International Journal of Cardiology 253 (2018) 50–54

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Sex differences in left main coronary artery stenting: Different characteristics but similar outcomes for women compared with men

Eun-Seok Shin [a], Cheol Whan Lee [b,*], Jung-Min Ahn [b], Pil Hyung Lee [b], Mineok Chang [b], Min-Ju Kim [c], Sung-Han Yoon [b], Duk-Woo Park [b], Soo-Jin Kang [b], Seung-Whan Lee [b], Young-Hak Kim [b], Seong-Wook Park [b], Seung-Jung Park [b]

[a] Department of Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Republic of Korea
[b] Heart Institute, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea
[c] Division of Biostatistics, Center for Medical Research and Information, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 15 January 2017
Received in revised form 23 May 2017
Accepted 12 June 2017

Keywords:
Left main coronary artery disease
Percutaneous coronary intervention
Drug-eluting stent
Sex difference

ABSTRACT

Background: The clinical outcomes for women compared with men undergoing left main PCI were sparse. We compared the characteristics and long-term outcomes in women versus men after percutaneous coronary intervention (PCI) with drug-eluting stents (DES) for unprotected left main CAD.
Methods: We identified 2328 patients (545 women; 1783 men) with unprotected left main CAD who received PCI with DES between January 2007 and December 2013 in the Interventional Cardiology Research In-cooperation Society-left MAIN revascularization (IRIS-MAIN) registry. The primary outcome was a composite of death from any cause, myocardial infarction, or stroke.
Results: The median follow-up time was 2.9 years (interquartile range: 1.0–4.1 years). Women were older, had a higher incidence of insulin-requiring diabetes mellitus and hypertension, and more commonly presented with acute coronary syndrome than men. Left main ostial lesion was more common in women, whereas left main bifurcation lesion with more extensive CAD was more common in men. The incidence of primary outcome was similar between the two groups (10.8% vs. 10.8%, respectively, log-rank $p = 0.587$). The results were similar after adjustment for baseline variables and consistent across major subgroups. The need for target lesion revascularization was significantly higher in women than in men (8.8% vs. 5.7%, respectively, $p < 0.05$) but the sex bias was not confirmed after adjusting for confounders.
Conclusions: Women, as compared to men, had different clinical and lesion characteristics but similar long-term outcomes after PCI with DES for left main CAD.

1. Introduction

Coronary artery bypass grafting (CABG) has been considered as the standard of care for left main coronary artery disease (CAD) [1–5]. Several randomized trials demonstrated that percutaneous coronary intervention (PCI) with drug-eluting stents (DES) showed favorable and similar long-term clinical outcomes compared with concurrent CABG [2,5]. Despite the safety and efficacy of left main PCI, however, only 24% of patients enrolled in each trial were women, and thereby data for women undergoing left main PCI were sparse [2,5]. It has been shown that women had different risk factors, presentations, atherosclerotic involvement, and outcomes compared with men in coronary artery disease [6–8]. However, little is known about sex differences in left main PCI.

In the present study, we investigated the sex differences in risk profile and long-term prognosis among patients with left main PCI with DES using the Interventional Research Incorporation Society-Left MAIN Revascularization (IRIS-MAIN) registry.

2. Methods

The study patients were recruited from the IRIS-MAIN registry (ClinicalTrials.gov number, NCT01341327). The registry was designed to evaluate the real-world outcomes of left main CAD and register all consecutive patients with left main CAD, defined as diameter stenosis >50% on coronary angiogram, between January 2007 and December 2013 from 50 academic and community hospitals in Asian countries (China, India, Indonesia, Japan, Malaysia, South Korea, Taiwan, and Thailand). All women and men undergoing PCI with DES were enrolled in the current analysis. The study protocol was approved by the institutional review boards of all participating centers, and written informed consent was obtained from all patients before entering the study.

* Corresponding author at: Division of Cardiology, Heart Institute, Asan Medical Center, University of Ulsan, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea.
E-mail address: cheolwlee@amc.seoul.kr (C.W. Lee).

http://dx.doi.org/10.1016/j.ijcard.2017.06.051
0167-5273/

PCI for left main CAD and other coronary artery diseases was performed according to the standard practical guidelines, as previously described [1,9]. The application of predilation, intravascular ultrasound, and intra-aortic balloon pumps, and the selection of a specific type of implanted stent, were at the discretion of the operator. Periprocedural anticoagulation was administered according to standard regimens. All patients undergoing PCI received a loading dose of aspirin and adenosine diphosphate (ADP) receptor antagonists before or during the intervention. After the procedure, aspirin was continued indefinitely and ADP receptor antagonists were prescribed for at least 12 months.

