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ORIGINAL RESEARCH

Gender-Disparities in the in-Hospital Clinical Outcome Among Patients with Chronic Kidney Disease Undergoing Percutaneous Coronary Intervention

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Purpose: The current study was to evaluate the gender-disparities in the in-hospital thrombotic and bleeding events among patients with chronic kidney disease (CKD) undergoing percutaneous coronary intervention (PCI).

Patients and Methods: Patients with CKD undergoing PCI were retrospectively enrolled. Baseline characteristics, and thrombotic and bleeding events occurred during hospitalization were collected and compared by gender.

Results: Compared to males (n = 558), females (n = 402) were older and more likely to have diabetes mellitus (37.1% vs 29.7%). Females had a lower estimated glomerular filtration rate (eGFR; 51.2 ± 7.9 vs 54.6 ± 5.1 mL/min/1.73m^2) and were more likely to undergo urgent PCI (66.7% vs 60.2%) and use glycoprotein IIb/IIIa inhibitor (15.4% vs 7.5%) at peri-PCI period. Compared to males, females had a higher rate of in-hospital mortality which was due to thrombotic events (9.0% vs 3.4%). Females also had a higher rate of moderate-to-severe hemorrhage (8.0% vs 3.2%). After multivariable adjustment, diabetes mellitus (odds ratio [OR] 1.15 and 95% confidence interval [CI] 1.07–1.29) and acute coronary syndrome (ACS) presentation (OR 1.53 and 95% CI 1.34–1.93) were associated with gender-disparities in composite thrombotic events. Ageing (OR 1.10 and 95% CI 1.02–1.33), diabetes mellitus (OR 1.21 and 95% CI 1.07–1.40) and glycoprotein IIb/IIIa inhibitor use (OR 1.13 and 95% CI 1.02–1.28) were associated with composite bleeding events.

Conclusion: Females with CKD undergoing PCI had a higher risk of experiencing in-hospital thrombotic and bleeding events than males.

Keywords: coronary heart disease, chronic kidney disease, prognosis, gender

Introduction

Despite progress has been achieved in the last three decades, coronary heart disease (CHD) remains a leading cause of morbidity and mortality in China and worldwide.[1–3] Prior studies have shown that chronic kidney disease (CKD), which is defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2, is a common comorbid condition in patients with CHD.[4–6] Presence of CKD substantially increases the risk of thrombotic and bleeding events in CHD patients undergoing percutaneous coronary intervention (PCI).[7–11] The underlying mechanisms are multifactorial, including enhanced systemic inflammation, coagulation disorder, endothelial dysfunction, and increased platelet reactivity among CKD patients.[12–14]

Gender-disparities in the prognosis among CHD patients undergoing PCI have been extensively reported in the Caucasian populations.[15–17] Recently, one study from Chinese patients with acute coronary syndrome (ACS) has shown that compared to males, females were less likely to receive optimal treatment during hospitalization, which resulted in a higher rate of in-hospital mortality.[18] These findings were also observed in another study from Chinese populations.[19] However, participants of these studies were from general populations, and these studies were focused on the gender-

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disparities in the in-hospital mortality. The gender-disparities in other clinically relevant outcomes such as acute stent thrombosis and bleeding events have not been assessed. Furthermore, the factors associated with the gender-disparities in clinical outcomes were unknown. Herein, the aims of the current study were to evaluate: 1) whether there was gender-disparity in the thrombotic and bleeding events during hospitalization between CKD females and males undergoing PCI; 2) if yes, what were the factors associated with the gender-disparity in the clinical outcomes.

Materials and Methods

Study Participants

This was a retrospective study. Because of retrospective design, no informed consent can be obtained. Therefore, informed consent was waived by the Institutional Review Board of the People's Hospital of Longhua District and the personal information of each individual patient was deidentified. The current study was approved by the Institutional Review Board of the People's Hospital of Longhua District. All the procedures were performed according to the Declaration of Helsinki. Patients who were diagnosed as CHD and CKD (according to the eGFR <60 mL/min/1.73m^2) at admission between June 2017 and June of 2019 were screened, and those who were diagnosed as end-stage renal disease (ESRD) or on hemodialysis or did not undergo coronary stenting during index hospitalization were excluded (the study flowchart is presented in Figure 1). In brief, patients with ESRD or on hemodialysis were excluded because these populations are quite different in terms of the clinical profile, treatment and outcome when compared to those with CKD but with preserved renal function.[20] Therefore, in order to reduce the heterogeneity of study participants, these population group was excluded. The diagnosis of CHD was based on clinical symptom plus the findings from computed coronary artery tomography or coronary angiography, which showed that the diameter of coronary artery was ≥50% stenosis.

