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*Original Article*

# Sex differences in clinical outcomes after rotational atherectomy of calcified coronary stenoses: from multicenter registry

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**Abstract:** Background: Recent improvements in devices and medications may diminish the risk of adverse events following percutaneous coronary intervention (PCI) in women. However, complex calcified coronary lesions are increasingly being encountered in clinical practice, which remain challenging for contemporary PCI. Rotational atherectomy (RA) of severely calcified lesions is an option that facilitates the technical success of PCI. We aimed to examine sex differences in long-term clinical prognoses after PCI with RA in the drug-eluting stent (DES) era. Methods and results: We evaluated J2T ROTA registry data from 1,090 patients with severely calcified de novo coronary artery stenoses who underwent PCI using RA at 3 hospitals between 2004 and 2015. After excluding patients who received regular hemodialysis, 788 patients, including 570 men and 218 women, were ultimately analyzed. The primary endpoint was major adverse cardiovascular and cerebrovascular events (MACCE), which included death, acute coronary syndrome (ACS), and stroke. The women were significantly older, and presented more frequently with chronic kidney disease, ACS, atrial fibrillation, lower body mass indexes, and worse lipid profiles than the men. During the observation period, MACCE occurred in 197 patients (25%) (118 deaths, 29 strokes, and 50 ACS). In the unmatched population, women had a higher MACCE rate than men (hazard ratio: 1.48, [95% confidence interval: 1.07-2.06]). However, sex was not associated with MACCE in the propensity score-matched population. Conclusion: In the DES era, differences between sexes were not observed in relation to long-term MACCE in patients undergoing PCI with RA for severely calcified coronary artery stenoses.

**Keywords:** Sex, percutaneous coronary intervention, rotational atherectomy

## Introduction

Worldwide, coronary artery disease (CAD) is the leading cause of death among men and women [1]. Sex is one of many factors that contribute to the pathophysiology of atherosclerosis [2] and platelet reactivity [3], and affect the clinical outcomes of patients with CAD. Previously, women were regarded to pose a higher procedural risk in relation to percutaneous coronary intervention (PCI) and a higher adverse event risk following the procedure than men [4, 5-7]. According to the most recent surveys, improvements in PCI-related devices and optimal medical therapy may have diminished the differences between the sexes in relation to clinical outcomes [8, 9]. However, in calcific coronary lesions, female gender reported to be an independent predictor of poor outcomes after PCI even in the contemporary drug-eluting stent (DES) era [10], despite the prevalence of coronary calcification is lower among women compared with that in men [11]. As the global population ages, complex calcified coronary lesions are increasingly being encountered in everyday clinical practice, and they remain challenging because of the poor deliverability of balloons and stents to the target lesions, incomplete

final stent expansions, and the malapposition of stent struts to the vessel wall. In addition, passing a DES through a calcified lesion may separate the polymer and/or drug coating from the stent strut. Rotational atherectomy (RA) is a strategic option that can facilitate the technical success of PCI in such severely calcified lesions [12, 13]. However, there are few reports that evaluate the sex difference in clinical outcomes after modification of calcific coronary stenosis by RA. Therefore, we aimed to examine differences between the sexes in relation to the long-term clinical prognoses after PCI with RA in extremely complex atherosclerotic arteries in the DES era.

## Methods

### *Study population and endpoints*

This study comprised a subanalysis of data from the J2T ROTA registry that comprises a multicenter retrospective cohort of 1,090 patients who underwent RA [14]. The inclusion criteria of this study was the patients with heavily calcified de novo lesions and significant stenosis (stenosis ≥70% of vessel diameter) treated with RA between 2004 and 2015 in each institutions. The decision to carry out RA was at the discretion of operators. The exclusion criteria of this study was the patient who received regular hemodialysis. Therefore, 302 patients who received regular hemodialysis were excluded, and 788 patients, including 570 men and 218 women, were ultimately analyzed. Then we compared the baseline characteristics, angiographic findings, procedural parameters and clinical outcomes. Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate < 60 mL/min/1.73 $m^2$, as calculated using the modification of the diet in renal disease equation modified with a Japanese coefficient using baseline serum creatinine [15]. Small vessel was defined as 2.5 mm or less diameter by angiographic assessment. Long stent use was defined as 23 mm or more total length of deployed stent.

The current study's primary endpoint was major adverse cardiovascular and cerebrovascular events (MACCE) after the index PCI. MACCE included any death, acute coronary syndrome (ACS), and stroke. The endpoints were analyzed on a per-patient basis, and the patients were grouped according to sex.