The primary outcome was a composite of death from any cause, myocardial infarction (MI), or stroke. Death was classified as either cardiac or non-cardiac death, with all death considered cardiac unless an unequivocal non-cardiac cause could be established. MI was defined as follows: 1) if occurring within 48 h after the index treatment, an increase in the creatine kinase–myocardial band (CK-MB) concentration of >5 times the upper reference limit with any of the followings: new pathological Q waves or new bundle branch block, new graft or new native coronary occlusion documented on angiography, and new regional wall motion abnormality or loss of viable myocardium on imaging studies [10]; 2) if occurring 48 h after the index treatment, an increase in the CK–MB concentration above the upper reference limit with ischemic symptoms or signs [11]. Stroke, as indicated by neurological deficits, was confirmed by a neurologist on the basis of imaging modalities. e. Stent thrombosis was evaluated according to the Academic Research Consortium definitions [12]. Repeat revascularization included any type of percutaneous or surgical revascularization procedures, regardless of whether the procedure was performed on a target lesion, a non-target lesion or a new lesion. All events were based on clinical diagnoses assigned by the patient's physician and were centrally adjudicated by an independent group of clinicians.

Baseline variables and outcome data were collected by a specialized personnel using a dedicated electronic case report form (e-CRF) at each center. Monitoring and verification of registry data were periodically performed in participating hospitals by the staff of the academic coordinating center (Clinical Research Center, Asan Medical Center, Seoul, Korea). Clinical follow-up was conducted during hospitalization and at 30 days, 6 months, and 12 months and every 6 months thereafter. At each visit, data pertaining to the patient's clinical status, all interventions, and adverse events were recorded.

Continuous variables were expressed as means ± one standard deviation; categorical variables were presented as counts and percentages. Continuous variables were compared using Student's *t*-test; categorical variables were compared using χ^2 statistics or Fisher's exact test, as appropriate. Cumulative probabilities for the outcomes were estimated by the Kaplan-Meier method, and the Kaplan-Meier curves of women and men groups were compared using the log-rank test. Multivariable Cox proportional hazard analysis was performed to appraise the sex differences simultaneously adjusting for all variables with significant ($p < 0.05$) or borderline significant ($p \leq 0.10$) association with sex at univariate analysis and including, by default, diabetic status as well as disease location(s) in the left main CAD. The results of these analyses were reported as hazard ratios (HRs) with 95% confidence intervals (CI). All computation was performed using SPSS 11.0 (SPSS, Chicago, IL, USA).

3. Results

We identified 2328 patients with left main CAD (women: $n = 545$, men: $n = 1783$) among 5134 patients with PCI with DES enrolled in the IRIS-MAIN registry. In the comparison with men, women were older and had more hypertension insulin-requiring diabetes mellitus and more frequently women presented with acute coronary syndrome (ACS). By contrast, women were less likely to be ever-smokers or to have history of previous MI, peripheral vascular disease, and chronic pulmonary disease. In addition, left main ostial lesion was more common in women, whereas left main bifurcation lesion with more extensive CAD (left main plus 3 vessel disease) was more common in men. Therefore, the left main stent only strategy was more common in women and more complex 2-stent technique in men. The total number of stents used was higher in men and total stent length was longer in men. In both groups, IVUS-guided PCI was as high as 80%. Patients were well treated with optimal medication without between-group differences (Tables 1 and 2).

During the median follow-up time of 2.9 years (interquartile range: 1.0–4.1 years), there were 199 deaths from any cause (8.1% in women vs. 8.7% in men, $p = 0.651$), 45 MIs (2.0% in women vs. 1.9% in men, $p = 0.869$), and 38 strokes (1.8% in women vs. 1.6% in men, $p = 0.670$). The incidence of primary outcome was 10.8% in women, and 10.8% in men ($p = 0.970$). After multivariate adjustment for the baseline differences between the two groups, the risk of the primary outcome was also similar. Subgroup analysis revealed similar rates of primary outcome between the two groups according to the extent and severity of left main CAD and the extent of CAD (Fig. 2). Individual

Table 1
Baseline clinical characteristics.

