



## Gender differences in clinical outcomes of acute myocardial infarction undergoing percutaneous coronary intervention: insights from the KAMIR-NIH Registry

Myunhee Lee<sup>1</sup>, Dae-Won Kim<sup>1,†</sup>, Mahn-Won Park<sup>1</sup>, Kyusup Lee<sup>1</sup>, Kiyuk Chang<sup>2</sup>, Wook Sung Chung<sup>2</sup>, Tae Hoon Ahn<sup>3</sup>, Myung Ho Jeong<sup>4</sup>, Seung-Woon Rha<sup>5</sup>, Hyo-Soo Kim<sup>6</sup>, Hyeon Cheol Gwon<sup>6</sup>, In Whan Seong<sup>7</sup>, Kyung Kuk Hwang<sup>8</sup>, Shung Chull Chae<sup>9</sup>, Kwon-Bae Kim<sup>10</sup>, Young Jo Kim<sup>11</sup>, Kwang Soo Cha<sup>12</sup>, Seok Kyu Oh<sup>13</sup>, Jei Keon Chae<sup>14</sup>, Ji-Hoon Jung<sup>15</sup>; on behalf of KAMIR-NIH registry investigators

<sup>1</sup>Division of Cardiology, Daejeon St. Mary's hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

<sup>2</sup>Division of Cardiology, Seoul St. Mary's hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

<sup>3</sup>Gachon University, Gil Medical Center, Incheon, South Korea

<sup>4</sup>Chonnam National University Hospital, Gwangju, South Korea d Korea University

<sup>5</sup>Korea University Guro Hospital, Seoul, South Korea

<sup>6</sup>Seoul National University Hospital, Seoul, South Korea

<sup>7</sup>Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea

<sup>8</sup>Chungnam National University Hospital, Daejeon, South Korea

<sup>9</sup>Chungbuk National University Hospital, Cheongju, South Korea

<sup>10</sup>Kyungpook National University Hospital, Daegu, South Korea

<sup>11</sup>Keimyung University Dongsan Medical Center, Daegu, South Korea

<sup>12</sup>Yeungnam University Hospital, Daegu, South Korea

<sup>13</sup>Pusan National University Hospital, Busan, South Korea

<sup>14</sup>Wonkwang University Hospital, Iksan, South Korea

<sup>15</sup>Chonbuk National University Hospital, Jeonju, South Korea

<sup>16</sup>Institute of Toxicology, Daejeon, South Korea

### Abstract

**Background** There are numerous but conflicting data regarding gender differences in outcomes following percutaneous coronary intervention (PCI). Furthermore, gender differences in clinical outcomes with acute myocardial infarction (AMI) following PCI in Asian population remain uncertain because of the under-representation of Asian in previous trials. **Methods** A total of 13,104 AMI patients from Korea Acute Myocardial Infarction Registry-National Institute of Health (KAMIR-NIH) between November 2011 and December 2015 were classified into male ( $n = 8021$ , 75.9%) and female ( $n = 2547$ , 24.1%). We compared the demographic, clinical and angiographic characteristics, 30-days and 1-year major adverse cardiac and cerebrovascular events (MACCE) in women with those in men after AMI by using propensity score (PS) matching. **Results** Compared with men, women were older, had more comorbidities and more often presented with non-ST segment elevation myocardial infarction (NSTEMI) and reduced left ventricular systolic function. Over the median follow-up of 363 days, gender differences in both 30-days and 1-year MACCE as well as thrombolysis in myocardial infarction minor bleeding risk were not observed in the PS matched population (30-days MACCE: 5.3% vs. 4.7%, log-rank  $P = 0.494$ , HR = 1.126, 95% CI: 0.800–1.585; 1-year MACCE: 9.3% vs. 9.0%, log-rank  $P = 0.803$ , HR = 1.032, 95% CI: 0.802–1.328; TIMI minor bleeding: 4.9% vs. 3.9%, log-rank  $P = 0.215$ , HR = 1.255, 95% CI: 0.869–1.814). **Conclusions** Among Korean AMI population undergoing contemporary PCI, women, as compared with men, had different clinical and angiographic characteristics but showed similar 30-days and 1-year clinical outcomes. The risk of bleeding after PCI was comparable between men and women during one-year follow up.

*J Geriatr Cardiol* 2020; 17: 680–693. doi:10.11909/j.issn.1671-5411.2020.11.006

**Keywords:** Acute myocardial infarction; Asian population; Gender difference; Percutaneous coronary intervention

<sup>†</sup>Correspondence to: mirinesilver@catholic.ac.kr. Received: August 25, 2020; Revised: November 8, 2020; Accepted: November 27, 2020; Published online: November 28, 2020

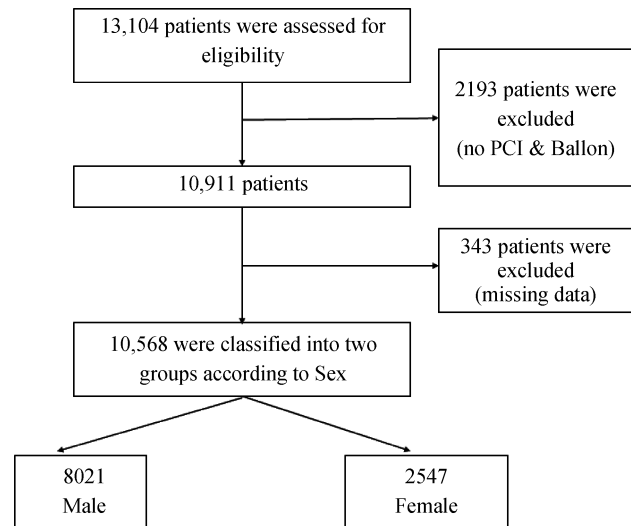
## 1 Introduction

Over the past decade, despite remarkable advances in medical and interventional therapeutics, ischemic heart disease (IHD) remains the leading cause of death worldwide and its prevalence is still increasing and becoming a major cause of morbidity and mortality.<sup>[1]</sup> Although the overall IHD mortality has declined over the past decade, the rate of decline for women compared with men has been slower in United States as well as in Korea, raising considerable interest about gender differences in clinical outcomes following IHD.<sup>[1,2]</sup> Percutaneous coronary intervention (PCI) is the cornerstone of improving outcomes in acute myocardial infarction. But there is still ongoing debate over the gender differences in outcomes after PCI. Previous studies have shown that female has worse clinical outcomes following PCI compared with male,<sup>[3-7]</sup> However, after adjustment of confounding variables (such as age, comorbidities and procedure characteristics), sex disparities in outcomes after PCI have showed inconclusive or negative results.<sup>[8-16]</sup> Owing to increased public awareness campaigns targeting women such as the American Heart Association's *Go red* campaign, a decrease in gender gap in the treatment, implementation of evidence-based pharmacologic therapies and the development of new interventional technologies, it is unclear whether the gender differences after PCI in AMI setting are still present in contemporary era. Therefore, we conducted this study to examine the association between sex and clinical outcomes after PCI among AMI patients using real world population in the current era.

## 2 Methods

### 2.1 Study design and patient population

The data were obtained from the database of the Korea Acute Myocardial Infarction Registry–National Institutes of Health (KAMIR-NIH). The KAMIR-NIH is a prospective, multi-center, web-based observational cohort study to develop the prognostic and surveillance index of Korean patients with AMI from 15 centers in Korea and was supported by a grant of Korea Centers for Disease Control and Prevention from May 2010 to June 2015. The study flow chart is displayed in Figure 1. Initially, 13,104 patients were included in this analysis. Among them, 2,193 patients who did not undergo PCI and 343 patients with missing data were excluded. The remaining 10,568 patients with AMI performing successful PCI were categorized into two groups according to sex (male: 8021 (75.9%), female: 2547 (24.1%)). All participated centers are high-volume centers for coronary angiography (CAG) with PCI and have used the same



**Figure 1. Study population.** PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty.

study protocol. This study was approved by the institutional review board (IRB) of each participating institution and was conducted according to the Declaration of Helsinki. Written informed consent was obtained from all participants. Trained study coordinators at each participating institution collected the data using a standardized format. Standardized definitions of all variables were determined by steering committee board of KAMIR-NIH.