The development of this registry complied with the ethical guidelines for epidemiological studies, and the relevant review boards of the 3 participating hospitals approved this study's protocol. All of the patients provided written informed consent in relation to the use of the data from their medical records before they were enrolled to participate in the study. The data were collected at each site using a standardized case report form that recorded the patients' demographic and clinical characteristics, and the procedural and follow-up data. The follow-up data were obtained at the time of enrollment and were collected from the patients' medical records and from physician or patient interviews. The investigators could access the data freely, and they oversaw the data analyses. The study's detailed inclusion and exclusion criteria, design, procedural details, and complete results have been published elsewhere.

### *Statistical analyses*

The quantitative data are presented as the means and the standard deviations, or as the medians with their interquartile ranges (IQRs). The categorical variables are presented as numbers and percentages. The independent Student's t-test and the non-parametric equivalent Mann-Whitney-U test were used to compare the groups with respect to the continuous variables, and the chi-squared test or Fischer's exact test were used to compare the groups with respect to the categorical variables, as appropriate. Kaplan-Meier curves were plotted to determine the cumulative incidence of MACCE, any death, ACS, and stroke from the time of the index procedure, and the differences between the groups were assessed using the log-rank test. Univariate Cox proportional hazards regression analyses were performed, and variables that reached a level of significance of $P < 0.10$ and were considered clinically significant were included in the multivariate model. Multivariate Cox proportional hazards regression analyses were performed to adjust for confounding factors and to identify independent risk factors for MACCE. Age, sex, the body mass index (BMI), hypertension, chronic kidney disease (CKD), ACS, atrial fibrillation, the left ventricular ejection fraction (LVEF), left main CAD, and the hemoglobin, creatinine, log-transformed brain natriuretic peptide (BNP), log-transformed C-reactive protein, and log-transformed

triglyceride levels, the administration of dual antiplatelet therapy, and the use of DES were used to adjust the multivariate model. In addition, propensity score (PS) matching was used to adjust for the baseline differences between the male and female patients. A logistic regression model generated the PS using independent variables that potentially influence the long-term outcomes after PCI, namely, age, the BMI, CKD, smoking, ACS, atrial fibrillation, and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEi/ARB) therapy. To create a PS matched cohort, the female patients were matched with the male patients using a 1:1 greedy matching technique [16]. A 2-sided value of $P < 0.05$ was considered statistically significant. The statistical analyses were performed using R software, version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

*Patients' baseline clinical characteristics*

**Table 1** presents the patients' baseline clinical characteristics, laboratory data, and oral medications at discharge following the index hospitalizations. The women were significantly older and they had significantly higher ACS, CKD, and atrial fibrillation rates than the men. Compared with the women, the men's average BMI and current smoker rate were significantly higher. The women had a higher BNP level, worse lipid profiles, except for the triglyceride level, and a lower hemoglobin level than the men. Regarding the prescription rates for the medications administered at discharge, the groups were comparable, except that the women had a significantly higher ACEi/ARB prescription rate than the men.

*Angiographic findings and procedural parameters*

The women had a higher rate of small vessel disease than the men. The groups did not differ regarding the distributions of the coronary arteries targeted for therapy and the rate of long stent use (**Table 2**). Compared with the men, the women had significantly smaller PCI system specifications, a smaller maximum burr size, and a higher rate of RA burr upsizing. The groups did not differ in terms of the types of stent implanted. The final thrombolysis in myocardial infarction (TIMI) 3 flows were comparable, and were about 96% in both groups.

*Unmatched patients' prognoses*

During the index hospitalization, the men and women had comparable adverse event rates, including death, myocardial infarction, cardiac tamponade, major bleeding, intra-aortic balloon pumping or percutaneous cardiopulmonary support, and emergency surgery (Supplementary Table 1). During the median observation period of 1,493 days (IQR 702-2,278 days), 197 patients had MACCE, comprising 134 men (23.5%) and 63 women (28.9%). In addition, 141 patients died, comprising 96 men (16.8%) and 45 women (20.7%). Kaplan-Meier analyses showed that the 5-year MACCE rate was significantly higher for the women (31.3%) than that for the men (22.3%) (log-rank $P = 0.019$) (**Figure 1**). In terms of the individual MACCE components, the mortality and ACS rates increased continuously in both groups during the observation period, and the rates did not differ between the men and women (**Figure 2**). Stroke was significantly more frequent in the women compared with the men during the observation period (log-rank $P = 0.008$).