Clinical Characteristics and PCI Data

Data were extracted from the electronic healthcare system of People's Hospital of Longhua District. Data were manually entered into the dataset by two independent investigators. Demographics (age and gender), risk factors (current cigarette smoking, obesity, hypertension, dyslipidemia and diabetes mellitus) and comorbidities (chronic heart failure, prior history of myocardial infarction [MI], ischemic stroke, peripheral artery disease, and prior history of revascularization) were extracted from the electronic healthcare system. In brief, obesity was defined as body mass index ≥28 kg/m^2 according to the WHO criteria for the Asian populations.[21] Hypertension was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg and/or using antihypertensive medication.[22] Dyslipidemia was defined as total cholesterol ≥5.2 mmol/L and/or low-density lipoprotein cholesterol (LDL-C) ≥2.6 mmol/L and/or using lipid lowering

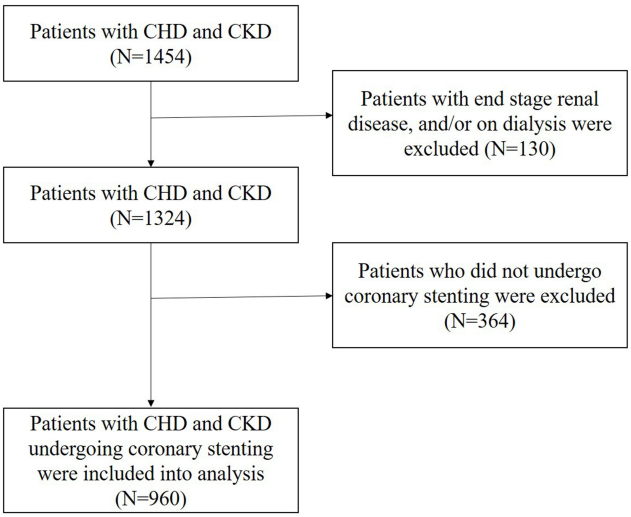

Figure 1 Study flowchart.
Abbreviations: CHD, coronary heart disease; CKD, chronic kidney disease.

medication.[23] Diabetes mellitus was defined as fasting plasma glucose ≥7.0 mmol/L and/or glycated hemoglobin A1c (HbA1c) ≥6.5% and/or using antidiabetic medication.[24] Laboratory data (serum hemoglobin, platelet count, LDL-C and HbA1c levels) were extracted from the electronic laboratory report system. Serum creatinine was used to calculate eGFR using the Modification Diet in Renal Disease formula. PCI data (radial arterial access, urgent or elective PCI, ACS presentation, number and type of stent implantation, number of coronary arteries ≥70% stenosis and peri-PCI antiplatelet drugs use) were extracted from the electronic coronary angiography report system. Medications used at admission and during hospitalization were extracted from the electronic healthcare record system.

Thrombotic and Bleeding Events During Hospitalization

In the current study, the in-hospital clinical outcomes were divided into two aspects. The first aspect was in-hospital thrombotic events, which included acute stent thrombosis, non-fatal MI and mortality due to thrombotic events. In brief, according to the Academic Research Consortium, the diagnosis of acute stent thrombosis was based on the symptoms suggestive of an ACS plus angiographic confirmation of stent thrombosis. The second aspect was in-hospital bleeding events, which included moderate-to-severe hemorrhage based on the GUSTO criteria (including intracranial hemorrhage, gastrointestinal hemorrhage, substantial hemodynamic compromise requires treatment or requires blood transfusion but without hemodynamic compromise)[25] and mortality due to bleeding events. All these events were adjudicated by two independent cardiologists who did not participate in the current study.

