2 Subgroup analysis of the predictive value aged <60 years, aged 60–75 years, and aged >75 years for future events in CAD patients. (a) Cardiovascular death, (b) nonfatal MI, (c) nonfatal stroke, (d) congestive heart failure, (e) MACE, and (f) total major events. CAD = coronary artery disease; MACE = major cardiovascular events; MI = myocardial infarction.

Third, our database did not record full-course mortality or noncardiac deaths, so we cannot provide relevant information to assess gender differences. Besides, post-PCI complications, such as hematoma at the femoral artery, pseudoaneurysm or arteriovenous (AV) fistula, infection, bleeding, renal damage from contrast dye, and so on, were not recorded initially. To fill this knowledge gap, further research is needed. Finally, our study was an observational cohort study not an intervention trial. Thus, a rehabilitation program was not included, and the impact of the cardiac rehabilitation was not estimated.

After successful PCI, younger women (aged <60 years) were especially associated with a higher risk of developing future adverse cardiovascular outcomes compared with men. Furthermore, the association of sex differences declined gradually with age. However, women still had worse outcomes than men after coronary intervention.

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Table 4

Clinical outcome in study population according to sex and age categories

	Male		Female		Model 1		Model 2		Model 3	
	n (%)	Event Rate /100 Pt-Yrs	n (%)	Event Rate /100 Pt-Yrs	HR 95%CI	*p*	HR 95%CI	*p*	HR 95%CI	*p*
PCI at age <60										
MI	59 (3.96%)	0.87	15 (6.41%)	1.47	1.67 (0.95–2.95)	0.076	2.01 (1.09–3.70)	**0.025**	1.99 (1.08–3.66)	**0.028**
Stroke	18 (1.21%)	0.26	3 (1.28%)	0.28	1.09 (0.32–3.70)	0.891	1.34 (0.37–4.90)	0.660	1.38 (0.38–5.05)	0.629
Cardiac death	21 (1.41%)	0.30	8 (3.42%)	0.75	2.41 (1.07–5.44)	0.034	3.23 (1.29–8.06)	**0.012**	3.19 (1.28–7.95)	**0.013**
HF	32 (2.15%)	0.47	9 (3.85%)	0.86	1.81 (0.86–3.79)	0.116	2.66 (1.18–5.98)	**0.018**	2.66 (1.18–5.99)	**0.018**
MACE	95 (6.38%)	1.41	24 (10.26%)	2.38	1.65 (1.05–2.58)	0.028	2.01 (1.24–3.27)	**0.005**	2.01 (1.24–3.27)	**0.005**
Total CV event	123 (8.26%)	1.85	32 (13.68%)	3.25	1.72 (1.16–2.53)	0.007	2.24 (1.46–3.42)	**0.000**	2.24 (1.46–3.42)	**0.000**
PCI at age 60-75										
MI	61 (4.49%)	0.98	34 (4.37%)	1.06	1.06 (0.70–1.62)	0.775	1.45 (0.90–2.35)	0.127	1.49 (0.92–2.41)	0.104
Stroke	31 (2.28%)	0.49	8 (1.03%)	0.25	0.52 (0.24–1.13)	0.099	0.64 (0.28–1.48)	0.297	0.63 (0.27–1.44)	0.271
Cardiac death	26 (1.91%)	0.41	28 (3.60%)	0.85	1.98 (1.16–3.38)	0.012	2.74 (1.48–5.05)	**0.001**	2.67 (1.45–4.93)	**0.002**
HF	83 (6.11%)	1.34	56 (7.20%)	1.78	1.31 (0.93–1.84)	0.122	1.55 (1.06–2.28)	**0.025**	1.55 (1.05–2.28)	**0.026**
MACE	113 (8.31%)	1.84	62 (7.97%)	1.95	1.04 (0.77–1.42)	0.785	1.42 (1.00–2.02)	**0.048**	1.42 (1.00–2.01)	**0.050**
Total CV event	183 (13.47%)	3.07	105 (13.50%)	3.45	1.10 (0.87–1.40)	0.425	1.41 (1.08–1.84)	**0.013**	1.40 (1.07–1.83)	**0.015**
PCI at age >75										
MI	115 (5.80%)	1.45	24 (3.99%)	1.22	0.83 (0.54–1.30)	0.418	0.98 (0.61–1.56)	0.934	1.01 (0.63–1.61)	0.967
Stroke	43 (2.17%)	0.53	17 (2.82%)	0.86	1.62 (0.92–2.85)	0.092	1.47 (0.81–2.66)	0.204	1.37 (0.75–2.48)	0.302
Cardiac death	99 (4.99%)	1.20	42 (6.98%)	2.10	1.54 (1.07–2.20)	0.020	1.51 (1.03–2.22)	0.035	1.41 (0.96–2.07)	0.077
HF	255 (12.85%)	3.33	75 (12.46%)	4.13	1.18 (0.91–1.53)	0.213	1.46 (1.10–1.92)	**0.008**	1.43 (1.08–1.89)	**0.012**
MACE	242 (12.20%)	3.08	78 (12.96%)	4.01	1.23 (0.95–1.59)	0.108	1.30 (0.99–1.70)	0.060	1.27 (0.97–1.67)	0.088
Total CV event	442 (22.28%)	6.00	138 (22.92%)	7.83	1.23 (1.01–1.49)	0.036	1.37 (1.12–1.69)	**0.002**	1.35 (1.10–1.65)	**0.005**

MI = nonfatal myocardial infarction; Stroke = nonfatal stroke; HF = Hospitalization for congestive heart failure.

MACE includes nonfatal MI, nonfatal stoke and cardiac death.

Total CV events includes MACE plus hospitalization for CHF.

The hazard ratio is for the female as compare with the male.

Model 1: Crude hazard ratio.

Model 2: adjusted with history of hypertension, diabetes, smoke.

Model 3: adjusted with history of hypertension, diabetes, smoke, and revascularization.

CHF = congestive heart failure; CV = cardiovascular; MI = nonfatal myocardial infarction; MACE = major cardiovascular events.

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