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Sex Difference Among Patients with Unprotected Left Main Coronary Artery Disease Undergoing Percutaneous Coronary Intervention in Northern China

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ABSTRACT

Background: Unprotected left main coronary artery (ULMCA) disease is associated with high mortality and morbidity. The aim of this study is to investigate the efficacy of percutaneous coronary intervention (PCI) on gender-specific patients with ULMCA in the Chinese population and provide a basis for further treatment of PCI in ULMCA disease.

Methods: 173 patients (female, N = 52; male, N = 121; mean age = 61.02 ± 7.95) with ULMCA disease, who underwent PCI between January 2010 and December 2014, were investigated in our study. The mean follow-up time was 23.8 ± 7.3 months. The baseline clinical characteristics, coronary angiography (CAG) and PCI procedures, and in-hospital and follow-up outcomes of gender-specific patients were evaluated.

Results: There were no statistically significant differences in baseline clinical characteristics with the exception of body weight, height, and smoking indexes between women and men. During PCI procedure, femoral artery puncture was more preferred in women than men ($P < .05$), whereas radial artery puncture was more preferred in men than women ($P < .05$). The characteristics of CAG and PCI procedures (except puncture path) were showed with no markedly difference between women and men. The incidences of MACCEs in male patients during the in-hospital and follow-up periods were slightly higher than those of the female patients although with no statistical differences.

Conclusion: In northern China, the incidence of ULMCA disease in men is likely to be higher than in women, whereas PCI for ULMCA disease shows similarly favorable outcomes in women as well as in men. During the PCI procedure, femoral artery puncture in women and radial artery puncture in men are recommended.

INTRODUCTION

Unprotected left main coronary artery (ULMCA) disease, belonging to left main coronary artery disease (LMCAD), is associated with high mortality and morbidity [Caracciolo 1995; Fajadet 2012]. It is defined as the absence patent of bypass grafts to either the left anterior descending or the left circumflex coronary artery, which could be found in 4 percent to 6 percent of all patients under¬going coronary angiography (CAG) [Proudfit 1967; Chieffo 2006; Ragosta 2006].

As the technical evolution of percutaneous coronary intervention (PCI) with drug-eluting stents (DES) and aggressive antiplate¬let therapy, PCI appears not only to be reserved for patients with poor surgical indication, but also a safe and effective method for ULMCA disease when patients are carefully selected [Eagle 2004]. Patients with ULMCA disease who have low risk for procedural complications and increased risk of adverse surgical outcomes are the candidates for PCI (class IIa) in American College of Cardiology (ACC)/American Heart Association (AHA)/Society for Cardiovascular Angiography and Interventions (SCAI) focused guidelines [Levine 2013]. Previous study of a nonrandomized registry comparing PCI and coronary artery bypass graft (CABG, a standard care for ULMCA) showed with similar results of patients with ULMCA undergoing PCI, even patients with PCI had a greater proportion of high-risk in the background [Lee 2006].

Sex difference could influence the dissection of coronary artery. Even with same body surface area, the coronary artery including left main coronary artery in women is much thinner than that in men [Herity 2003]. Female patients with coronary heart diseases are more easily accompanied with risk factors. Sudden death could occur with approximately 2/3 of female patients with coronary heart diseases without any symptoms [Mosca 2007]. However, estrogen with the protective effects of hemangiectasis and improved blood flow on angiocarpy has been found in previous studies [Haynes 2000; Manson 2007]. Our aim in the study is to investigate the efficacy of PCI on gender-specific patients with ULMCA disease in the ethnic Han population of northern China and provide the basis for further therapy of PCI in ULMCA disease with different sex.