Statistical Analysis

Continuous variables were presented as means ± standard deviation (SD), and categorical variables were presented as number and percentage. Student *t*-test was used for comparison of continuous variables and the chi-square test was used for comparison of categorical variables. Univariate and multivariate regression analyses were performed to evaluate the factors associated with the gender-disparities in the in-hospital thrombotic and bleeding events, respectively. When calculating composite thrombotic events, individuals with non-fatal MI secondary to acute stent thrombosis was considered as one event. In the univariate regression analysis, factor with a P value <0.1 was entered into the multivariate regression analyses, and odds ratio (OR) and associated 95% confidence interval (CI) was reported. Male was considered as the reference group. All statistical analyses were performed using the SPSS24.0 software (IBM Statistics) and a two-sided P value <0.05 was considered statistically significant.

Results

Comparisons of Baseline Characteristics by Gender

As presented in Table 1, compared to males, females were older (64.8 ± 12.5 years vs 60.6 ± 13.8 years). They were less likely to be current smokers (11.2% vs 54.1%) and have a prior PCI history. While they were more likely to have diabetes mellitus (37.1% vs 29.7%) and have a higher HbA1c value (6.7 ± 1.6 vs 6.2 ± 1.7%). Females had a lower hemoglobin concentration and there was no difference in the platelet count.

Comparisons of Medications Used at Admission and During Hospitalization by Gender

As presented in Table 2, medications used at admission were similar by gender except for a lower use of statins in females (23.9% vs 31.5%). During hospitalization, guideline-recommended medications used were increased in both males and females. Nevertheless, compared to males, females still had a lower use of statins. Females were more likely to receive ticagrelor (36.8% vs 27.2%) but less likely to use clopidogrel (63.2% vs 72.8%).

Comparisons of Peri-PCI Characteristics by Gender

As shown in Table 3, compared to males, females were less likely to use radial artery access (58.0% vs 72.9%), and they were more likely to present as non-ST-segment elevation MI (NSTEMI; 32.1% vs 24.4%), undergo urgent PCI (49.3% vs 42.3%) and receive glycoprotein IIb/IIIa inhibitor at peri-PCI period (15.4% vs 7.5%).

Table 1 Comparisons of Baseline Characteristics by Gender

Variables	Males (n = 558)	Females (n = 402)
Age (years)	60.6 ± 13.8	64.8 ± 12.5*
Current smoker, n (%)	302 (54.1)	45 (11.2)*
Obesity, n (%)	218 (39.1)	167 (41.5)
Hypertension, n (%)	365 (65.4)	266 (66.2)
Dyslipidemia, n (%)	214 (38.4)	164 (40.8)
Diabetes mellitus, n (%)	166 (29.7)	149 (37.1)*
Chronic heart failure, n (%)	98 (17.6)	75 (18.7)
Myocardial infarction, n (%)	115 (20.6)	72 (17.9)
Ischemic stroke, n (%)	121 (21.7)	84 (20.9)
Peripheral artery disease, n (%)	76 (13.6)	64 (15.9)
Prior PCI, n (%)	106 (19.0)	52 (12.9)*
Prior CABG, n (%)	5 (1.4)	8 (2.0)
eGFR (mL/min/1.73m^2)	54.6 ± 5.1	51.2 ± 7.9
UACR (mg/g)	24.5 ± 6.2	27.1 ± 6.8
HbA1c (%)	6.2 ± 1.7	6.7 ± 1.6*
LDL-C (mmol/L)	3.1 ± 1.5	3.3 ± 1.5
Hemoglobin (g/dL)	14.6 ± 2.5	12.3 ± 3.4*
Platelet (10^9/L)	202 ± 42	210 ± 55

Note: *P < 0.05 versus male patients.
Abbreviations: PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; UACR, urine albumin creatine ratio; HbA1c, glycated hemoglobin A1c; LDL-C, low density lipoprotein-cholesterol.

Comparisons of Clinical Outcomes by Gender

As presented in Table 4, compared to males, females had a longer duration of hospitalization (5.8 days vs 4.6 days). Females had a higher rate of in-hospital mortality due to thrombotic events, and the composite thrombotic events were higher in females (9.0% vs 3.4%). Females also had a higher rate of moderate-to-severe hemorrhage (8.0% vs 3.2%). Among the moderate-to-severe hemorrhagic events, females had a higher rate of gastrointestinal bleeding (6.5% vs 1.8%) and there was no difference in intracranial hemorrhage by gender (1.5% vs 1.4%).