### 2.2 PCI procedure and medical treatment

CAG and PCI were performed according to the standard guidelines at the time of procedure.<sup>[17]</sup> Antiplatelet therapy and administration of periprocedural anticoagulation were administered in accordance with the standard regimens. Aspirin (loading dose, 200 mg) plus clopidogrel (loading dose, 300 or 600 mg) or ticagrelor (loading dose 180 mg) or prasugrel (loading dose 60 mg) were prescribed for all patients before or during PCI. After the procedure, aspirin (100–200 mg/day) was maintained indefinitely. Patients with drug-eluting stent (DES) were prescribed clopidogrel (75 mg/day), ticagrelor (90 mg twice/day), prasugrel (10 mg/day) for at least 12 months. The choice of procedural applications related to PCI such as pre-dilation, direct stenting, post-adjunct balloon inflation, use of imaging devices (e.g., intravascular ultrasound, optical coherence tomography, fractional flow reserve), and administration of glycoprotein IIb/IIIa-receptor blockers and the cardiac medications were left to the discretion of the treating physician.

### 2.3 Definitions

The diagnosis of AMI was based on the detection of a raise and/or fall of cardiac biomarkers (creatine kinase-my-

cardiac band (CK-MB) and troponin I or T) with at least one value above the 99<sup>th</sup> percentile upper reference limit and with at least one of the following: symptoms of ischemia, new ischemic ECG changes, development of pathological Q waves, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology.<sup>[18]</sup> Diabetes mellitus (DM) was defined as a fasting glucose concentration of  $\geq 7.0$  mmol/L, a blood glucose concentration of  $\geq 11.0$  mmol/L on a 75 g, 2 h oral glucose tolerance test, or the use of antidiabetic therapy. Hypertension (HTN) was defined as a history of a systolic blood pressure of  $\geq 140$  mmHg, a diastolic pressure of  $\geq 90$  mmHg, or the use of antihypertensive therapy. Dyslipidemia was defined as a fasting total cholesterol concentration of  $\geq 220$  mg/dL, a fasting triglyceride concentration of  $\geq 150$  mg/dL, or the use of antihyperlipidemic therapy. Chronic kidney disease (CKD) was defined as a glomerular filtration on admission of  $< 60$  mL/min per  $1.73$  m<sup>2</sup>. The glomerular filtration rate was calculated according to the abbreviated Modification of Diet and Renal Disease Study formula.<sup>[19]</sup>

#### 2.4 Primary and secondary endpoints

The primary endpoint was a one year major adverse cardiac and cerebrovascular events (MACCE), composite of cardiac death (CD), myocardial infarction (MI), target vessel revascularization (TVR) and cerebrovascular accident (CVA). All deaths were considered as cardiac unless an unequivocal non-cardiac cause was established. CD was defined as any death due to a proximate cardiac cause such as MI, low-output failure, arrhythmia, unwitnessed death and all procedure-related deaths, including those related to concomitant treatment.<sup>[20]</sup> MI was defined as newly developed Q wave, raised CK-MB, troponin I or T above the normal ranges, typical ischemic symptom accompanied with ST elevation. TVR was defined as percutaneous or surgical revascularization of the stented lesion including 5 mm margin segments and more proximal or distal, newly developed lesion. CVA were defined as a stroke or cerebrovascular accident with loss of neurological function caused by an ischemic or hemorrhagic event with residual symptoms at least 24 h after onset or leading to death. The secondary endpoints were all-cause death, heart failure, stent thrombosis and thrombolysis in myocardial infarction (TIMI) major and minor bleeding<sup>[21]</sup> at one year. Heart failure was defined as sudden worsening of the signs and symptoms of heart failure, which was measured as a left ventricular ejection fraction (LVEF) of less than 40% during follow-up. Stent thrombosis was evaluated according to the Academic Research Consortium Definitions.<sup>[22]</sup> TIMI minor bleeding was defined as overt clinical bleeding associated with a fall

in hemoglobin of 3% to less than or equal to 5 g/dL or in hematocrit of 9% to less than or equal to 15% (absolute). All adverse events were confirmed through the source documents, including medical records and telephone interviews, and were also adjudicated by the Steering Committee of Chonnam National University Hospital.

#### 2.5 Statistical analyses

Continuous variables are expressed as mean  $\pm$  SD and categorical data are presented as absolute values and percentages. Differences between the groups of categorical variables were analyzed by chi-square or Fisher exact test as appropriate and differences between the groups of continuous variables were analyzed by the 2-tailed Student's *t* test. The incidences of the primary endpoints according to sex were estimated at 12 months and were displayed in tables and Kaplan-Meier curves. The log-rank test was performed to compare the incidences of the endpoints between the groups. Based on the significant variables ( $P < 0.05$ ), propensity score (PS) analysis was performed to reduce bias due to confounding variables. Baseline demographic, clinical and angiographic characteristics were compared within the PS matched group. PS was computed by non-parsimonious multiple logistic regression analysis (C-statistics = 0.927). Matching was performed with the use of a 1:1 nearest neighbor matching, from initial 7 to 1 digit. We confirmed the model reliability with goodness of-fit test ( $P = 0.273$ ). In the matched cohort, paired comparisons were performed with the use of McNemar's test for binary variables and a paired *t*-test for continuous variables. All analyses were two-tailed, and clinical significance was defined as  $P < 0.05$ . All statistical analyses were performed using a Statistical Analysis Software (SAS, version 9.4, SAS Institute, Cary, NC, USA).

### 3 Results

From May 2010 to June 2015, a total 10,568 patients with AMI at 15 medical centers in Korea who underwent successful revascularization were enrolled in this analysis.

#### 3.1 Baseline characteristics of study population

Baseline demographic, clinical and laboratory characteristics were significantly different between sexes (Table 1). Compared with men, women were significantly older ( $71.8 \pm 10.1$  vs.  $60.7 \pm 11.9$  years,  $P < 0.001$ ), more likely to have DM, HTN and CKD, which were known risk factors of coronary artery disease (CAD). At the time of AMI presentation, women were more frequently presented with non-ST-segment elevation myocardial infarction (NSTEMI), severe left ventricular (LV) systolic dysfunction (LVEF  $\leq$

**Table 1. Baseline demographic, clinical and laboratory characteristics in AMI patients in Crude and Propensity Score matched Population.**

