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GENDER DIFFERENCES IN CLINICAL CHARACTERISTICS AND IN-HOSPITAL OUTCOMES OF PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION IN VIETNAM

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ABSTRACT

Background: Little is known about gender differences of coronary heart disease patients undergoing percutaneous coronary intervention (PCI) in low-and middle-income nations, despite its rapid uptake across Asia. **Objective:** to report on gender clinical characteristics and in-hospital outcomes for patients undergoing percutaneous coronary intervention at a leading cardiac centre in Vietnam. **Methods:** Information on characteristics, treatments, and outcomes of patients undergoing percutaneous coronary intervention was collected into the first registry. Subgroup analysis was conducted to explore gender differences. **Results:** Between September 2017 and May 2018, 1,022 patients undergoing percutaneous coronary intervention were recruited from a total of 1,041 procedures. The mean age was 68.3 years, and two thirds were male. Female patients were older, lower educational level, monthly income and involved with more manual jobs than male ($p<0.0001$). Despite having less serve clinical presentations, female tent to have more comorbidities and a higher incidence of major bleeding than males ($p<0.05$). **Conclusions: t**he findings may contribute to evaluating PCI-related practices, identifying the gaps in sex-specific care for cardiovascular health, and potentially developing appropriate treatment guidelines.

Keywords: Percutaneous coronary intervention; Clinical characteristic; Outcomes; Vietnam

INTRODUCTION

Percutaneous coronary intervention (PCI) has been demonstrated to be an effective treatment for coronary heart disease (CHD) worldwide since its inception in the late 1970s[1,2]. The procedure has become more widely used in Asia, where CHD was the leading cause of death (approximately 16.2% of all deaths in 2016)[3,4], with around one million PCIs undertaken in 2016 alone[5]. Notwithstanding the apparent benefits of PCI, post-procedural cardiac complications remain a concern, including death, myocardial infarction (MI) and bleeding[6,7].

Accumulating data in the USA and Europe have shown that the occurrence of these adverse cardiac events differed according to many factors, including gender[6,8,9]. In Asia, cardiac registries in some high-income countries have also reported similar findings[10,11], while relevant data remains limited in lower-and middle-income countries. Additionally, most medical care provided for CHD patients in Asian countries is based on the European or North American guidelines developed from large domestic registries[12-14]. It is not clear whether the non-Asian data reflects the Asian experience, nor whether the guidelines are well suited to the Asian population. Thus, data from real-world practice in less developed countries are very important to establish current benchmarks and determine appropriate management and preventive strategies for these populations.

Vietnam is a middle-income nation in South-East Asia, where PCI has been widely used in modern cardiac based treatments for CHD, the second leading cause of death[15]. The aim of this paper is to provide insights concerning the gender differences in clinical characteristics and in-hospital outcomes of patients undergoing PCI in Vietnam based on the first PCI registry conducted at a leading cardiac hospital in Vietnam.

METHODS

Participants, time and location of study

Participants were patients underwent percutaneous coronary intervention at the Vietnam National Heart Institute (VNHI), Hanoi, Vietnam during September 2017-May 2018. The study was conducted at VNHI, the leading cardiac centre nationwide,

where the highest quality of healthcare services are provided for around 17,000 cardiovascular inpatients and 80,000 out-patients annually[16].

It was a pilot registry study. Potential participants were patients who underwent PCI at VNHI during the study period and met the following criteria: Vietnamese residents aged 18 years and over; Had at least one active phone contact number; and able to communicate, understand the information sheet and did not opt-out of future follow-ups by the time of discharge. There were no exclusion criteria.

Data collection

This single-centre, hospital-based registry adapted the data collection forms currently used in the Victorian Cardiac Outcomes and Melbourne Interventional Group registries, Australia[17,18]. Information on demographic, clinical and procedural information, and outcomes of patients who underwent PCI was recorded on standardised data abstraction forms with standard definitions for all fields. Information was collected via patient interviews, extracting medical records, reading the PCR disks.

Information collection

Patient characteristics

Information on participant demographics, medical history, cardiovascular risk factors (diabetes, hypertension, dyslipidemia, cerebrovascular disease), clinical symptoms and presentation (acute coronary syndrome (ACS), cardiogenic shock, cardiac arrest), left ventricular ejection fraction, and pre-procedural renal status was collected via both patient interviews and medical records.