Variables	Women ($n = 545$)	Men ($n = 1783$)	*p*-Value
Age, years	64.7 ± 11.8	63.3 ± 10.5	0.016
Body mass index, kg/m^2	24.7 ± 3.6	24.4 ± 2.8	0.054
Atrial fibrillation	9 (1.7)	52 (2.9)	0.090
Hypertension	376 (69.0)	1073 (60.2)	<0.001
Diabetes	185 (33.9)	602 (33.8)	0.937
Insulin treated diabetes	41 (7.5)	91 (5.1)	0.033
Dyslipidemia	269 (49.4)	862 (48.3)	0.679
Current smoking	25 (4.6)	541 (30.3)	<0.001
Previous myocardial infarction	27 (5.0)	144 (8.1)	0.014
Previous coronary intervention	98 (18.0)	290 (16.3)	0.347
Previous stroke	43 (7.9)	152 (8.5)	0.640
Previous heart failure	15 (2.8)	36 (2.0)	0.306
Family history of coronary artery disease	49 (9.0)	182 (10.2)	0.406
Peripheral vascular disease	13 (2.4)	88 (4.9)	0.011
Chronic pulmonary disease	3 (0.6)	54 (3.0)	0.001
Chronic renal failure	23 (4.2)	69 (3.9)	0.713
Shock at presentation	3 (0.6)	10 (0.6)	>0.99
Clinical diagnosis			
Stable angina or silent ischemia	215 (39.4)	808 (45.3)	0.016
Acute coronary syndrome	330 (60.6)	975 (54.7)	0.016
Lesion location			
Ostium	211 (38.7)	427 (23.9)	<0.001
Shaft	130 (23.9)	473 (26.5)	0.212
Bifurcation	319 (58.5)	1202 (67.4)	<0.001
Disease extent			
Left main only	90 (16.5)	175 (9.8)	<0.001
Left main plus 1 vessel disease	116 (21.3)	456 (25.6)	0.042
Left main plus 2 vessel disease	202 (37.1)	623 (34.9)	0.364
Left main plus 3 vessel disease	137 (25.1)	529 (29.7)	0.041
Left ventricular ejection fraction, %	60.8 ± 9.1	59.2 ± 9.7	0.004
Medication at discharge			
Aspirin	537 (98.7)	1737 (97.6)	0.127
Thienopyridines	527 (96.9)	1698 (95.4)	0.134
Cilostazole	171 (31.5)	546 (30.8)	0.751
Beta blocker	291 (54.7)	974 (55.5)	0.736
Calcium channel blocker	255 (48.4)	786 (45.5)	0.238
ACEi or ARB	198 (37.1)	658 (37.9)	0.728
Statin	239 (57.2)	718 (55.2)	0.476

Categorical variables: Chi-square test or Fisher's exact test.
Continuous variables: *t*-test.
Data are mean ± SD or number (percentage).
ACEi = angiotensin-converting enzyme inhibitor; ADP = adenosine diphosphate; ARB = angiotensin II receptor blocker.

Table 2
Procedural characteristics.

Variables	Women ($n = 545$)	Men ($n = 1783$)	*p* value
Use of intravascular ultrasound	438 (80.4)	1423 (79.8)	0.776
Stent technique			
Left main stent only	142 (26.1)	303 (17.0)	<0.001
Simple cross over technique	295 (54.1)	1048 (58.8)	0.055
2-stent technique	108 (19.8)	432 (24.2)	0.033
Total number of treated lesion	1.6 ± 0.8	1.7 ± 0.9	0.114
Total stent number per patient	2.1 ± 1.2	2.3 ± 1.3	0.004
Total stent length per patient, mm	49.8 ± 33.8	55.3 ± 35.5	0.001
Stent diameter, mm	3.4 ± 0.4	3.5 ± 0.3	0.004
Maximal stent pressure, mm Hg	15.9 ± 4.2	16.2 ± 4.6	0.264
Maximal stent diameter, mm	3.8 ± 0.5	3.9 ± 0.5	0.001
Final kissing balloon	163 (29.9)	609 (34.2)	0.065
Complete revascularization	388 (71.2)	1257 (70.5)	0.756
Hemodynamic support[a]	24 (4.4)	91 (5.1)	0.509
Stent type			
1st generation drug-eluting stent	156 (28.8)	441 (24.9)	0.067
2nd generation drug-eluting stent	385 (71.2)	1330 (75.1)	0.067

Categorical variables: Chi-square test or Fisher's exact test.
Continuous variables: *t*-test.
Data are mean ± SD or number (percentage).
[a] Insertion of intra-aortic balloon pump or extracorporeal membrane oxygenation.