Characteristics	Overall		P-value	Standardized difference	PSM		P-value	Standardized difference
	Male (n = 8021)	Female (n = 2547)			Male (n = 1317)	Female (n = 1317)		
Age, yrs	60.7 ± 11.9	71.8 ± 10.1	< 0.001	1.014	69.0 ± 10.3	68.9 ± 10.8	0.883	-0.006
BMI, kg/m <sup>2</sup>	24.3 ± 3.2	23.3 ± 3.6	< 0.001	-0.285	23.4 ± 3.0	23.7 ± 3.7	0.098	0.065
Killip classification								
I	6579 (82.0%)	1864 (73.2%)	< 0.001	0.247	971 (73.7%)	971 (73.7%)	0.239	0.0752
II	588 (7.3%)	267 (10.5%)			118 (9.0%)	135 (10.3%)		
III	426 (5.3%)	278 (10.9%)			130 (9.9%)	134 (10.2%)		
IV	428 (5.3%)	138 (5.4%)			98 (7.4%)	77 (5.8%)		
Clinical presentation								
NSTEMI	3686 (46.0%)	1377 (54.1%)	< 0.001	-0.163	693 (52.6%)	690 (52.4%)	0.938	0.0046
STEMI	4335 (54.0%)	1170 (45.9%)			624 (47.4%)	627 (47.6%)		
Family history of CAD	591 (7.4%)	107 (4.2%)	< 0.001	-0.136	70 (5.3%)	64 (4.9%)	0.654	-0.0210
Diabetes	2023 (25.2%)	896 (35.2%)	< 0.001	0.218	441 (33.5%)	456 (34.6%)	0.555	0.0240
Hypertension	3558 (44.4%)	1696 (66.6%)	< 0.001	0.459	800 (60.7%)	792 (60.1%)	0.771	-0.012
Dyslipidemia	909 (11.3%)	291 (11.4%)	0.898	0.003	125 (9.5%)	156 (11.8%)	0.059	0.076
Smoking	6039 (75.3%)	264 (10.4%)	< 0.001	-1.738	241 (18.3%)	264 (20.0%)	0.115	0.044
CKD	1131 (14.1%)	748 (29.4%)	< 0.001	0.377	368 (27.9%)	336 (25.5%)	0.177	-0.055
Previous MI	488 (6.1%)	126 (4.9%)	0.033	-0.050	81 (6.2%)	78 (5.9%)	0.868	-0.010
Prior HF	255 (3.2%)	172 (6.8%)	< 0.001	0.165	73 (5.5%)	92 (7.0%)	0.143	0.0600
Previous PCI	658 (8.2%)	194 (7.6%)	0.343	-0.022	121 (9.2%)	104 (7.9%)	0.261	-0.046
Atrial fibrillation	360 (4.5%)	122 (4.8%)	0.525	0.014	85 (6.5%)	64 (4.9%)	0.096	-0.069
Prior CVA	432 (5.4%)	208 (8.2%)	< 0.001	0.111	108 (8.2%)	106 (8.0%)	0.943	-0.006
HbA1c	6.5% ± 1.5%	6.6% ± 1.5%	< 0.001	0.082	6.5% ± 1.5%	6.5% ± 1.6%	0.838	0.008
NT-proBNP, pg/mL	1493.6 ± 4788.3	3754.9 ± 6480.1	< 0.001	0.397	3186.1 ± 6188.5	3545.8 ± 6435.8	0.133	0.057
Hb, g/dL	14.5 ± 1.9	12.3 ± 1.7	< 0.001	-1.197	12.9 ± 2.0	12.8 ± 1.8	0.062	-0.065
hsCRP, mg/L	1.1 ± 3.1	1.7 ± 3.4	< 0.001	0.174	1.6 ± 3.7	1.7 ± 3.4	0.457	0.029
Total cholesterol, mg/dL	180.2 ± 44.1	181.9 ± 48.6	0.479	0.038	174.2 ± 46.7	175.0 ± 47.9	0.646	0.017
Triglyceride, mg/dL	140.4 ± 127.4	120.4 ± 100.3	< 0.001	-0.175	118.9 ± 125.8	120.6 ± 102.5	0.694	0.015
LDL cholesterol, mg/dL	114.2 ± 39.0	114.9 ± 41.8	0.829	0.016	108.2 ± 38.9	109.2 ± 41.0	0.475	0.027
HDL cholesterol, mg/dL	41.9 ± 11.3	44.9 ± 13.1	< 0.001	0.245	43.3 ± 13.0	43.8 ± 11.7	0.328	0.037
Aspirin	8012 (99.9%)	2545 (99.9%)	> 0.999	0.011	1314 (99.8%)	1315 (99.8%)	> 0.999	0.0174
Clopidogrel	6024 (75.1%)	2135 (83.8%)	< 0.001	0.217	1094 (83.1%)	1082 (82.2%)	0.574	-0.024
Ticagrelor/prasugrel	3078 (38.4%)	707 (27.8%)	< 0.001	-0.227	397 (30.1%)	398 (30.2%)	> 0.999	0.002
β-blocker	6829 (85.1%)	2128 (83.5%)	0.052	-0.044	1059 (80.4%)	1079 (81.9%)	0.339	0.039
Calcium channel blocker	434 (5.4%)	153 (6.0%)	0.252	0.026	86 (6.5%)	86 (6.5%)	> 0.999	0.000
ACE inhibitor/ARB	6462 (80.6%)	2024 (79.5%)	0.225	-0.027	1024 (77.8%)	1030 (78.2%)	0.809	0.011
Statin	7518 (93.7%)	2330 (91.5%)	< 0.001	-0.086	1184 (89.9%)	1190 (90.4%)	0.745	0.015
Oral anticoagulant	195 (2.4%)	69 (2.7%)	0.434	0.018	36 (2.7%)	37 (2.8%)	> 0.999	0.005
GpIIb-IIIa inhibitor	1294 (16.1%)	307 (12.1%)	< 0.001	-0.117	160 (12.1%)	174 (13.2%)	0.445	0.032
LVEF ≤ 40%	1137 (14.2%)	449 (17.6%)	< 0.001	0.095	253 (19.2%)	252 (19.1%)	> 0.999	-0.003
LVEF	52.2% ± 10.6%	51.4% ± 11.3%	0.003	-0.071	51.4% ± 11.1%	50.9% ± 11.5%	0.229	-0.046

Data are presented as mean ± SD, median (interquartile range), or n (%) where appropriate. ACE inhibitor: angiotensin-converting enzyme inhibitor; AMI: acute myocardial infarction; ARB: angiotensin receptor blocker; BMI: body mass index; CAD: coronary artery disease; CKD: chronic kidney disease; CVA: cerebrovascular accident; GpIIb-IIIa inhibitor: glycoprotein IIb/IIIa inhibitor; Hb: hemoglobin; HbA1c: glycated hemoglobin; HDL: high-density lipoprotein; HF: heart failure; hsCRP: high sensitivity C-reactive protein; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; NSTEMI: non-ST-segment elevation myocardial infarction; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; PCI: percutaneous coronary intervention; PSM: propensity score matching; STEMI: ST-segment elevation myocardial infarction.

40%, 17.6% vs. 14.2%), had a higher incidence of a Killip class  $\geq$  II, showed a higher level of proBNP and had lower hemoglobin. More women had a prior history of heart failure and CVA whereas men had a higher percentage of history of previous MI. During the index AMI hospitalization, women were treated more often with potent P2Y12 inhibitor (such as prasugrel and ticagrelor), while men more frequently received glycoprotein IIb/IIIa inhibitors. At discharge, both men and women were prescribed with similar percentage of antiplatelet agents,  $\beta$ -blocker and RAAS (renin angiotensin aldosterone system) inhibitors. There was no difference of baseline low-density lipoprotein cho-

lesterol level between sexes whereas women had a slightly higher baseline high sensitivity C-reactive protein (hsCRP) level than men, but the mean hsCRP level was less than 2 mg/L at baseline in both groups. There were also significant differences in baseline angiographic characteristics between men and women as displayed in Table 2. The most common infarct-related artery was the left anterior descending artery (LAD) and women showed relatively higher proportion of LAD in target vessels and higher rates of multi-vessel diseases. But there were no significant differences in the total number of stents and stent lengths between men and women.

**Table 2. Baseline angiographic characteristics in AMI patients in Crude and Propensity Score matched population.**

Characteristic	Overall		P-value	Standardized difference	PSM		P-value	Standardized difference
	Male (n = 8021)	Female (n = 2547)			Male (n = 1317)	Female (n = 1317)		
Target vessel								
LAD	5550 (69.2%)	1879 (73.8%)	< 0.001	0.102	953 (72.4%)	954 (72.4%)	> 0.999	0.002
LCX	3434 (42.8%)	1197 (47.0%)	< 0.001	0.084	586 (44.5%)	606 (46.0%)	0.453	0.031
RCA	4280 (53.4%)	1368 (53.7%)	0.758	0.007	710 (53.9%)	724 (55.0%)	0.617	0.021
LMCA	390 (4.9%)	107 (4.2%)	0.170	-0.032	83 (6.3%)	68 (5.2%)	0.245	-0.049
Lesion classification								
A	101 (1.3%)	33 (1.3%)	0.886	0.003	22 (1.7%)	21 (1.6%)	> 0.999	-0.006
B1	928 (11.6%)	321 (12.6%)	0.159	0.032	170 (12.9%)	167 (12.7%)	0.909	-0.007
B2	2968 (37.0%)	992 (38.9%)	0.077	0.040	478 (36.3%)	485 (36.8%)	0.813	0.011
C	4023 (50.2%)	1201 (47.2%)	0.008	-0.060	647 (49.1%)	644 (48.9%)	0.938	-0.005
Pre TIMI flow of culprit vessel								
0	3780 (47.1%)	1080 (42.4%)	< 0.001	0.097	524 (39.8%)	568 (43.1%)	0.574	0.071
I	861 (10.7%)	299 (11.7%)			179 (13.6%)	164 (12.5%)		
II	1207 (15.0%)	434 (17.0%)			229 (17.4%)	212 (16.1%)		
III	2173 (27.1%)	734 (28.8%)			385 (29.2%)	373 (28.3%)		
Post TIMI flow of culprit vessel								
0	7 (0.1%)	3 (0.1%)	0.008	0.074	1 (0.1%)	1 (0.1%)	0.961	0.027
I	13 (0.2%)	8 (0.3%)			4 (0.3%)	4 (0.3%)		
II	178 (2.2%)	84 (3.3%)			35 (2.7%)	41 (3.1%)		
III	7823 (97.5%)	2452 (96.3%)			1277 (97.0%)	1271 (96.5%)		
Pre-PCI TIMI 0 or 1	4641 (57.9%)	1379 (54.1%)	0.001	-0.075	703 (53.4%)	732 (55.6%)	0.278	0.044
Post-PCI TIMI 0 or 1	20 (0.2%)	11 (0.4%)	0.138	0.031	5 (0.4%)	5 (0.4%)	> 0.999	0.000
Post -PCI TIMI 3	7823 (97.5%)	2452 (96.3%)	< 0.001	0.073	1277 (97.0%)	1271 (96.5%)	0.586	0.026
Number of diseased vessel								
One-vessel disease	4044 (50.4%)	1161 (45.6%)	< 0.001	0.114	610 (46.3%)	611 (46.4%)	0.475	0.054
Two-vessel disease	2447 (30.5%)	806 (31.6%)			425 (32.3%)	401 (30.4%)		
Three-vessel disease	1400 (17.5%)	542 (21.3%)			256 (19.4%)	281 (21.3%)		
Three-vessel disease with LM	130 (1.6%)	38 (1.5%)			26 (2.0%)	24 (1.8%)		
Total number of stents	1.18 $\pm$ 0.41	1.20 $\pm$ 0.44	0.024	0.056	1.19 $\pm$ 0.43	1.20 $\pm$ 0.45	0.560	0.022
Stent size								
Length, mm	29.3 $\pm$ 14.1	29.9 $\pm$ 14.4	0.103	0.041	29.9 $\pm$ 15.0	29.9 $\pm$ 14.7	0.998	-0.0001
Diameter, mm	3.1 $\pm$ 0.6	2.9 $\pm$ 0.5	< 0.001	-0.338	3.0 $\pm$ 0.5	3.0 $\pm$ 0.5	0.484	-0.027