Procedures and medications

The strategy for the specific coronary intervention (e.g. choice of stent, medication) was at the discretion of the interventionists. Injured lesion segments were coded following the classification of the Syntax Score[19] and guidelines for the lesion type of American College of Cardiology/ American Heart Association (ACC/AHA)[20]. A procedure was considered successful if there was a residual stenosis of less than 10% following coronary

stenting and the rate of coronary blood perfusion of Thrombosis in Myocardial Infarction 2 or 3 flow. Pre and post procedural medical therapies such as oral antiplatelet, aspirin, anti-thrombin, and glycoprotein IIb/IIIa inhibitors were evaluated according to the 2016 ACC/AHA guidelines[21]. Medications and procedural data were obtained by extracting medical records and reading secured procedural disks.

Clinical outcomes

Medical records were extracted to document in-hospital complications including death, new or recurrent MI, cardiogenic shock, bleeding, post-procedural renal impairment, new requirement for dialysis, unplanned target vessel revascularisation (revascularisation for the previously cured coronary artery) by PCI or coronary artery bypass grafts (CABG), stent thrombosis, and stroke.

Statistical analysis

Data on demographic, clinical, procedures and outcomes were presented as numbers (and percentages) for categorical variables, and means (with standard deviations) for continuous variables. Descriptive statistics were used to summarise characteristics of the study participants. Fisher exact or Chi-square tests were undertaken to compare categorical variables, and Student's t tests or analysis of variance (ANOVA) were applied to compare continuous variables. All p-values were two-tailed with significance defined as $p \leq 0.05$. All statistical analyses were performed using the SPSS statistical package (SPSS Version 20.0 for Windows; SPSS Inc., Chicago, IL).

Research ethics

The study protocol was approved by the Curtin University Ethics Committee before the commencement of data collection (HRE 2017-0378). Patients had the right to opt out of the study without impacting on their care. Data collection was conducted by a team of specifically trained local investigators at VNHI.

RESULTS

Patient characteristics by gender

Table 1. Clinical characteristics (n= 1022)

	Female	Male	P value*
Patients	326 (31.9)	696 (68.1)	_
Age (years), mean ± SD	70.9 ± 9.4	67.0 ± 10.5	<0.0001 †
Kinh people	321 (98.5)	667 (95.8)	0.045
From provinces outside Hanoi	233 (71.5)	563 (80.9)	0.001
Education			
Primary school and lower	47 (14.4)	36 (5.2)	<0.0001
Secondary school	122 (37.4)	245 (35.2)	
High school	40 (12.3)	124 (17.8)	
College and higher	117 (35.9)	291 (41.8)	
Current/ past occupation			
Officer worker	120 (36.8)	269 (38.6)	<0.0001
Manual worker	67 (20.6)	96 (13.8)	
Farmer	107 (32.8)	148 (21.3)	
Tradesperson	17 (5.2)	47 (6.8)	
Others	15 (4.6)	136 (19.5)	
Poverty [a]	19 (5.8)	25 (3.6)	0.175
Low income [b]	279 (85.6)	483 (69.4)	<0.0001
Body mass index (kg/m^2)			
Low (<18.5)	38 (11.7)	69 (9.9)	0.071
Normal (18.5- 22.9)	178 (54.6)	340 (48.9)	
High (≥ 23.0)	110 (33.7)	287 (41.2)	

Data are presented as n (%), otherwise specified.

* Comparing female and male subjects; [a] Obtained certificates of poor and near poor household; [b] Individual monthly income < 216 USD with the exchange rate of 23.150 VND; [c] Creatinine > 200µmol/L.

A total of 1,022 patients were enrolled into the registry. Of these, 19 patients had a second PCI, meaning a total of 1,041 procedures, treating 1,276 lesions.

Demographics and clinical characteristics of participants are summarized in Table 1. Two-thirds of the study population were male. The participants' mean age (±SD) was 68.3 years (10.3) and females were approximately 4 years older than men (p<0.0001). Compared with males, females had a lower education level, monthly income and were more likely to do manual work (p<0.0001).