*Predictors of major adverse cardiovascular and cerebrovascular events*

The univariate Cox proportional hazards regression analyses showed that the female sex was associated with a higher incidence of MACCE (hazard ratio [HR]: 1.44, 95% confidence interval [CI]: 1.06-1.93, $P = 0.022$). The multivariate Cox proportional hazards regression analyses showed that the female sex was not an independent predictor of MACCE (HR: 1.10, 95% CI: 0.62-1.92, $P = 0.74$), and that age (HR: 1.07, 95% CI: 1.03-1.11, $P < 0.001$), atrial fibrillation (HR: 1.92, 95% CI: 1.02-3.41, $P = 0.045$), and the LVEF (HR: 0.95, 95% CI: 0.93-0.97, $P < 0.001$) were independent predictors of MACCE (**Table 3**).

*Propensity score matched cohort analysis*

PS matching generated 207 matched pairs of men and women. After PS matching, none of the variables, except the hemoglobin level, the lipid profiles, the BNP level, and small vessel disease, differed significantly between the men and women (Supplementary Tables 2 and 3).

**Table 1.** Patients' baseline clinical characteristics

| Variables | Male n = 570 | Female n = 218 | *p* value |
|---|---|---|---|
| Age, years | 70.4 ± 9.1 | 75.3 ± 6.9 | <0.001 |
| BMI, kg/m$^2$ | 23.6 ± 2.9 | 23.0 ± 3.7 | 0.028 |
| Diabetes | 323 (57%) | 130 (60%) | 0.45 |
| Insulin use | 96 (17%) | 39 (18%) | 0.73 |
| Hypertension | 461 (81%) | 179 (82%) | 0.69 |
| Dyslipidemia | 408 (72%) | 160 (73%) | 0.61 |
| Current smoker | 129 (23%) | 17 (8%) | <0.001 |
| Family history of coronary artery disease | 135 (24%) | 51 (24%) | 0.96 |
| ACS presentation | 68 (12%) | 41 (19%) | 0.012 |
| Chronic kidney disease | 140 (25%) | 72 (33%) | 0.019 |
| Prior myocardial infarction | 139 (24%) | 56 (26%) | 0.66 |
| Prior PCI | 168 (31%) | 68 (31%) | 0.62 |
| Prior CABG | 64 (11%) | 18 (8%) | 0.22 |
| Atrial fibrillation | 61 (11%) | 36 (17%) | 0.025 |
| LVEF, % | 57.6 ± 11.9 | 57.3 ± 12.8 | 0.76 |
| Low LVEF (<40%) | 55 (11%) | 21 (11%) | 0.95 |
| Laboratory data | | | |
| Hemoglobin, g/dl | 13.0 (11.9-14.2) | 11.5 (10.4-12.4) | <0.001 |
| Creatinine, mg/dL | 0.95 ± 0.40 | 0.91 ± 0.74 | 0.28 |
| Total cholesterol, mg/dL | 170.5 ± 34.5 | 179.8 ± 44.3 | 0.002 |
| Triglycerides, mg/dL | 126.2 ± 71.3 | 119.9 ± 74.4 | 0.28 |
| HDL-C, mg/dL | 46.9 ± 13.9 | 50.6 ± 13.9 | 0.001 |
| LDL-C, mg/dL | 99.8 ± 31.5 | 107.4 ± 37.9 | 0.045 |
| HbA1c, % | 6.54 ± 1.05 | 6.61 ± 1.07 | 0.48 |
| C-reactive protein, mg/dL | 0.66 ± 2.09 | 0.75 ± 1.51 | 0.56 |
| BNP, pg/ml | 53.3 (23.6-146.6) | 123.3 (48.1-307.4) | <0.001 |
| Medical therapy at discharge | | | |
| β-blocker | 303 (53%) | 110 (51%) | 0.57 |
| Ca-antagonist | 280 (49%) | 117 (54%) | 0.20 |
| ACEi/ARB | 367 (65%) | 160 (74%) | 0.009 |
| Statin | 401 (71%) | 153 (71%) | 0.88 |
| Nitrates/Nicorandil | 284 (50%) | 109 (50%) | 0.97 |
| Aspirin | 547 (96%) | 203 (94%) | 0.24 |
| Thienopyridine | 531 (93%) | 199 (91%) | 0.37 |
| Dual antiplatelet therapy | 515 (90%) | 192 (88%) | 0.35 |
| Cilostazol | 23 (4%) | 11 (5%) | 0.51 |
| Oral anticoagulant | 46 (8%) | 25 (11%) | 0.14 |

ACEi/ARB = angiotensin converting enzyme/angiotensin receptor blocker; ACS = acute coronary syndrome; BMI = body mass index; CABG = coronary artery bypass graft; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.

The rates of MACCE and its individual components did not differ between the PS matched men and women (**Figure 3**, Supplementary Figure 1).