Data are presented as mean  $\pm$  SD, median (interquartile range), or *n* (%) where appropriate. Lesion based on American College of Cardiology/American Heart Association lesion classification. AMI: acute myocardial infarction; LAD: left anterior descending artery; LCX: left circumflex artery; LMCA: left main coronary artery; RCA: right coronary artery; PSM: propensity score matching; TIMI: thrombolysis in myocardial infarction.

### 3.2 Clinical outcomes of the crude population

The unadjusted 1-year clinical outcomes among AMI patients who underwent successful PCI are shown in Table 3 (upper panel). The cumulative rate of primary composite outcome was significantly higher in women than in men (463 (5.8%) vs. 255 (10.0%), HR (95% CI): 1.788 (1.534–2.083),  $P < 0.001$ , Table 3 (upper panel)). Individually, the unadjusted cumulative incidence of cardiac death, MI and CVA within one year of the index MI event was significantly higher among women than among men (Table 3 (upper panel) and Figure 2). The contrast in the primary composite outcome between men and women was mainly driven by the increased risk for cardiac death in women (266 (3.3%) vs. 160 (6.3%), HR (95% CI): 1.928 (1.585–2.346),  $P < 0.001$ , Table 3 (upper panel) and Figure 2). In the secondary outcomes, the overall mortality rate was significantly higher in women than in men. (220 (8.6%) vs. 380 (4.7%), HR (95% CI): 1.863(1.578–2.199),  $P < 0.001$ , Table 3 (upper panel)). Heart failure and TIMI minor bleeding occurred more frequently in women than in men (heart failure:

172 (6.8%) vs. 255 (3.2%), HR (95% CI): 2.214 (1.751–2.578),  $P < 0.001$ , TIMI minor: 117 (4.6%) vs. 216 (2.7%), HR (95% CI): 1.707 (1.363–2.138),  $P < 0.001$ ; Table 3 (upper panel)) whereas there was no difference in stent thrombosis and TIMI major bleeding between men and women (Table 3 (upper panel)). The Kaplan-Meier curve for the 1-year primary composite endpoint and individual components of primary endpoint are shown in Figure 2.

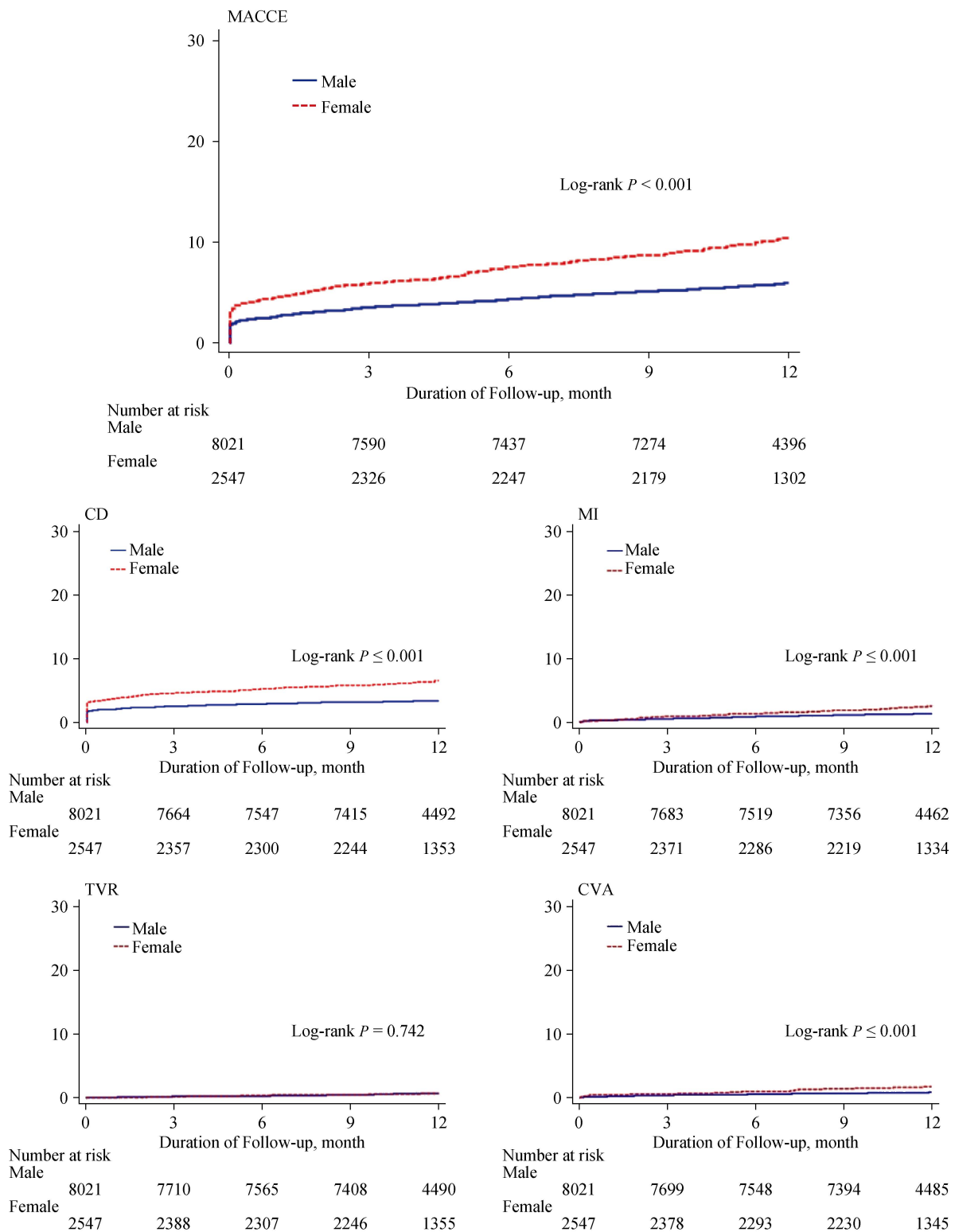
### 3.3 Clinical outcomes of the propensity score matched population

The 1-year clinical outcomes among AMI patients who underwent successful PCI after PS matching are shown in Table 3 (lower panel) and Figure 3. PS matching yielded 1,317 pairs with balanced baseline characteristics including demographic, clinical, laboratory and angiographic features (Table 2 (right panel)). After PS matching, female sex was no longer significantly associated with a higher risk of MACCE (HR (95% CI): 1.032 (0.802–1.328),  $P = 0.803$ , Table 3 (lower panel)). All observed differences in each