MATERIALS AND METHODS

Subjects: Patients with ULMCA disease who underwent PCI from January 2010 to December 2014 were investigated in Cangzhou Central Hospital. Patients were included if all the following criteria were met: (1) patients were diagnosed

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Table 1. Baseline clinical characteristics of the 173 patients

Baseline clinical characteristics	Women (N = 52)	Men (N = 121)	*P*
Ages (years)	60.52 ± 6.65	61.24 ± 8.47	.586
Weight (kg)	67.84 ± 11.18	76.17 ± 9.43	.001
Height (cm)	158.82 ± 7.12	170.53 ± 5.49	.000
Body mass index (kg/m^2)	25.55 ± 2.86	26.71 ± 3.76	.163
Risk factors for CVD (N,%)			
Hypertension	32(61.5%)	66(54.5%)	.395
Diabetes mellitus	13(25.0%)	21(17.6%)	.246
Hyperlipidemia	4(7.7%)	5(4.1%)	.553
Family history of CHD	13(23.1%)	25(20.7%)	.527
Smoker	8(15.4%)	60(49.6%)	.000
Anamnesis (N,%)			
MI history	6(11.5%)	7(5.8%)	.317
PCI history	10(19.2%)	19(15.7%)	.569
CABG history	0(0)	4(3.3%)	.438
Auxiliary examination			
cTnI (ng/L)	5.13 ± 12.50	5. 15.42	.831
LVEF (%)	61.58 ± 10.17	63.00 ± 9.34	0.472

PCI: percutaneous coronary intervention; CVD: cardiovascular disease; CHD: coronary heart disease cardiac; cTnI: troponin I; LVEF: left ventricular ejection fraction.

Table 2. CAG and PCI procedures profiles among patients (N = 173)

Factors	Women (N = 52)	Men (N = 121)	*P*
Puncture path (N, %)			
Femoral artery	19(36.5%)	26(21.5%)	.039
Radial artery	33(63.5%)	95(78.5%)	.039
Target vascular lesions			
Diameter (mm)	2.45 ± 0.61	2.65 ± 0.78	.137
Length (mm)	9.35 ± 3.76	9.79 ± 4.35	.488
Degree of stenosis (%)	71.50 ± 20.49	74.02 ± 20.02	.453
Site of lesion (N,%)			
Ostium	14(26.9%)	30(24.8%)	.768
Shaft	12(23.1%)	24(19.8%)	.630
Distal bifurcation	26(50.0%)	67(55.4%)	.516
Number of vessels intervened (N,%)			
Single vessel (LM alone)	6(11.5%)	13(10.7%)	.878
Multivessel (N, %)			
(a) LM + 1 additional vessel	11(21.2%)	32(26.4%)	.460
(b) LM + 2 additional vessels	18(34.6%)	34(28.1%)	.391
(c) LM + 3 additional vessels	17(32.7%)	42(34.7%)	.797
PCI technique (N, %)			
Single stent crossing over LCX	31(59.6%)	67(55.4%)	.606
V-stenting	0(0)	2(1.7%)	.875
Crush-stenting	6(11.5%)	17(14.0%)	.656
Culottes-stenting	0(0)	1(0.8%)	1.000
Kissing balloon	9(17.3%)	21(17.4%)	.994
Type of stent (N, %)			
Bare metal stent	0(0)	0(0)	
Drug-eluting stents	52(100%)	121(100%)	
Stents diameter (mm)	3.31±0.44	3.42±0.54	.148
Total stents length (mm)	23.12±7.27	23.52±7.60	.783
Numbers of stents	1.12±0.32	1.16±0.41	.515
Complication (N, %)			
Pseudoaneurysm	2(3.8%)	1(0.8%)	.447
In-stent restenosis	0(0)	1(0.8%)	1.000
Subacute thrombus	0(0)	1(0.8%)	1.000
Infection in puncture site	0(0)	0(0)	
Local hematoma in puncture site	2(3.8%)	0(0)	.163

LM: left main coronary artery; PCI: percutaneous coronary intervention.