## Discussion

This study's major findings from patients who underwent PCI with RA showed that 1) the female patients had higher risk profiles than the male patients; 2) the in-hospital outcomes were comparable for the women and men; and 3) the women had a significantly higher MACCE rate than the men. However, the multivariate analysis and the analysis of the PS matched men and women revealed that the female sex was not independently associated with the MACCE rate.

**Table 2.** Angiographic findings and procedural parameters

| Variables | Male n = 570 | Female n = 218 | *p* value |
|---|---|---|---|
| Target vessel | | | 0.27 |
| LAD | 410 (72%) | 155 (71%) | |
| Circumflex | 59 (10%) | 20 (9%) | |
| RCA | 76 (13%) | 40 (18%) | |
| LMCA | 56 (10%) | 31 (14%) | |
| Multivessel disease | 425 (75%) | 167 (77%) | 0.55 |
| Chronic total occlusion | 34 (6%) | 10 (5%) | 0.45 |
| Small vessel (< 2.5 mm) | 108 (19%) | 73 (34%) | < 0.001 |
| Long stent use (< 23 mm) | 423 (76%) | 160 (75%) | 0.95 |
| Guiding catheter size | | | 0.005 |
| 6Fr. | 198 (36%) | 106 (49%) | |
| 7Fr. | 322 (59%) | 100 (46%) | |
| 8Fr. | 30 (5%) | 11 (5%) | |
| Max. burr size | | | 0.002 |
| 1.25 mm | 42 (7%) | 23 (11%) | |
| 1.5 mm | 229 (40%) | 110 (50%) | |
| 1.75 mm | 183 (32%) | 64 (29%) | |
| 2.0 mm | 96 (17%) | 15 (7%) | |
| 2.15 mm | 14 (2%) | 3 (1%) | |
| 2.25 mm | 4 (1%) | 3 (1%) | |
| Max. burr size, mm | 1.67 ± 0.23 | 1.60 ± 0.21 | < 0.001 |
| RA burr size-up | 158 (28%) | 84 (39%) | 0.0032 |
| Scoring balloon after RA | 73 (13%) | 28 (14%) | 0.89 |
| Stent type | | | |
| Bare-metal stent | 66 (12%) | 18 (8%) | 0.17 |
| 1st-generation DES | 299 (52%) | 104 (48%) | 0.23 |
| SES | 201 (35%) | 73 (33%) | 0.64 |
| PES | 111 (19%) | 35 (16%) | 0.27 |
| 2nd-generation DES | 196 (34%) | 87 (40%) | 0.15 |
| Co-Cr EES | 131 (23%) | 50 (23%) | 0.99 |
| Pr-Cr EES | 59 (10%) | 25 (11%) | 0.65 |
| Other DES | 6 (1%) | 12 (6%) | < 0.001 |
| Final TIMI 3 flow | 552 (97%) | 207 (95%) | 0.21 |

Co-Cr = cobalt chromium; DES = drug eluting stent; EES = everolimus eluting stent; LAD = left anterior descending coronary artery; LMCA = left main coronary artery; PES = paclitaxel eluting stent; Pr-Cr = platinum chromium; RA = rotational atherectomy; RCA = right coronary artery; SES = sirolimus eluting stent; TIMI = Thrombolysis in myocardial infarction.

Previous studies that have assessed differences in clinical outcomes after PCI between the sexes have generated inconsistent results mainly because of the variations in the study populations selected [4, 17, 18]. Moreover, patients with severely calcified vessels have generally been excluded from studies evaluating sex-based differences in outcomes after PCI with DES implantations [19, 20]; therefore, few data are available that describe differences between the sexes in relation to long-term outcomes among patients with severely calcified vessels. In the current study, compared with the male patients, the female patients were older, and their comorbidity rates were higher; these findings are consistent with some clinical profiles of female patients in contemporary trials [17, 18], despite our study included higher risk patients who had severely calcified coronary arteries that required RA. In the DES era, the evolution of devices and techniques for PCI and progress in optimizing medical therapy have been proved to be able to suppress the differences between the sexes [4, 9]. Indeed, multivariate analysis and the analysis of the PS matched population revealed that sex was not associated with MACCE in this study. In addition, the sexes did not differ regarding the mortality and ACS rates, even before adjustments for the confounders. RA is now a standard procedure in contemporary practice; therefore, sex differences may not have been observed, even for complex PCI in severely calcified vessels. The significantly higher rate of stroke in the women compared with that in the men may be explained by the higher prevalence of atrial fibrillation among the women. However, the PS matched cohort analysis showed that the women did not have a higher stroke rate than the men after PCI with RA.