**Table 3. One-year clinical outcomes in AMI patients in Crude and Propensity Score matched population.**

Crude population	Male (n = 8021)	Female (n = 2547)	P-value	Log rank P-value	HR	95% CI		P-value
						Lower	Upper	
Primary endpoint	463 (5.8%)	255 (10.0%)	< 0.001	< 0.001	1.788	1.534	2.083	< 0.001
Cardiac death	266 (3.3%)	160 (6.3%)	< 0.001	< 0.001	1.928	1.585	2.346	< 0.001
Myocardial infarction	104 (1.3%)	59 (2.3%)	< 0.001	< 0.001	1.851	1.345	2.548	< 0.001
Target vessel revascularization	52 (0.6%)	15 (0.6%)	0.844	0.742	0.944	0.531	1.677	0.844
Cerebrovascular accident	62 (0.8%)	39 (1.5%)	< 0.001	< 0.001	2.055	1.377	3.067	< 0.001
All-cause death	380 (4.7%)	220 (8.6%)	< 0.001	< 0.001	1.863	1.578	2.199	< 0.001
Heart failure	255 (3.2%)	172 (6.8%)	< 0.001	< 0.001	2.124	1.751	2.578	< 0.001
Stent thrombosis	25 (0.3%)	10 (0.4%)	0.486	0.536	1.297	0.623	2.701	0.487
TIMI major	10 (0.1%)	1 (0.0%)	0.244	0.478	0.315	0.040	2.460	0.271
TIMI minor	216 (2.7%)	117 (4.6%)	< 0.001	< 0.001	1.707	1.363	2.138	< 0.001
Propensity-Score matching	Male (n = 1317)	Female (n = 1317)	P-value	Log rank P-value	HR	95% CI		P-value
Primary endpoint	119 (9.0%)	123 (9.3%)	0.841	0.803	1.032	0.802	1.328	0.804
Cardiac death	83 (6.3%)	78 (5.9%)	0.747	0.684	0.938	0.689	1.278	0.686
Myocardial infarction	23 (1.7%)	30 (2.3%)	0.410	0.331	1.308	0.760	2.251	0.333
Target vessel revascularization	5 (0.4%)	6 (0.5%)	> 0.999	0.764	1.199	0.366	3.928	0.765
Cerebrovascular accident	13 (1.0%)	19 (1.4%)	0.377	0.287	1.464	0.723	2.964	0.290
All-cause death	126 (9.6%)	111 (8.4%)	0.340	0.318	0.879	0.681	1.135	0.323
Heart failure	73 (5.5%)	92 (7.0%)	0.143	0.127	1.260	0.927	1.714	0.140
Stent thrombosis	5 (0.4%)	6 (0.5%)	> 0.999	0.759	1.203	0.367	3.943	0.760
TIMI major	1 (0.1%)	1 (0.1%)	> 0.999	> 0.999	1.000	0.063	15.988	> 0.999
TIMI minor	51 (3.9%)	64 (4.9%)	0.255	0.215	1.255	0.869	1.814	0.226

Data are presented as n (%). AMI: acute myocardial infarction; TIMI: thrombolysis in myocardial infarction.



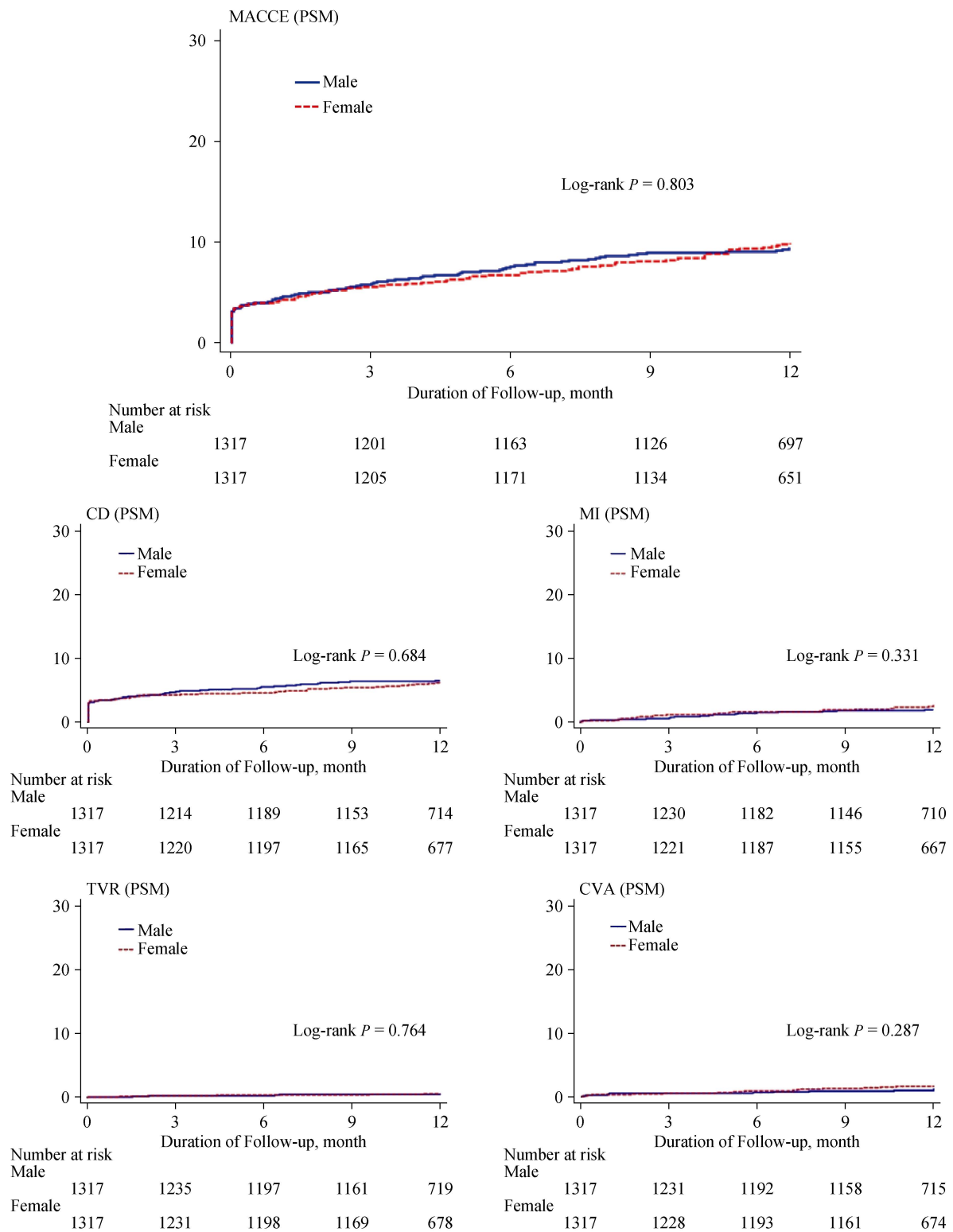
**Figure 2. Kaplan-Meier curve for the 12-month probability of each endpoint in patients with MI undergoing primary PCI comparing men and women before propensity score matching.** CD: cardiac death; CVA: cerebrovascular accident; MACCE: major adverse cardiac and cerebrovascular events; MI: myocardial infarction; PCI: percutaneous coronary intervention; TVR: target vessel revascularization.

primary and secondary outcomes were no longer significant after PS matching: HR (95% CI): 0.938 (0.689–1.278),  $P$

= 0.684 for CD; HR (95% CI): 1.308 (0.760–2.251),  $P$  = 0.331 for MI; HR (95% CI): 1.464 (0.723–2.964),  $P$  =

0.287 for CVA; HR (95% CI): 0.879 (0.681–1.135),  $P = 0.340$  for all-cause death; HR (95% CI): 1.260 (0.927–1.714),

$P = 0.127$  for heart failure (Table 3 (lower panel), Figure 3). We performed a landmark analysis with a prespecified



**Figure 3. Kaplan-Meier curve for the 12-month probability of each endpoint in propensity score matched patients with AMI undergoing primary PCI comparing men and women.** AMI: acute myocardial infarction; CD: cardiac death; CVA: cerebrovascular accident; MACCE: major adverse cardiac and cerebrovascular events; PCI: percutaneous coronary intervention; PSM: propensity score matching; TVR: target vessel revascularization.



**Table 4. One-month landmark clinical outcomes in AMI patients in Propensity Score Matched population.**

Propensity-Score Matching	Male (n = 1317)	Female (n = 1317)	P-value	Log rank P-value	HR	95% CI		P-value
						Lower	Upper	
Primary endpoint	57 (4.3%)	53 (4.0%)	0.773	0.701	0.930	0.640	1.352	0.704
Cardiac death	47 (3.6%)	47 (3.6%)	> 0.999	0.999	1.000	0.667	1.498	1.000
Myocardial infarction	4 (0.3%)	3 (0.2%)	> 0.999	0.708	0.752	0.168	3.359	0.709
Target vessel revascularization	0	0	-	-	-	-	-	-
Cerebrovascular accident	6 (0.5%)	4 (0.3%)	0.754	0.531	0.669	0.189	2.371	0.534
All-cause death	66 (5.0%)	62 (4.7%)	0.786	0.720	0.940	0.664	1.329	0.725
Heart failure	73 (5.5%)	92 (7.0%)	0.143	0.127	1.260	0.927	1.714	0.140
Stent thrombosis	0	3 (0.2%)	0.250	-	-	-	-	-
TIMI major	1 (0.1%)	1 (0.1%)	> 0.999	> 0.999	1.000	0.063	15.988	>0.999
TIMI minor	51 (3.9%)	63 (4.8%)	0.294	0.251	1.235	0.854	1.787	0.262

Data are presented as n (%). AMI: acute myocardial infarction; TIMI: thrombolysis in myocardial infarction.

landmark set at one month to evaluate whether sex is associated with short term morbidity and mortality related to PCI in PS matched population. As shown in Table 4 and Figure 4, landmark analysis confirmed that gender difference was not observed in the short-term (30-day) as well as long-term (1-year) clinical outcomes (MACCE, each component of MACCE and bleeding outcomes).

