Long-Term Outcomes of Single-Vessel Percutaneous Coronary Intervention on Culprit Vessel vs. Multivessel Percutaneous Coronary Intervention in Non-ST-Segment Elevation Acute Coronary Syndrome Patients With Multivessel Coronary Artery Disease

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Background: The optimal percutaneous coronary intervention (PCI) strategy for multivessel lesions in the setting of non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS) remains controversial. This study sought to compare long-term prognosis between single-vessel PCI (SV-PCI) and multivessel PCI (MV-PCI) in patients with multivessel coronary artery disease (MV-CAD) presenting with NSTEMI-ACS in a real-world population.

Methods and Results: NSTEMI-ACS patients with MV-CAD undergoing PCI in Fuwai Hospital in 2013 were consecutively enrolled. SV-PCI was defined as targeting only the culprit vessel, whereas MV-PCI was defined as treating ≥ 1 coronary artery(s) in addition to the culprit vessel at the index procedure. The primary endpoint was the incidence of major adverse cardiovascular and cerebrovascular events (MACCE) at 2 years, consisting of all-cause death, cardiac death, myocardial infarction, unplanned revascularization, or stroke. A total of 3,338 patients were included. Both SV-PCI and MV-PCI were performed in 2,259 patients and 1,079 patients, respectively. During a median follow up of 2.1 years, the MACCE rates and adjusted risk were not significantly different between the SV-PCI and MV-PCI groups (13.1% vs. 14.0%, $P=0.735$; adjusted HR=0.967, 95% CI: 0.792–1.180). Similar results were observed in propensity-score matching and inverse probability of treatment weighting analyses. Subgroup analysis revealed a consistent effect on 2-year MACCE across different subgroups.

Conclusions: In NSTEMI-ACS patients with MV-CAD, MV-PCI is not superior to SV-PCI in terms of long-term MACCE.

Key Words: Multivessel percutaneous coronary intervention; Non-ST-segment elevation acute coronary syndrome; Percutaneous coronary intervention strategy

Percutaneous coronary intervention (PCI) has become a standard of treatment for patients with non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS).^{1–3} Among patients with obstructive coronary artery disease (CAD), 21–58% have multivessel CAD (MV-CAD).^{4–8} There is evidence suggesting that incomplete revascularization has a negative effect on long-term outcomes.⁹ Nevertheless, multivessel PCI (MV-PCI) is associated with higher risk of procedure-related complications, which may affect its efficacy and safety.¹⁰ Thus, there remains a need to find the optimal PCI strategy for those

patients to make a trade-off between minimizing the adverse events related to MV-PCI and maximizing the long-term benefits.

The application of different PCI strategies (i.e., culprit-only vs. multivessel) varies among different institutions in everyday clinical practice. The current American and European guidelines recommend considering MV-PCI (Class IIb, B),¹ or to tailor the PCI strategy to the clinical status, comorbidities, and the disease severity, analogous to the principles of stable CAD (SCAD),³ because of lacking evidence from randomized control trials. Results from

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previous cohort studies have been inconsistent, with some reporting no significant difference in long-term outcomes between the groups,^{8,11–13} some reporting reduced repeat revascularization after MV-PCI,^{4,14–16} whereas others have reported lower mortality with MV-PCI.^{5,6,17,18} Therefore, we aimed to compare long-term prognosis between single-vessel PCI (SV-PCI) and MV-PCI in patients with MV-CAD presenting with NSTEMI-ACS.