RA is a strategic option for severely calcified coronary arteries; however, concerns about complications remain unresolved [21]. In addition, several studies' findings have demonstrated a higher risk of complications in women who undergo PCI [22, 23]. A recent publication reported that female patients had an increased risk of procedural complications following RA compared with male patients [24]. However, our results suggest that the in-hospital prognoses for the female patients, including complications, were comparable with those for the male patients. While intravascular ultra-

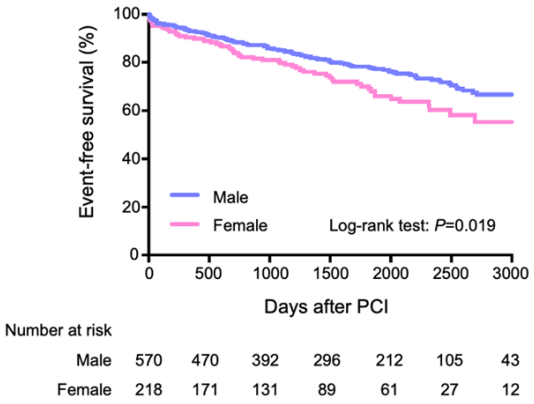


**Figure 1.** Major adverse cardiovascular and cerebrovascular event (MACCE) rates in the unmatched male and female patient groups. The Kaplan-Meier curves show the MACCE-free rates in male and female patients. PCI indicates percutaneous coronary intervention.

sound was used in 73% of the patients in our study, it was used in up 20% of the patients in previous study [24]. Imaging guidance is necessary when selecting suitably sized RA burrs and balloon catheters to prevent serious vessel dissections and perforations, especially during RA. Hence, the rates of imaging-guided PCI may partly explain the differences in the procedural complication rates between this study and previous studies. Female patients have smaller vessels; consequently, smaller maximum RA burr sizes were used in the current study. However, a higher rate of RA burr upsizing was observed in the female patients compared with that in the male patients. Therefore, the therapeutic approach of starting with small RA burrs and upsizing, if needed, might be key to implementing safe procedures in female patients. Given the balance between the risks and benefits, we should not hesitate to perform RA on all indicated patients of both sexes.

*Limitations*

Several study limitations must be considered. First, as this was a retrospective study, it could not establish the efficacy of RA compared with other techniques, and the study was, instead, limited to evaluating the prognoses of patients who underwent RA. Second, the angiographic analyses did not involve a core laboratory, and the indications for RA, PCI, or clinical follow-up depended on each hospital's attending physicians' assessments; the absence of data analyses by a core laboratory may have adversely affected the accuracy of the reported outcomes. Finally, this study still included the limited numbers of patients who received PCI; therefore, the findings from this study should be validated in prospective, large-scale multicenter studies.

## Conclusions

The results from this study, which was undertaken during the DES era, showed the sexes did not differ regarding long-term MACCE following PCI with RA in severely calcified coronary artery stenoses. For better long-term prognoses, optimal interventions should be considered to manage calcified stenoses in all indicated patients of both sexes.

*Competency in medical knowledge*

In the DES era, differences between the sexes are not apparent in relation to long-term MACCE following PCI with RA. We should not hesitate to perform RA on all indicated patients of both sexes.

*Translational outlook*

Differences between the sexes in relation to long-term MACCE are not observed in patients who undergo PCI with RA. Imaging guidance and stepwise burr upsizing might be essential for safe procedures in women. The findings from this study should be validated in prospective, large-scale multicenter studies.

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## Disclosure of conflict of interest

Juntendo University School of Medicine (Dr. Okai, Dr. Dohi, Dr. Okazaki, Dr. Tamura, Dr. Miyauchi, and Dr. Daida) and Teikyo University School of Medicine (Dr. Nakashima, Dr. Okabe, Dr. Nagura, Dr. Nara, Dr. Kawashima, Dr. Kyono, and Dr. Kozuma) received institutional research funds from Boston Scientific Japan. Dr. H. Kyono and K Kozuma have received modest honorarium for lecture from Boston Scientific Japan. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