### 3.4 Bleeding outcomes

We examined the cumulative incidence of TIMI major and minor bleeding event within one-year post index PCI. In general, there were few bleeding events for both men and women. Women had a higher risk of TIMI minor bleeding (4.6% vs. 2.7%,  $P < 0.001$ , Table 3 (upper panel)), but there is no difference in TIMI major bleeding between gender (Table 3 (upper panel)). After PS matching two populations, sex was no longer significantly associated with bleeding events (Table 3 (lower panel)).

### 3.5 Subgroup analysis of propensity score matched population

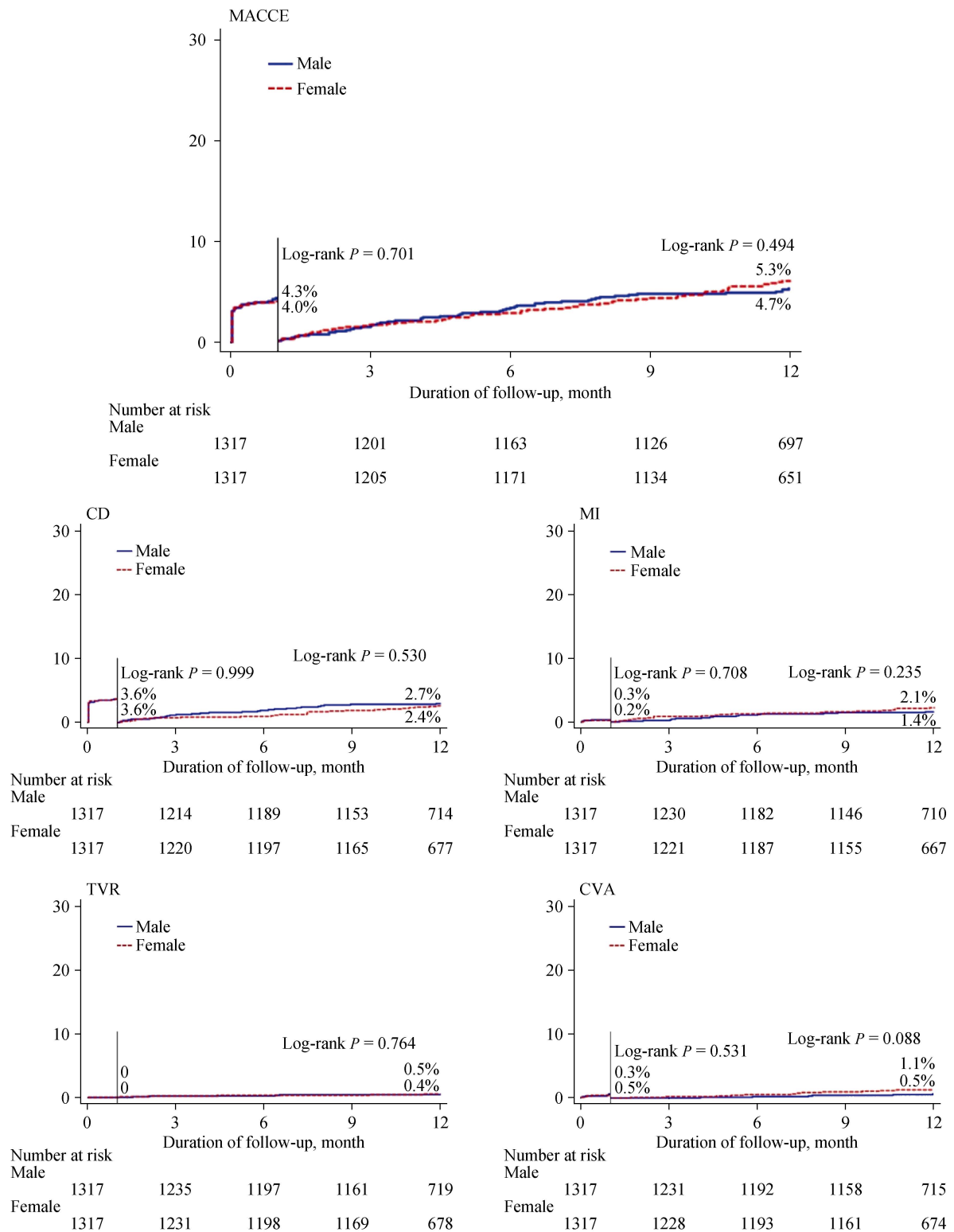
After PS matching, the association of female sex with risk of 1-year MACCE was similar between patients with and those without CAD risk factors (such as DM, HTN, dyslipidemia and smoking status), older ( $\geq 70$  years) and younger patients, patients with preserved LV systolic function and with reduced LV systolic function. (Figure 5) Particularly, among ST-segment elevation myocardial infarction (STEMI) patients, female had marginally significant increased risk compared with men. (HR (95% CI): 1.326 (0.921–1.908),  $P$  value for interaction = 0.055).

## 4 Discussion

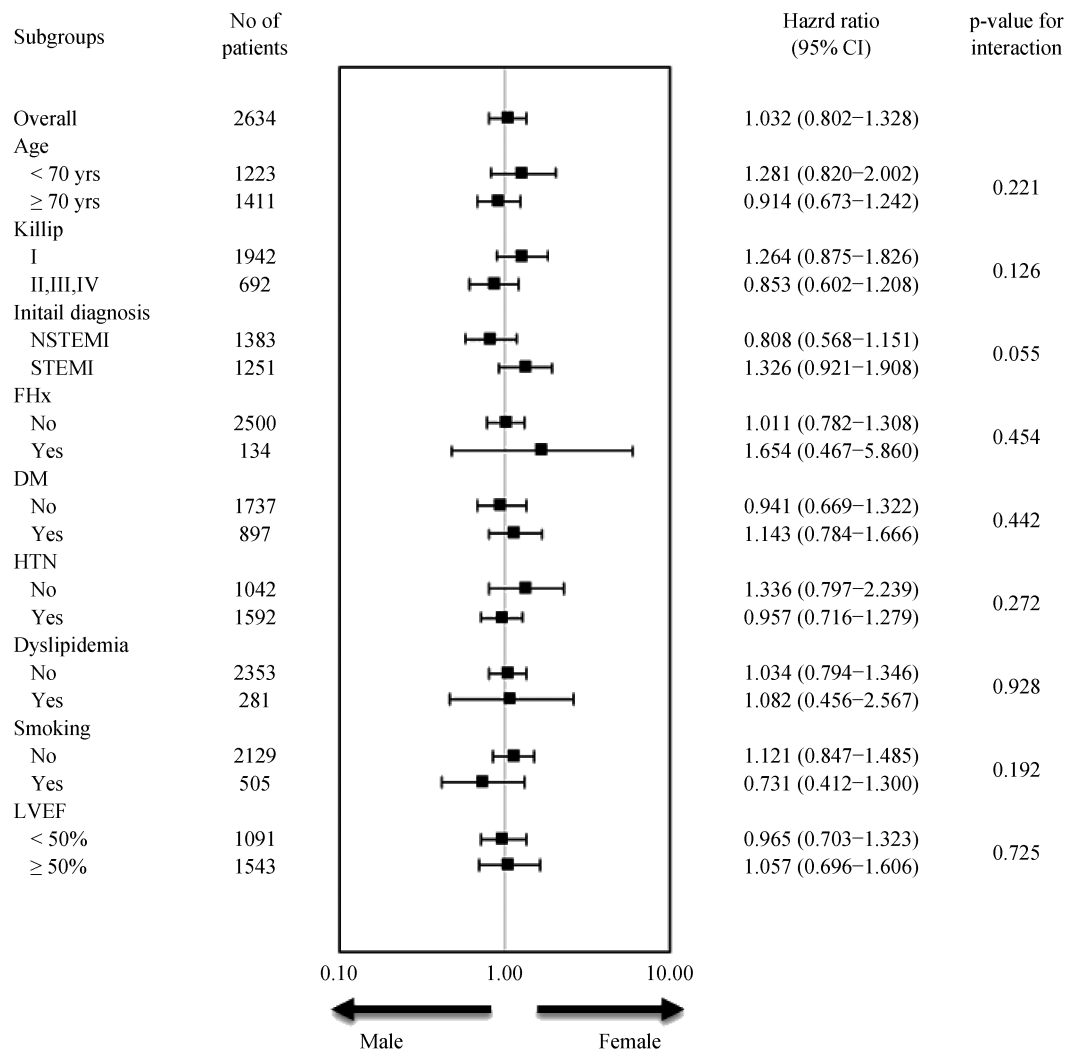
This present study demonstrated as follows: (1) clinical