Comparisons of Clinical Outcomes According to CKD Grade

According to eGFR, participants were categorized as CKD 3a (45–59 mL/min/1.73m^2, n=475), CKD 3b (30–45 mL/min/1.73m^2, n = 385) and CKD 4 (15–29 mL/min/1.73m^2, n = 100). Compared to the CKD3a group, the rate of composite thrombotic (4.8% vs 5.2% vs 10.0%; P < 0.001) and bleeding events (5.1% vs 5.7% vs 7.0%; P = 0.03) was higher in the CKD3b and CKD 4 groups.

Factors Associated with Gender-Disparities in the in-Hospital Thrombotic and Bleeding Events

As presented in Table 5, in the univariate regression analysis, ageing, diabetes mellitus, decreasing eGFR, ACS presentation and ticagrelor treatment during hospitalization were associated with a higher risk of composite thrombotic events in females. After multivariate regression analyses, only diabetes mellitus and ACS presentation remained significantly associated with a higher risk of composite thrombotic events in females.

In the univariate regression analysis, ageing, diabetes mellitus, decreasing eGFR and hemoglobin concentration, ACS presentation, glycoprotein IIb/IIIa inhibitor use at peri-PCI period, and ticagrelor and proton pump inhibitor use during hospitalization were associated with a higher risk of composite bleeding events in females. After multivariate regression analyses, ageing, diabetes mellitus and glycoprotein IIb/IIIa inhibitor use at peri-PCI period remained significantly associated with a higher risk of composite bleeding events in females.

Table 2 Comparisons of Medications Used at Admission and During Hospitalization by Gender

Medications	Males (n = 558)	Females (n = 402)
At admission		
Aspirin, n (%)	130 (23.3)	90 (22.4)
Clopidogrel, n (%)	77 (13.8)	52 (12.9)
Ticagrelor, n (%)	29 (5.2)	21 (5.2)
Statins, n (%)	176 (31.5)	96 (23.9)*
ACEi/ARB, n (%)	137 (24.6)	98 (24.4)
Beta-blocker, n (%)	105 (18.8)	85 (21.1)
Oral hypoglycemic drugs, n (%)	122 (21.9)	83 (20.6)
Insulin, n (%)	38 (6.8)	30 (7.5)
Diuretic, n (%)	54 (9.7)	46 (11.4)
Calcium channel blocker, n (%)	140 (25.1)	103 (25.6)
Oral anticoagulants, n (%)	21 (3.8)	17 (4.2)
Proton pump inhibitor, n (%)	42 (7.6)	35 (8.7)
In-hospital		
Aspirin, n (%)	558 (100)	402 (100)
Clopidogrel, n (%)	406 (72.8)	254 (63.2)*
Ticagrelor, n (%)	152 (27.2)	148 (36.8)*
Statins, n (%)	527 (94.4)	351 (87.3)*
ACEi/ARB, n (%)	426 (76.3)	310 (77.1)
Beta-blocker, n (%)	453 (81.2)	328 (81.6)
Oral hypoglycemic drugs, n (%)	126 (22.6)	100 (24.9)
Insulin, n (%)	50 (9.0)	35 (8.7)
Diuretic, n (%)	63 (11.3)	52 (12.9)
Calcium channel blocker, n (%)	143 (25.6)	104 (25.9)
Oral anticoagulants, n (%)	21 (3.8)	16 (4.0)
Proton pump inhibitor, n (%)	96 (17.2)	56 (13.9)

Note: *P < 0.05 versus male patients.
Abbreviation: ACEi/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