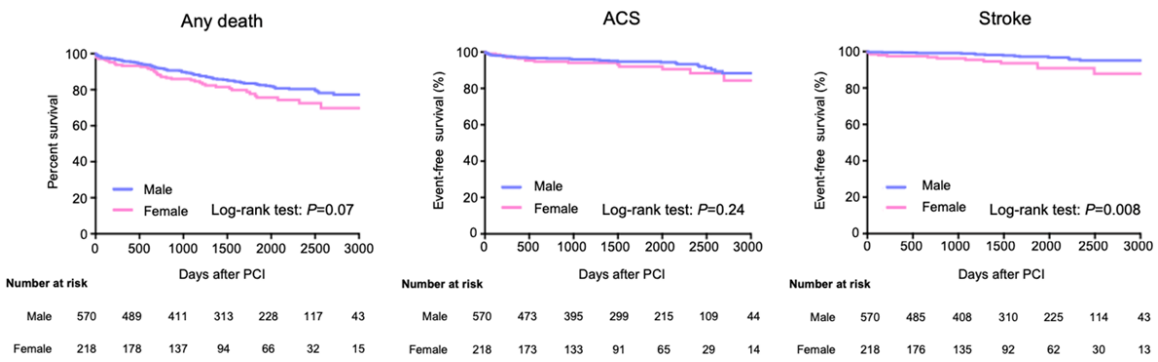


**Figure 2.** The rates of each major adverse cardiovascular and cerebrovascular event (MACCE) component in the unmatched male and female patients. The Kaplan-Meier curves show the event-free rates for any death, acute coronary syndrome, and stroke in the male and female patients. ACS indicates acute coronary syndrome; PCI, percutaneous coronary intervention.

**Table 3.** Predictors of macce

| Variables | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | *p* Value | HR | 95% CI | *p* Value |
| Age | 1.08 | 1.06-1.10 | < 0.001 | 1.07 | 1.03-1.11 | < 0.001 |
| Female | 1.44 | 1.06-1.93 | 0.022 | 1.10 | 0.62-1.92 | 0.74 |
| BMI | 0.92 | 0.87-0.96 | < 0.001 | 0.97 | 0.90-1.04 | 0.35 |
| Hypertension | 1.49 | 1.02-2.27 | 0.041 | 1.47 | 0.69-3.58 | 0.33 |
| Chronic kidney disease | 1.96 | 1.46-2.61 | < 0.001 | 1.22 | 0.64-2.28 | 0.54 |
| ACS | 2.92 | 2.06-4.05 | < 0.001 | 1.35 | 0.75-2.33 | 0.31 |
| Atrial fibrillation | 1.65 | 1.10-2.38 | 0.017 | 1.92 | 1.02-3.41 | 0.045 |
| LVEF | 0.97 | 0.96-0.98 | < 0.001 | 0.95 | 0.93-0.97 | < 0.001 |
| LMCA | 1.80 | 1.24-2.62 | 0.002 | 0.89 | 0.46-1.60 | 0.70 |
| Hemoglobin | 0.74 | 0.67-0.82 | < 0.001 | 0.99 | 0.83-1.18 | 0.96 |
| Creatinine | 1.50 | 1.29-1.69 | < 0.001 | 0.95 | 0.42-1.64 | 0.89 |
| $BNP_{log}$ | 3.68 | 2.71-4.97 | < 0.001 | 1.41 | 0.81-2.44 | 0.22 |
| $CRP_{log}$ | 2.03 | 1.64-2.50 | < 0.001 | 1.47 | 0.98-2.17 | 0.06 |
| $Triglyceride_{log}$ | 0.33 | 0.17-0.64 | 0.001 | 1.75 | 0.55-5.44 | 0.34 |
| Dual anti platelet therapy at discharge | 0.42 | 0.30-0.61 | < 0.001 | 0.57 | 0.30-1.15 | 0.11 |
| DES use | 0.68 | 0.48-0.97 | 0.036 | 0.79 | 0.42-1.60 | 0.50 |

ACS = acute coronary syndrome; BMI = body mass index; BNP = brain natriuretic peptide; CRP = C-reactive protein; DES = drug eluting stent; LVEF = left ventricular ejection fraction; LMCA = left main coronary artery.

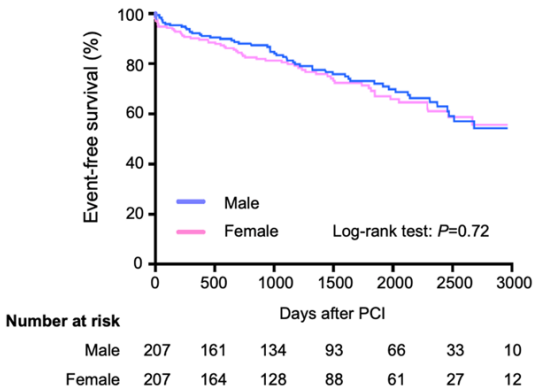


**Figure 3.** Major adverse cardiovascular and cerebrovascular event (MACCE) rates in the propensity score (PS) matched male and female patients. The Kaplan-Meier curves show the MACCE-free rates in the male and female patients after PS matching. PCI indicates percutaneous coronary intervention.

## Abbreviations

ACEi/ARB, angiotensin converting enzyme inhibitor/angiotensin-receptor blocker; ACS, acute coronary syndrome; BMI, body mass index; CRP, C-reactive protein; DES, drug eluting stent;

LVEF, left ventricular ejection fraction; MACCE, major adverse cardiovascular and cerebrovascular event; PCI, percutaneous coronary intervention; PS, propensity score; RA, rotational atherectomy.