with ULMCA identified by CAG; (2) patients with hemodynamic instability (emergency indication); (3) patients refused to receive CABG or had high perioperative risks for CABG. The performance of PCI needed to be considered of coronary anatomy, patients' condition, risks for surgery, and hemodynamic indication by both interventional cardiologists and cardiac surgeons. Patients were excluded if one or more of the following criteria were met: (1) intolerance to antiplatelet drug or allergy to aspirin, Clopidogrel; (2) severe hepatic and renal dysfunction or allergy to contrast medium; (3) hemorrhagic disorder; (4) malignancies; (5) contraindica¬tion to surgical treatment. The study was approved by the institutional review board of Cangzhou Central Hospital. Written informed consent was obtained from each patient before the surgical procedures and for the use of personal information for research purposes.

PCI procedure and medical treatment: PCI procedure for ULMCA was conducted by traditional techniques [Yin 2015]. Preoperatively, all patients were treated with 300 mg oral aspirin and 600 mg oral Clopidogrel. A maintenance dose of 100 mg/day aspirin and 75 mg/day Clopidogrel were performed during surgery. Unfractionated heparin with 70 units to 100 units per kg was administrated during the surgery. After PCI, all patients received 100 mg/day to 300 mg/day aspirin for one month. Antiplatelet regimen included lifetime aspirin of 100 mg/day if no contraindications were present and 75 mg/day of Clopidogrel for at least 12 months beginning from one month after surgery.

Assessment and clinical follow-up: Clinical follow-up via office visits or telephone contact was scheduled for all

Table 3. In-hospital and follow-up outcomes between female and male patients (N = 173)

	Women (N = 52)	Men (N = 121)	*P*
In-hospital (N,%)			
MACCE	3(5.8)	1(0.8)	.152
Cardiac death	0(0)	0(0)	
Noncardiac death	1(1.9)	0(0)	.663
MI	2(3.8)	1(0.8)	.447
Target-lesion revascularization	0(0)	0(0)	
Follow-up (N,%)			
MACCE	4(7.7)	3(2.5)	.240
Cardiac death	1(1.9)	0(0)	
Noncardiac death	0(0)	0(0)	.663
MI	0(0)	0(0)	
Target-lesion revascularization	3(5.8)	3(2.5)	.528

MACCE: major adverse cardiac and cerebrovascular events; MI: myocardial infarction.

patients within 36 months after hospital discharge. Major adverse cardiac and cerebrovascular events (MACCE) including all death, myocardial infarction (MI), and target-lesion revascularization were recorded. All deaths were considered cardiac unless an unequivocal non-cardiac cause could be established. MI was defined with recurrent symptoms of new ST-segment elevation or re-elevation of total creatine kinase of greater than three times the upper limit of normal value. Target-lesion revascularization was defined as a repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion, and the target lesion was defined as the treated segment from 5 mm proximal segments to the stent and to 5 mm distal segments to the stent [Cutlip 2007].

Statistical analysis: All data was analyzed by using SPSS software (version 16.0, SPSS, Inc., Chicago, IL). Continuous variables were expressed as means ± standard deviation (SD) and analyzed with Student's t-test. Categorical variables were expressed as a number or percentage and analyzed with chi-square analysis. $P < .05$ was considered as statistically significant.

RESULTS

Baseline clinical data: A total of 173 patients (female, N = 52; male, N = 121; mean age = 61.02 ± 7.95) were enrolled in this study. Demographic and clinical characteristics of the patients are presented in Table 1. Body mass index and height were significantly lower in women than in men. Smokers were more frequently among men ($P < .05$). There were no significant differences between women and men regarding other indexes such as age, risk factors (except smoking), and the results of auxiliary examination and histories of diseases.

The characteristics of CAG and PCI procedures: The characteristics of CAG and PCI procedures are presented in Table 2. The femoral artery puncture was more preferred in women than men ($P < .05$), whereas radial artery puncture was more preferred in men than women ($P < .05$). No significant differences were observed regarding the target vascular lesions, site of lesion, numbers of vessels intervened, types and numbers of stents, PCI technique, stents diameter, total stents length, kissing balloon, or complications between women and men. Incidences of pseudoaneurysm and subacute hematoma from puncture sites were slightly higher in women than in men, although there was no statistical significance.