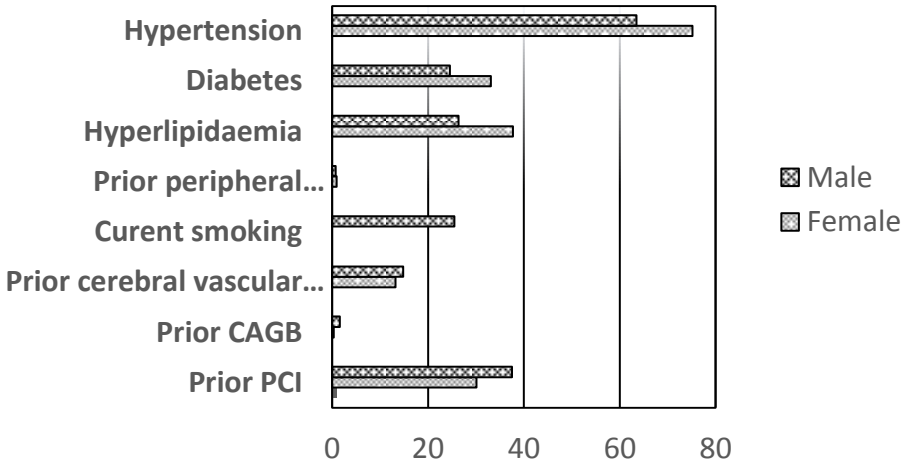

Figure 1. Risk factors of study participants

Additionally, females also had a higher prevalence of risk factors such as hypertension, diabetes, and hyperlipidaemia ($p<0.05$) with the exception of current smoking and previous PCI ($p<0.05$) compared to males (Figure 1).

Lesion, procedural characteristics and medications prior to PCI

Table 2. Lesion, procedural characteristics and medications prior to PCI (n= 1276*)

	Female (n=406)	**Male (n=870)**	**P value**
Lesions	406 (31.8)	870 (68.2)	_
Percutaneous entry location			
Radial	263 (79.2)	561 (79.1)	>0.999
Femoral	69 (20.8)	148 (20.9)	
Target vessel			
Left main	29 (7.1)	123 (14.2)	<0.0001
Left anterior descending	208 (51.2)	387 (44.5)	0.030
Right coronary	118 (29.1)	288 (33.1)	0.164
Circumflex	80 (19.7)	191 (22.0)	0.394
PCI with ≥ 2 lesions	69 (17.0)	149 (17.1)	>0.999

Type B2 and C lesions	381 (93.8)	821 (94.5)	0.745
Chronic total occlusion	10 (2.5)	51 (5.9)	0.012
Restenotic lesions	11 (2.7)	53 (6.1)	0.014
Stents used for each lesion			
≤ 1	271 (66.7)	517 (59.5)	0.015
≥ 2	135 (33.3)	352 (40.5)	
Mean (± SD)	1.42 (± 0.64)	1.54 (± 0.74)	0.002
Stent length > 20mm	375 (95.2)	806 (96.2)	0.502
Mean stent length (± SD)	34.5 (± 8.9)	34.7 (± 8.7)	0.656
Angiographic success	405 (99.8)	862 (99.2)	0.448
Drug-eluting stent use	394 (97.3)	837 (97.1)	0.998
Balloon only	11 (2.7)	25 (2.9)	
Guidance of IVUS	13 (3.2)	33 (3.8)	0.654
Medications			
Fibrinolytic therapy	1 (50.0)	1 (50.0)	0.536
Glycorprotein IIb/ IIIa			
Antithrombin therapy	111 (34.3)	266 (37.5)	0.227
Ticagrelor	35 (10.5)	141 (19.9)	<0.0001
Clopidogrel/ Ticlopidine	284 (85.5)	549 (77.4)	0.003
Aspirin	320 (96.4)	695 (98.0)	0.172

**missing information of one lesion*

Data are presented as n (%), unless specified. IVUS: Intravascular Ultrasound

There were 1,276 lesions which required subsequent treatment within 1041 procedures (Table 2).

Compared with females, males were more likely to have disease in the left main coronary artery, chronic total occlusions, stent restenosis, and ≥ 2 stents per lesion ($p<0.05$). They tended to receive ticagrelor, while their female counterparts were relatively more likely to be prescribed with clopidogrel prior to PCI (both $p<0.05$).

In-hospital outcomes and medications post PCI

Table 3. In-hospital outcomes and medications post PCI (n= 1041)