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**Supplementary Table 1.** In-hospital outcomes

| In-hospital outcomes | Male n = 570 | Female n = 218 | *p* value |
|---|---|---|---|
| In-hospital death | 11 (1.9%) | 9 (4.1%) | 0.08 |
| Myocardial infarction | 12 (2.1%) | 7 (3.3%) | 0.35 |
| Cardiac tamponade | 6 (1.1%) | 0 (0.0%) | 0.13 |
| Major bleeding | 5 (0.9%) | 4 (1.8%) | 0.26 |
| IABP/PCPS use | 15 (2.6%) | 5 (2.3%) | 0.79 |
| Emergency operation | 2 (0.6%) | 3 (1.4%) | 0.11 |

IABP = intraaortic balloon pumping; PCPS = percutaneous cardiopulmonary support.

**Supplementary Table 2.** Patients' baseline clinical characteristics after ps matching

| Variables | Male n = 207 | Female n = 207 | *p* value |
|---|---|---|---|
| Age, years | 75.1 ± 7.7 | 74.9 ± 6.9 | 0.79 |
| BMI, kg/m$^2$ | 23.0 ± 2.8 | 23.2 ± 3.6 | 0.58 |
| Diabetes | 124 (60%) | 125 (60%) | 0.92 |
| Insulin use | 37 (18%) | 39 (19%) | 0.80 |
| Hypertension | 168 (81%) | 172 (83%) | 0.61 |
| Dyslipidemia | 149 (72%) | 154 (74%) | 0.58 |
| Current smoker | 18 (9%) | 17 (8%) | 0.86 |
| Family history of coronary artery disease | 45 (22%) | 49 (24%) | 0.64 |
| ACS presentation | 39 (19%) | 39 (19%) | 1.00 |
| Chronic kidney disease | 67 (30%) | 66 (32%) | 0.92 |
| Prior myocardial infarction | 45 (22%) | 54 (26%) | 0.30 |
| Prior PCI | 65 (31%) | 65 (31%) | 1.00 |
| Prior CABG | 26 (13%) | 18 (9%) | 0.20 |
| Atrial fibrillation | 26 (13%) | 34 (16%) | 0.26 |
| LVEF, % | 56.6 ± 12.4 | 57.4 ± 12.9 | 0.57 |
| Low LVEF (< 40%) | 25 (14%) | 20 (11%) | 0.41 |
| Laboratory data | | | |
| Hemoglobin, g/dl | 12.6 (11.4-13.7) | 11.5 (10.5-12.4) | < 0.001 |
| Creatinine, mg/dL | 1.00 ± 0.43 | 0.89 ± 0.74 | 0.07 |
| Total cholesterol, mg/dL | 164.5 ± 33.7 | 181.5 ± 41.4 | < 0.001 |
| Triglycerides, mg/dL | 114.3 ± 58.6 | 122.7 ± 75.1 | 0.67 |
| HDL-C, mg/dL | 47.5 ± 14.9 | 50.8 ± 13.9 | 0.02 |
| LDL-C, mg/dL | 97.0 ± 33.3 | 108.4 ± 38.3 | 0.001 |
| HbA1c, % | 6.53 ± 1.00 | 6.64 ± 1.08 | 0.30 |
| C-reactive protein, mg/dL | 0.75 ± 2.10 | 0.77 ± 1.54 | 0.89 |
| BNP, pg/ml | 73.4 (29-194) | 114.9 (45.7-275.5) | 0.01 |
| Medical therapy at discharge | | | |
| β-blocker | 109 (53%) | 103 (50%) | 0.56 |
| Ca-antagonist | 102 (49%) | 114 (54%) | 0.24 |
| ACEi/ARB | 155 (75%) | 153 (74%) | 0.82 |
| Statin | 151 (73%) | 150 (73%) | 0.91 |
| Nitrates/Nicorandil | 114 (55%) | 105 (51%) | 0.38 |
| Aspirin | 199 (96%) | 195 (94%) | 0.36 |
| Thienopyridine | 191 (92%) | 191 (92%) | 1.00 |