Table 3 Comparisons of Peri-PCI Characteristics

Variables	Males (n = 558)	Females (n = 402)
Radial artery access, n (%)	407 (72.9)	233 (58.0)*
Urgent PCI status, n (%)	236 (42.3)	198 (49.3)*
ACS presentation		
STEMI, n (%)	252 (39.8)	174 (39.1)
NSTEMI, n (%)	136 (24.4)	129 (32.1)*
UA, n (%)	198 (35.5)	144 (35.8)
Number of stent implantation	1.6 ± 0.8	1.5 ± 0.6
Number of arteries ≥ 70% stenosis	1.9 ± 0.6	1.8 ± 0.7
Peri-PCI antiplatelet medications use		
Glycoprotein IIb/IIIa inhibitor, n (%)	42 (7.5)	62 (15.4)*
Clopidogrel loading, n (%)	176 (31.5)	126 (31.3)
Ticagrelor loading, n (%)	105 (18.8)	70 (17.4)

Note: * P < 0.05 versus male patients.
Abbreviations: ACS, acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; UA, unstable angina.

Table 4 Comparisons of in-Hospital Clinical Outcome by Gender

Clinical Outcomes	Males (n = 558)	Females (n = 402)
Length of hospital stay (days)[#]	4.6 (3.1–6.5)	5.8 (3.4–7.2)*
Composite thrombotic events, n (%)	19 (3.4)	34 (9.0)*
In-hospital mortality, n (%)	12 (2.2)	29 (7.2)*
Acute stent thrombosis, n (%)	6 (1.1)	5 (1.2)
Non-fatal MI, n (%)	7 (1.3)	7 (1.7)
Composite bleeding events, n (%)	20 (3.6)	33 (8.2)*
In-hospital mortality, n (%)	2 (0.4)	1 (0.2)
Moderate-to-severe hemorrhage, n (%)	18 (3.2)	32 (8.0)*

Note: [#] presented in median and interquartile range; * P < 0.05 versus male patients.
Abbreviation: MI, myocardial infarction.

Table 5 Factors Associated with the Composite Thrombotic and Bleeding Events in Females vs Males

Factors	Univariate Regression		Multivariate Regression	
Composite thrombotic events	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Age	1.27 (1.08–1.45)	0.03	1.07 (0.96–1.19)	0.21
Smoking status	0.96 (0.92–1.05)	0.28		
Obesity	1.14 (0.95–1.25)	0.17		
Hypertension	1.06 (0.97–1.10)	0.21		
Diabetes mellitus	1.36 (1.18–1.75)	0.01	1.15 (1.07–1.29)	0.03
Myocardial infarction	0.92 (0.83–1.07)	0.30		
Prior PCI	0.91 (0.85–1.14)	0.22		
eGFR	1.48 (1.26–1.80)	0.009	1.12 (0.97–1.24)	0.15
Hemoglobin	1.06 (0.94–1.12)	0.25		
ACS presentation	1.99 (1.51–2.38)	< 0.001	1.53 (1.34–1.93)	0.008
Glycoprotein IIb/IIIa inhibitor use	0.97 (0.90–1.05)	0.17		
Ticagrelor use (in-hospital)	0.90 (0.83–0.96)	0.03	0.97 (0.91–1.05)	0.26
Statins use (in-hospital)	1.12 (0.95–1.25)	0.07	1.04 (0.92–1.13)	0.41
Oral hypoglycemic use (in-hospital)	1.08 (0.90–1.13)	0.19		
Proton pump inhibitor use (in-hospital)	1.00 (0.91–1.05)	0.42		
Composite bleeding events	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Age	1.29 (1.09–1.54)	0.02	1.10 (1.02–1.33)	0.04
Smoking status	0.95 (0.91–1.03)	0.56		
Obesity	1.07 (0.94–1.22)	0.27		
Hypertension	1.01 (0.90–1.14)	0.40		
Diabetes mellitus	1.50 (1.24–1.99)	0.002	1.21 (1.07–1.40)	0.02
Myocardial infarction	0.93 (0.88–1.07)	0.39		
Prior PCI	0.99 (0.92–1.13)	0.16		
eGFR	1.43 (1.21–1.75)	0.01	1.13 (0.97–1.26)	0.06
Hemoglobin	1.22 (1.10–1.36)	0.04	1.09 (0.97–1.21)	0.17
ACS presentation	1.18 (1.02–1.30)	0.03	1.02 (0.91–1.10)	0.32
Glycoprotein IIb/IIIa inhibitor use	1.24 (1.16–1.52)	0.01	1.13 (1.02–1.28)	0.04
Ticagrelor use (in-hospital)	1.25 (1.10–1.53)	0.02	1.09 (0.98–1.16)	0.44
Statins use (in-hospital)	1.03 (0.92–1.16)	0.17		
Oral hypoglycemic use (in-hospital)	1.05 (0.95–1.06)	0.13		
Proton pump inhibitor use (in-hospital)	1.10 (1.03–1.28)	0.03	1.01 (0.92–1.07)	0.25