and treatment profiles differed between female and male in the Korean AMI patients undergoing primary PCI in the DES-era: women were older and sicker at presentation, had a higher prevalence of NSTEMI, lower LVEF, had more comorbidities such as DM, HTN, CKD and CVA, while men had a higher percentage of obesity, smokers; (2) female showed a higher unadjusted 30-days and 1-year outcomes but showed comparable 30-days and 1-year outcome compared with men in PS matched population (unadjusted incidences of all-cause death, cardiovascular death, and MACCE were all higher in women, whereas these outcome measures became comparable between the women and the men in PS matched population); and (3) women were also more likely to have minor bleeding than men, yet after adjustment, female sex was no longer associated with a higher risk of bleeding events.

Numerous reports have been published regarding the gender disparities in clinical outcomes of CAD patients following PCI, but they showed inconclusive and inconsistent results.<sup>[8–16]</sup> Traditionally, female sex has been regarded as a prognostic factor of worse clinical outcome after PCI. The suggested reasons for adverse clinical outcome compared with men has been often ascribed to women's older age at presentation,<sup>[23–25]</sup> comorbidities,<sup>[23,24]</sup> less frequent administration of guideline-recommended medical therapy<sup>[24,26,27]</sup> and less frequent application of invasive procedures such as PCI.<sup>[26–28]</sup> But, recent studies tended to report that female sex was not associated with worse outcome after PCI.<sup>[29–32]</sup> However, gender differences in AMI have not been established in an Asian population in the era of second-generation DES. Therefore, we conducted this study to investigate the impact of sex on clinical outcomes after emergency PCI in Korean patients with AMI. Our findings have several important implications. First, although Asian generally has



**Figure 4. Kaplan-Meier curve and the one-month landmark analysis of probability of each endpoint in propensity score matched patients with MI undergoing primary PCI comparing men and women.** CD: cardiac death; CVA: cerebrovascular accident; LVEF: left ventricular ejection fraction; MACCE: major adverse cardiac and cerebrovascular events; MI: myocardial infarction; PCI: percutaneous coronary intervention; TVR: target vessel revascularization.



**Figure 5. Subgroup analysis of the primary outcome.** CAD: coronary artery disease; DM: diabetes mellitus; FHx: family history; HTN: hypertension; LVEF: left ventricular ejection fraction; STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction.

known to have a higher prevalence of CAD, more cardiovascular comorbidities and poorer outcomes compared with Caucasians after PCI,<sup>[33–35]</sup> previous studies regarding the gender differences have been performed in western population, including a relatively small percentage of Asian subgroup. Furthermore, the risk profiles of Korean patients differ from those in Western populations (e.g., Korean patients are older, smoke less frequently, and have less traditional risk factors such as HTN, dyslipidemia and a prior history of MI/CVA/PCI, except for DM). Thus, gender differences in clinical outcomes after PCI in Korean need to be investigated. In the present study, we demonstrated the gender differences no longer exist in contemporary era and female gender itself is not an independent risk factor of

clinical outcomes as well as bleeding complications after PCI based on nationwide, multicenter Korean AMI registry. Second, gender differences in outcomes following PCI differ according to the initial clinical presentation. It has been previously shown that outcomes did not differ between male and female patients with stable angina, unstable angina and NSTEMI.<sup>[16,36,37]</sup> In contrast, among STEMI patients, female exhibited worse prognosis, even after adjustment for multiple variables.<sup>[7,27,38–40]</sup> In this prospective cohort study, female had a significantly higher unadjusted risk of major cardiovascular events and mortality than men. These could be explained by female's advanced age, severe initial presentation and underlying comorbidities compared with men. But after PS matching, gender differences in outcomes were

no longer observed not only patients with STEMI but also those with NSTEMI. There are plausible explanations for the absence of gender disparity in STEMI patients in this study. First, all participated centers have highly qualified interventional cardiologists (at least five years of experiences of PCI) and high-volume centers (over 300 cases of PCI annually) for CAG with PCI. In Korea, primary PCI facilities are available throughout the country, which enables more timely access to revascularization even in high-risk patients. This situation in Korea might contribute to reduce periprocedural complications and enhance clinical outcomes after PCI in female patients. Second, in this study, study participants exclusively comprised patients receiving newer-generation DES during PCI. Naito *et al.* reported that in plain old balloon angioplasty (POBA)-era female exhibited lower event-free survival rate compared with men, but the difference has diminished in bare metal stent (BMS)-era, disappeared in DES-era.<sup>[31]</sup> Because women with AMI have culprit coronary arteries with smaller diameters and thus a potentially high risk of procedure related complications such as rupture, bleeding and restenosis, female patients may benefit more than male patients from the use of DES. This newer-generation DES would enable female patients to tolerate high risk PCI more safely and effectively. Advance in devices and techniques related to PCI, improvement of evidence-based medical therapies, and increased awareness in patients with AMI, have resulted in a reduction in short- and long-term morbidity and mortality.

#### 4.1 Study limitations

There are several limitations in this study. First, our results are obtained from a prospective analysis of an observational PCI registry that was subject to missing or incomplete information. Therefore, potential residual biases from measured confounders and biases due to unmeasured confounders might influence the results. To reduce selection bias and residual biases assessing causal effects in observational studies, we used PS-matched (1: 1) analysis. Furthermore, this registry can provide “real world” data on a wide spectrum of unselected patients that underwent PCI procedures in Korea. Second, the 1-year follow-up period was relatively short to determine the long-term clinical outcomes according to gender difference. Further long-term studies will be needed to confirm these findings. Third, because the present study was conducted in a wide diversity of hospital settings and laboratory tests performed separately by the different hospitals, it has an intrinsic limitation itself due to heterogeneity in angiographic, laboratory and procedural parameters and it could have affected outcomes.

## 5 Conclusions

In this study of contemporary national based AMI patients undergoing PCI, women presenting with AMI were older, had more comorbidities than men, reflecting higher unadjusted 30-days and 1-year mortality rate even following successful PCI. But, gender differences in clinical outcomes after AMI were no longer observed in PS matched population. Our study suggested that gender differences in outcomes after PCI is no longer existed in modern DES-era.

## Acknowledgements

This research was funded by Research of Korea Centers for Disease Control and Prevention and the Korea Health Technology R & D Project (2016-ER6304- 01), Ministry of Health & Welfare (HI13C1527), South Korea. The authors declared no conflicts of interests.

## References

- 1 Mozaffarian D, Benjamin EJ, Go AS, *et al.* Heart disease and stroke statistics--2015 update: a report from the American Heart Association. *Circulation* 2015; 131: e29–322.
- 2 Lee SW, Kim HC, Lee HS, Suh I. Thirty-year trends in mortality from cardiovascular diseases in Korea. *Korean Circ J* 2015; 45: 202–209.
- 3 Malenka DJ, O'Connor GT, Quinton H, *et al.* Differences in outcomes between women and men associated with percutaneous transluminal coronary angioplasty. A regional prospective study of 13,061 procedures. Northern New England Cardiovascular Disease Study Group. *Circulation* 1996; 94: II99–II104.
- 4 Cowley MJ, Mullin SM, Kelsey SF, *et al.* Sex differences in early and long-term results of coronary angioplasty in the NHLBI PTCA Registry. *Circulation* 1985; 71: 90–97.
- 5 Kelsey SF, James M, Holubkov AL, *et al.* Results of percutaneous transluminal coronary angioplasty in women. 1985-1986 National Heart, Lung, and Blood Institute's Coronary Angioplasty Registry. *Circulation* 1993; 87: 720–727.
- 6 Milcent C, Dormont B, Durand-Zaleski I, Steg PG. Gender differences in hospital mortality and use of percutaneous coronary intervention in acute myocardial infarction: microsimulation analysis of the 1999 nationwide French hospitals database. *Circulation* 2007; 115: 833–839.
- 7 Venetsanos D, Sederholm Lawesson S, Alfredsson J, *et al.* Association between gender and short-term outcome in patients with ST elevation myocardial infarction participating in the international, prospective, randomised Administration of Ticagrelor in the catheterisation Laboratory or in the Ambulance for New ST elevation myocardial Infarction to open the