Outcomes	Female (n=332)	Male (n=709)	p
New renal impairment	11 (3.3)	22 (3.1)	>0.999
New dialysis	1 (0.3)	8 (1.1)	0.286
Cardiogenic shock	1 (0.3)	3 (0.4)	>0.999
New/ recurrent MI	2 (0.6)	1 (0.1)	0.24
Unplanned PCI	1 (0.3)	1 (0.1)	>0.999
Stent thrombosis	2 (0.6)	0 (0.0)	0.102
Major bleeding	12 (3.6)	9 (1.3)	0.023
Stroke	1 (0.3)	4 (0.6)	>0.999
Death	3 (0.9)	3 (0.4)	0.39
Hospital length (day), median	2.0	2.0	0.69
Hospital length > 2 days	34.3	32.4	0.59
Medications			
Aspirin	329 (99.7)	704 (99.7)	>0.999
Clopidogrel/ Ticlopidine	290 (87.8)	545 (77.2)	<0.0001
Ticagrelor	40 (12.2)	161 (22.9)	<0.0001
Beta Blockers	138 (41.8)	259 (37.0)	0.125
Angiotensin-receptor blockers	308 (93.6)	644 (91.6)	0.317
Statin	330 (100.0)	703 (99.6)	0.556
Other lipid lowering therapy	3 (0.9)	0 (0.0)	0.032
Oral anticoagulation therapy	2 (0.6)	2 (0.3)	0.956

Data are presented as n (%), unless specified.

Major bleeding rate was higher in females than males ($p<0.05$). Ticagrelor was commonly used in males, while clopidogrel was frequently prescribed in the latter ($p<0.0001$).

DISCUSSION

This study was the first to provide gender differences in several demographic and socioeconomic factors, clinical presentation and treatment which may be potentially important in the design of optimal care in developing settings.

Patterns of gender differences in demographic, socioeconomic and clinical factors are consistent with prior research [8,22,23]. For

example, our study showed females receiving PCI accounted for nearly one-third of total participants, those females were generally older and had more comorbidities than males. In our data, the female to male ratio was 0.47, which contrasts with the general Vietnamese population group age 64 and above which has a female to male ratio of 1.6[24]. This lower incidence of PCI in females might be explained by the relatively lower priority in families of females compared to males in Vietnamese culture. This may be exacerbated by the high cost requirement of the procedure itself and other hospital treatments in the national centre as VNHI. More males were transferred from other provinces to VNHI for PCI in comparison to females ($p= 0.001$), which may support this theory. Additionally, presenting females were on average 4 years older than males ($p< 0.0001$). The protective impact of oestrogen in females in delaying the onset of cardiovascular disease is likely to be part of the explanation[25]. The 4-year age gap also partly explains more comorbidities seen in females such as hypertension, diabetes and hyperlipidaemia in our study. The Global Registry of Acute Coronary Events (GRACE) indicated that, in the group of patients undergoing cardiac intervention, females had higher rates of diabetes, hypertension, but were less likely to smoke[9]. Data from several systematic review with meta-analysis also confirmed that females with cardiovascular risk factors were more likely to have incident CHD than males[26,27].

Regarding clinical presentations, in general, females receiving PCI had lower procedural risks relative to males. Results from the GRACE registry indicated that females were more likely to have normal/mild diseases and less likely to have injured lesion in left main vessel[9]. Although this is not direct comparison as GRACE contained patients undergoing catheterization only, our finding is in line with that result. Similarly, a nationwide study in patients undergoing PCI in Korea reported that males had more chronic lesions in left main vessel, and required a higher number of stents than females[23]. Data from a national cardiovascular registry in America also revealed that females had a lower risk of angiographic features, and needed shorter stents[8].

In term of in-hospital outcomes, previous studies have largely reported that, females were at a higher risk of having complications or worse PCI-specific outcomes, e.g. death, bleeding or cardiogenic shock than males[8,22,28]. Likewise, females in our study were more likely to have major bleeding relative to males. It is possible that females were older, had a higher prevalence of coronary risk factors, and a smaller body size as well as smaller arteries than males at the time of PCI procedure[8,23]. It is also worth noting that most current PCI-based devices and medication therapies have been designed relatively equally between males and females, without a specific gender indication[29]. Thus, more focused efforts should be taken to prevent and reduce bleeding complications in female patients with PCI.

STUDY LIMITATIONS

There are some limitations to our study. Despite data was collected at the national and biggest cardiac interventional centre in Vietnam, our findings might not be representative of the whole nation, particularly in terms of lesion type and uptake of cutting-edge interventions as VNHI is a single centre only. Furthermore, some uncertainties and recall errors of the patients in self-reporting the socioeconomic status as well as cardiovascular risk factors might occur, which can contribute to the differences observed. Additional dedicated studies should be conducted to provide more overall views of PCI practices in Vietnam.

CONCLUSION

Our study based on the first Vietnamese PCI registry provides an opportunity to understand insights of gender differences in clinical characteristics and in-hospital outcomes of the patients undergoing PCI in Vietnam. The findings may contribute to evaluating PCI-related practices, identifying the gaps in sex-specific care for cardiovascular health, and potentially developing appropriate treatment guidelines.

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