Abbreviations: OR, odds ratio; CI, confidence interval; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; ACS, acute coronary syndrome.

Discussion

Although prior studies have reported the gender-disparities in the in-hospital mortality in the Chinese general population,[18,19] the current study for the first time specifically evaluates the gender-disparities in the in-hospital thrombotic and bleeding events in the Chinese CKD patients undergoing PCI. There are two main findings. Among CKD populations undergoing PCI, compared to males, females had a higher risk of composite thrombotic and bleeding events during hospitalization. In addition, the gender-disparities in the clinical outcomes were associated with traditional risk factors, suggesting that there are opportunities to narrow the gender-disparities through better controlling these risk factors.

Compared to males, females commonly experience a higher risk of ischemic events post-PCI therapy. For example, using data from the National Cardiovascular Disease Registry, Roswell et al reported that among patients with STEMI, females had a longer duration of contact-to-device process, resulting in a higher mortality rate.[26] Combing data from the United Kingdom and Sweden cohort studies, Kunadian et al reported that compared to males, females experienced a higher rate of mortality at 30-days and 1-year after PCI therapy.[27] After adjusting for potential covariates, female sex remained an independent risk factor for a higher mortality risk. Recently, Hao et al reported that Chinese females, who were hospitalized for ACS, received less optimal therapy than their male counterparts.[18] In addition, females experienced a higher risk of in-hospital mortality, which were due to the gender-disparities in the clinical profiles and therapy during hospitalization. Importantly, in the CKD populations, findings of the current study showed that the risk of in-hospital mortality due to thrombotic events was higher in females. There are some theories to explain this disparity. First of all, as shown in Table 1 that females were older and more likely than males to have other comorbidities such as diabetes mellitus. Notably, these two factors are associated with significantly higher risk of mortality in CHD populations undergoing PCI.[28] In specific, the adverse effects of diabetes mellitus are greater in women than in men. Indeed, prior studies suggest that diabetes mellitus has greater influences on blood pressure elevation, endothelial dysfunction and systemic inflammation in women than in men, which might contribute to the higher thrombotic events in women.[29] In addition, diabetic females commonly have a higher level atherogenic dyslipidemia than men, which also leads to a higher risk of thrombotic event.[30] Second, females were less likely than males to receive guideline-recommended medication therapy during hospitalization. For example, compared to males, the use of statins was lower in females. It is well documented that statins therapy is associated with improvement in prognosis for CHD populations.[31] Third, females were less likely to use radial artery access and more likely to undergo urgent PCI than males. Prior studies have demonstrated that the use of radial artery access was associated with lower incidence of thrombotic event at peri-PCI period and urgent PCI per se might represent a high thrombotic risk.[32]

Extending prior studies which only evaluated the in-hospital mortality risk, the current study also compared the rate of acute stent thrombosis and non-fatal MI between females and males. Prior studies have suggested that CKD patients had a higher risk of developing stent thrombosis than those with normal kidney function.[4,8] The current study did not find any significant gender-disparities in acute stent thrombosis and non-fatal MI. The reasons might be due to the fact that females were more likely to receive glycoprotein IIb/IIIa inhibitor at peri-PCI period and ticagrelor during hospitalization. Notably, these two medications have potent and rapid effects on inhibiting platelet, which in turn might reduce the incidence of thrombotic events in female patients.