In-hospital and follow-up outcomes: As shown in Table 3, the following was reported: One female patient with a noncardiac cause of death, two female patients and one male patient with MI, and no patients with target-lesion revascularization during the in-hospital period. There was no significant difference with overall in-hospital MACCE incidence between women and men (5.8 percent versus 0.8 percent, $P = .152$). The mean follow-up time was 23.8 ± 7.3 months. During the follow-up period, the following was reported: One female patient with a cardiac cause of death, and three female and three male patients with target-lesion revascularization. There was no statistical difference regarding the overall long-term MACCE incidence between women and men (7.7 percent versus 2.5 percent, $P = .240$).

DISCUSSION

Our study demonstrated there was no statistical difference in baseline clinical data except the body mass, height, quantity, and smoking indexes. There is an imbalance in the quantity of patients with ULCMA disease between women and men. Soleimani et al [Soleimani 2009] showed that men were more likely than women to develop the ULCMA disease. In our study, the number of women (52/173) was markedly less than the number of male patients (121/173), which was consistent with the findings of Soleimani et al [Soleimani 2009]. The imbalance may be related to the protective effect of female estrogen on the cardiovascular system. The mean age of patients with ULCMA disease showed no difference between women and men (60.52 ± 6.65 versus 61.24 ± 8.47), which was consistent with previous domestic research [Xuebin 2014]. Nevertheless, Sheiban et al. [Sheiban 2010] found the age of female patients was significantly greater than male patients (73.9 ± 11 versus 69.9 ± 11.0). The discrepancy is probably owing to the different economic conditions, living standards, racial factors, and gonadal hormones between different countries.

During the PCI procedure, women were more likely to receive femoral artery puncture and men were more likely to receive radial artery puncture path in our study. The thinner radial arteries of women, which would lead to difficulty in surgery and postoperative care, are not recommended in PCI. On the contrary, the thicker radial arteries of men are appropriate for PCI. Previous studies have shown that the fatality rates of puncture paths between femoral artery and

radial artery present no significant difference [Agostoni 2004; Ziakas 2004]. However, antispasmodic drugs are needed in the perioperative period with radial artery surgery.

Sex difference is a controversial factor in the prognosis of PCI. Kelsey et al. [Kelsey 1993] found that the short-term prognosis of PCI in women was worse than men. Narins et al [Narins 2006] showed that women had higher mortality of PCI and higher incidence of non-fatal MACCE than men in various age groups. The worse prognosis of PCI in women may be related to the complex factors such as the physical states, the thin and curved coronary artery, and complications [D'Ascenzo 2011; Benamer 2011]. Nevertheless, Singh et al [Singh 2008] found there was no significant difference between male and female patients regarding the fatality rate of PCI. Sheiban et al [Sheiban 2010] suggested that sex difference was not an independent predictive factor for patients with ULMCA, and PCI offered similarly favorable clinical results in women as well as in men. The conflicting results may be due to the varying usage of DES and the technical improvement of PCI [Jacobs 2002]. In our study, DES was used in all patients. The incidences of MACCEs during the in-hospital period and the follow-up period did not show any obvious differences between women and men, indicating that PCI had the similar therapeutic effect and prognosis on gender-specific patients with ULMCA disease.

Our study has some limitations. It was single-center, retrospective analysis which might affect the results due to unmeasured confounder. The small sample size might lead to a lack of statistically significant differences between women and men in these outcome measures. Finally, the follow-up time was relatively short for the analysis in the study.

CONCLUSION

In northern China, the incidence of ULMCA disease in men is likely to be higher than in women, while PCI for ULMCA shows similarly favorable clinical outcomes in women as well as in men. During the PCI procedure, femoral artery puncture in women and radial artery puncture in men are recommended.

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