- Coronary artery (ATLANTIC) trial: a prespecified analysis. *BMJ Open* 2017; 7: e015241.
- 8 Peterson ED, Lansky AJ, Kramer J, *et al.* Effect of gender on the outcomes of contemporary percutaneous coronary intervention. *Am J Cardiol* 2001; 88: 359–364.
  - 9 Jacobs AK, Johnston JM, Haviland A, *et al.* Improved outcomes for women undergoing contemporary percutaneous coronary intervention: a report from the National Heart, Lung, and Blood Institute Dynamic registry. *J Am Coll Cardiol* 2002; 39: 1608–1614.
  - 10 Iyanoye A, Moreyra AE, Swerdel JN, *et al.* Gender disparity in the use of drug-eluting stents during percutaneous coronary intervention for acute myocardial infarction. *Catheter Cardiovasc Interv* 2015; 86: 221–228.
  - 11 Bell MR, Holmes DR, Jr., Berger PB, *et al.* The changing in-hospital mortality of women undergoing percutaneous transluminal coronary angioplasty. *JAMA* 1993; 269: 2091–2095.
  - 12 Arnold AM, Mick MJ, Piedmonte MR, Simpfordorfer C. Gender differences for coronary angioplasty. *Am J Cardiol* 1994; 74: 18–21.
  - 13 Singh M, Rihal CS, Gersh BJ, *et al.* Mortality differences between men and women after percutaneous coronary interventions. A 25-year, single-center experience. *J Am Coll Cardiol* 2008; 51: 2313–2320.
  - 14 Park JS, Kim YJ, Shin DG, *et al.* Gender differences in clinical features and in-hospital outcomes in ST-segment elevation acute myocardial infarction: from the Korean Acute Myocardial Infarction Registry (KAMIR) study. *Clin Cardiol* 2010; 33: E1–E6.
  - 15 Mrdovic I, Savic L, Asanin M, *et al.* Sex-related analysis of short- and long-term clinical outcomes and bleeding among patients treated with primary percutaneous coronary intervention: an evaluation of the RISK-PCI data. *Can J Cardiol* 2013; 29: 1097–1103.
  - 16 Vasiljevic-Pokrajcic Z, Mickovski N, Davidovic G, *et al.* Sex and age differences and outcomes in acute coronary syndromes. *Int J Cardiol* 2016; 217 Suppl: S27–S31.
  - 17 Levine GN, Bates ER, Blankenship JC, *et al.* 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *J Am Coll Cardiol* 2011; 58: e44–e122.
  - 18 Thygesen K, Alpert JS, Jaffe AS, *et al.* Fourth universal definition of myocardial infarction (2018). *Eur Heart J* 2019; 40: 237–269.
  - 19 Brosius FC, Hostetter TH, Kelepouris E, *et al.* Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease. *Circulation* 2006; 114: 1083–1087.
  - 20 Cutlip DE, Windecker S, Mehran R, *et al.* Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007; 115: 2344–2351.
  - 21 Wiviott SD, Antman EM, Gibson CM, *et al.* Evaluation of prasugrel compared with clopidogrel in patients with acute coronary syndromes: design and rationale for the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet Inhibition with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38). *Am Heart J* 2006; 152: 627–635.
  - 22 Laskey WK, Yancy CW, Maisel WH. Thrombosis in coronary drug-eluting stents: report from the meeting of the circulatory system medical devices advisory panel of the food and drug administration center for devices and radiologic health, december 7-8, 2006. *Circulation* 2007; 115: 2352–2357.
  - 23 Kang SH, Suh JW, Yoon CH, *et al.* Sex differences in management and mortality of patients with ST-elevation myocardial infarction (from the Korean Acute Myocardial Infarction National Registry). *Am J Cardiol* 2012; 109: 787–793.
  - 24 Shih JY, Chen ZC, Chang HY, *et al.* Risks of age and sex on clinical outcomes post myocardial infarction. *Int J Cardiol Heart Vasc* 2019; 23: 100350.
  - 25 Kunadian V, Qiu W, Lagerqvist B, *et al.* Gender Differences in Outcomes and Predictors of All-Cause Mortality After Percutaneous Coronary Intervention (Data from United Kingdom and Sweden). *Am J Cardiol* 2017; 119: 210–216.
  - 26 Shaw LJ, Shaw RE, Merz CN, *et al.* Impact of ethnicity and gender differences on angiographic coronary artery disease prevalence and in-hospital mortality in the American College of Cardiology-National Cardiovascular Data Registry. *Circulation* 2008; 117: 1787–1801.
  - 27 Jneid H, Fonarow GC, Cannon CP, *et al.* Sex differences in medical care and early death after acute myocardial infarction. *Circulation* 2008; 118: 2803–2810.
  - 28 Anand SS, Xie CC, Mehta S, *et al.* Differences in the management and prognosis of women and men who suffer from acute coronary syndromes. *J Am Coll Cardiol* 2005; 46: 1845–1851.
  - 29 Bandyopadhyay D, Chakraborty S, Amgai B, *et al.* Acute myocardial infarction in the young—National Trend Analysis with gender-based difference in outcomes. *Int J Cardiol* 2020; 301: 21–28.
  - 30 Stehli J, Martin C, Brennan A, *et al.* Sex Differences Persist in Time to Presentation, Revascularization, and Mortality in Myocardial Infarction Treated With Percutaneous Coronary Intervention. *J Am Heart Assoc* 2019; 8: e012161.
  - 31 Naito R, Miyauchi K, Konishi H, *et al.* Gender difference in long-term clinical outcomes following percutaneous coronary intervention during 1984–2008. *Atherosclerosis* 2016; 247: 105–110.
  - 32 Hess CN, McCoy LA, Duggirala HJ, *et al.* Sex-based differences in outcomes after percutaneous coronary intervention for acute myocardial infarction: a report from TRANSLATE-ACS. *J Am Heart Assoc* 2014; 3: e000523.
  - 33 Mahajan AM, Claessen BE, Chandrasekhar J, *et al.* Outcomes by Gender and Ethnicity After Percutaneous Coronary Inter-

- vention. *Am J Cardiol* 2019; 123: 1941–1948.
- 34 Gasevic D, Khan NA, Qian H, *et al.* Outcomes following percutaneous coronary intervention and coronary artery bypass grafting surgery in Chinese, South Asian and White patients with acute myocardial infarction: administrative data analysis. *BMC Cardiovasc Disord* 2013; 13: 121.
- 35 Krishnamurthy A, Keeble C, Burton-Wood N, *et al.* Clinical outcomes following primary percutaneous coronary intervention for ST-elevation myocardial infarction according to sex and race. *Eur Heart J Acute Cardiovasc Care* 2019; 8: 264–272.
- 36 Tang XF, Song Y, Xu JJ, *et al.* Effect of sex difference in clinical presentation (stable coronary artery disease vs. unstable angina pectoris or non-ST-elevation myocardial infarction vs. ST-elevation myocardial infarction) on 2-year outcomes in patients undergoing percutaneous coronary intervention. *J Interv Cardiol* 2018; 31: 5–14.
- 37 Acharjee S, Teo KK, Jacobs AK, *et al.* Optimal medical therapy with or without percutaneous coronary intervention in women with stable coronary disease: A pre-specified subset analysis of the Clinical Outcomes Utilizing Revascularization and Aggressive druG Evaluation (COURAGE) trial. *Am Heart J* 2016; 173: 108–117.
- 38 Kanic V, Suran D, Krajnc I, Kompara G. ST-elevation myocardial infarction in a real world population - An observational retrospective study with a sex perspective. *Eur J Intern Med* 2019; 66: 81–84.
- 39 Shehab A, Bhagavathula AS, Alhabib KF, *et al.* Age-related sex differences in clinical presentation, management, and outcomes in st-segment-elevation myocardial infarction: pooled analysis of 15 532 patients from 7 arabian gulf registries. *J Am Heart Assoc* 2020; 9: e013880.
- 40 Cenko E, Yoon J, Kedev S, *et al.* Sex differences in outcomes after STEMI: effect modification by treatment strategy and age. *JAMA Intern Med* 2018; 178: 632–639.