Diabetes mellitus and ACS presentation were the two main factors associated with a higher risk of composite thrombotic events in females. These findings suggested that improving the management of traditional risk factors would be beneficial for narrowing the gender-disparities in clinical outcomes. Indeed, as presented in Table 1, females had a higher prevalence of diabetes mellitus; however, the use of hypoglycemic medications was similar by gender, suggesting that females were under-treatment than their male counterparts. Improvement in diabetic therapy might be helpful to narrow this disparity. In addition, females were more likely to present as ACS, suggesting that promoting the awareness of latent cardiovascular problems might increase the utilization of secondary prevention and timely re-reperfusion therapy.

Notably, considering the high risk of thrombotic events among CKD patients undergoing PCI, prolonged dual antiplatelet therapy might be beneficial for decreasing the thrombotic risk. Indeed, Cesaro et al reported that in a real-

world study including patients with prior MI, prolonged dual antiplatelet therapy with low-dose ticagrelor was effective and safe for preventing thrombotic events, with no risk of increasing major bleeding events at follow-up.[33] These findings suggest that prolongation of aspirin and low-dose ticagrelor therapy might be helpful to reduce the thrombotic risk among females with CKD while without increasing bleeding risk, which deserves further evaluation.

Prior studies have indicated that the use of radial artery access was associated with a reduced risk of acute kidney injury (AKI) among CKD patients.[34,35] In the current study, females were less likely than males to use the radial artery access. Unfortunately, we did not evaluate the incidence of AKI in the current study. It is noted that incident AKI was associated with a higher mortality risk. Therefore, it was possible that the higher mortality risk in female patients might be partly explained by their lower use of radial artery access. Notwithstanding, when we categorized participants based on eGFR at baseline, the results indicated that there was a trend toward increasing thrombotic and bleeding events with decreasing renal function. These findings demonstrate the influences of renal function on the clinical outcomes.

Different from prior studies which merely evaluated the gender-disparities in the in-hospital mortality or thrombotic events,[18,19,26] the current study also evaluated the bleeding events by gender. Compared to males, females had a higher risk of bleeding events during hospitalization, especially gastrointestinal bleedings. Results from prior studies also supported the current findings. Xu et al reported that compared to males, females undergoing PCI had a high risk of bleedings at two-years follow-up.[36] Wanha et al also found that although the 1-year bleeding risk between females and males was similar after PCI therapy, females experienced a higher risk of in-hospital bleeding events.[37] Extending prior reports, the current study was also focused on elucidating the factors associated with the gender-disparities in bleeding events. As presented in Table 4, ageing, diabetes mellitus and glycoprotein IIb/IIIa inhibitor use at peri-PCI period were associated with the gender-disparities in the composite bleeding events. Notably, numerous studies have shown that ageing, diabetes mellitus and peri-PCI use of potent antiplatelet drug (eg, glycoprotein IIb/IIIa inhibitor) were associated with a high bleeding risk in both short- and long-term follow-up.[38–42]

Recognizing the overlapped risk factors for thrombotic and bleeding events (diabetes mellitus) and the tradeoff of using potent antiplatelet drug (thrombotic risk vs bleeding risk), the clinical implications of the current findings were as follow: 1) among females with CKD undergoing PCI, optimizing diabetic management might mitigate the thrombotic and bleeding risk simultaneously; 2) among females with CKD undergoing PCI, it should be prudent to use potent antiplatelet drug at peri-PCI period, and it is essential to balance the harm and benefit in an individual level.

There are some limitations of the current study. First, the observational design could not allow us to draw any causal relationship between the identified factors and outcome of interest. Second, since this was a retrospective study, the potential recalled and selection biases might influence the current findings. Third, we had only evaluated the in-hospital clinical outcome, and whether these findings could be extrapolated to the clinical outcome at follow-up were unknown. Fourth, findings from the current single-center study should be corroborated in other research groups. Fifth, despite we have extensively adjusted for potential covariates, unmeasured and unknown factors might still exist and influence the association between potential risk factor and the clinical outcome. Last but not the least, in the current study, patients with ESRD or on hemodialysis were excluded. Therefore, findings of the current study cannot be extrapolated to these populations.

Conclusion

In conclusion, the current study shows that in CKD patients undergoing PCI, compared to males, females have a higher risk of thrombotic and bleeding events during hospitalization, which were associated with traditional risk factors. Further studies are needed to evaluate whether intervening these risk factors could narrow the gender-disparities in the clinical outcomes.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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