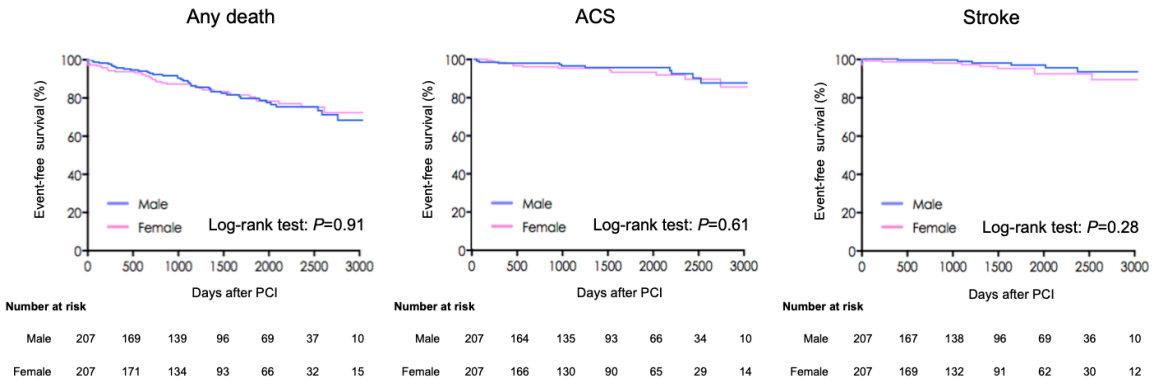
| | | | |
|---|---|---|---|
| Dual antiplatelet therapy | 184 (89%) | 184 (89%) | 1.00 |
| Cilostazol | 7 (3%) | 11 (5%) | 0.33 |
| Oral anticoagulant | 26 (13%) | 24 (12%) | 0.76 |

PS = propensity score; ACEi/ARB = angiotensin converting enzyme inhibitor/angiotensin receptor blocker; ACS = acute coronary syndrome; BMI = body mass index; CABG = coronary artery bypass graft; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.

**Supplementary Table 3.** Angiographic findings and procedural parameters after ps matching

| Variables | Male n = 207 | Female n = 207 | *p* value |
|---|---|---|---|
| Target vessel | | | 0.32 |
| LAD | 145 (70%) | 148 (72%) | |
| Circumflex | 28 (14%) | 19 (9%) | |
| RCA | 27 (13%) | 37 (18%) | |
| LMCA | 28 (14%) | 30 (14%) | |
| Multivessel disease | 142 (69%) | 158 (76%) | 0.08 |
| Chronic total occlusion | 7 (3%) | 9 (4%) | 0.61 |
| Small vessel (< 2.5 mm) | 41 (20%) | 70 (35%) | 0.001 |
| Long stent use (< 23 mm) | 154 (76%) | 151 (75%) | 0.86 |
| Guiding catheter size | | | 0.50 |
| 6Fr. | 84 (44%) | 99 (48%) | |
| 7Fr. | 101 (52%) | 96 (47%) | |
| 8Fr. | 8 (4%) | 11 (5%) | |
| Max. burr size | | | 0.38 |
| 1.25 mm | 19 (9%) | 23 (10%) | |
| 1.5 mm | 92 (45%) | 106 (50%) | |
| 1.75 mm | 65 (32%) | 59 (29%) | |
| 2.0 mm | 26 (13%) | 15 (7%) | |
| 2.15 mm | 3 (1%) | 3 (1%) | |
| 2.25 mm | 1 (1%) | 3 (1%) | |
| Max. burr size, mm | 1.63 ± 0.22 | 1.60 ± 0.22 | 0.17 |
| RA burr size-up | 62 (30%) | 78 (38%) | 0.10 |
| Scoring balloon after RA | 28 (14%) | 24 (12%) | 0.65 |
| Stent type | | | |
| Bare-metal stent | 18 (9%) | 17 (8%) | 0.85 |
| 1st-generation DES | 110 (53%) | 102 (49%) | 0.43 |
| SES | 71 (34%) | 71 (34%) | 1.00 |
| PES | 45 (22%) | 35 (17%) | 0.21 |
| 2nd-generation DES | 74 (36%) | 79 (38%) | 0.61 |
| Co-Cr EES | 46 (22%) | 46 (22%) | 1.00 |
| Pr-Cr EES | 21 (10%) | 23 (11%) | 0.75 |
| Other DES | 5 (1%) | 9 (6%) | 0.28 |
| Final TIMI 3 flow | 203 (98%) | 195 (95%) | 0.07 |

DES = drug eluting stent; EES = everolimus eluting stent; LAD = left anterior descending coronary artery; LMCA = left main coronary artery; PES = paclitaxel eluting stent; PS = propensity score; RA = rotational atherectomy; RCA = right coronary artery; SES = sirolimus eluting stent; TIMI = Thrombolysis in myocardial infarction.




**Supplementary Figure 1.** Each component of MACCE in PS-matched male and female. The Kaplan-Meier curves show event-free rate of any death, ACS, and stroke in male and female patients after PS-matching. ACS indicates acute coronary syndrome; MACCE, major adverse cardiovascular and cerebrovascular event.