Methods

Study Population

Data of 10,724 consecutive patients from a single center (Fuwai Hospital, Beijing, China) undergoing PCI from January 2013 to December 2013 were consecutively collected. Although some NSTEMI-ACS patients with MV-CAD underwent CABG in our hospital, here we only focused those who underwent PCI in the current analysis. Among them, 3,338 patients with NSTEMI-ACS and MV-CAD were enrolled after excluding patients with ST-segment elevation acute myocardial infarction (STEMI) (n=1,445), SCAD (n=4,295), no significant lesion (n=119) or single-vessel

disease (n=1,272), those whose data for the PCI strategy were missing (n=189), as well as those who did not have successful procedures (n=66) (**Figure 1**). MV-CAD was defined as having angiographically significant stenosis ($\geq 50\%$) in at least 2 major epicardial coronary arteries or their branches, with or without involvement of the left main artery. Successful procedure was defined as an angiographically residual stenosis $\leq 30\%$ with Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow. None of the involved patients had cardiogenic shock, a glomerular filtration rate < 30 mL/min/1.73 m², or received prior coronary artery bypass grafting. The Institutional Review Board approved the study protocol. All patients provided written informed consent before the intervention.

All procedures and medications were performed or managed according to current standard practice guidelines. The choice between SV-PCI and MV-PCI was at the operators' discretion based on each patient's clinical status and comorbidities, as well as the disease severity. SV-PCI was defined as targeting only the culprit vessel, whereas MV-PCI was defined as treating ≥ 1 coronary artery(s) in addition to the culprit vessel at the index procedure. The

Table 1. Baseline Characteristics Stratified by PCI Strategy

Characteristics	All patients (n=3,338)			Matched patients (n=1,576)		
	SV-PCI (n=2,259)	MV-PCI (n=1,079)	P value	SV-PCI (n=788)	MV-PCI (n=788)	P value
Age,^{A,B} years	59.7±9.9	59.3±10.1	0.2947	59.1±9.9	59.1±10.1	0.9099
Female,^{A,B} n (%)	594 (26.3)	267 (24.7)	0.3385	167 (21.2)	167 (21.2)	1.0000
Body mass index,^{A,B} kg/m²	25.8±3.1	26.1±3.4	0.0203*	26.2±3.1	25.9±3.1	0.0877
NSTEMI,^A n (%)	218 (9.7)	136 (12.6)	0.0095*	71 (9.0)	98 (12.4)	0.0279*
Risk factors, n (%)						
Current smoker ^{A,B}	1,281 (56.7)	590 (54.7)	0.2699	461 (58.5)	456 (57.9)	0.7985
Diabetes ^B	749 (33.2)	348 (32.3)	0.6029	246 (31.2)	257 (32.6)	0.5522
Hypertension ^B	1,557 (68.9)	747 (69.2)	0.8579	560 (71.1)	540 (68.5)	0.2725
Hyperlipidemia ^B	1,530 (67.7)	728 (67.5)	0.8810	526 (66.8)	535 (67.9)	0.6288
Medical history, n (%)						
Prior myocardial infarction ^B	339 (15.0)	182 (16.9)	0.1659	133 (16.9)	139 (17.6)	0.6892
Prior stroke ^{A,B}	284 (12.6)	142 (13.2)	0.6337	105 (13.3)	104 (13.2)	0.9408
Prior PCI ^{A,B}	503 (22.3)	175 (16.2)	<0.0001*	149 (18.9)	151 (19.2)	0.8979
Laboratory tests before PCI						
Leukocyte, ×10 ⁹ /L	6.8±1.8	6.8±1.8	0.1580	6.8±1.8	6.9±1.9	0.0986
Platelet, ×10 ⁹ /L	204.8±54.3	205.4±51.7	0.7594	202.2±52.2	205.6±52.2	0.1919
Hemoglobin, g/L	142.3±15.5	141.7±15.5	0.2516	143.9±14.9	142.2±15.4	0.0326
Creatinine, μmol/L	75.3±16.4	75.0±15.3	0.6297	75.7±16.5	75.8±15.0	0.8285
eGFR, ^{A,B} mL/min/1.73 m ²	90.2±15.3	90.9±14.9	0.2185	91.1±14.8	90.8±14.7	0.7277
LVEF, ^{A,B} %	63.7±6.5	63.5±6.5	0.3840	63.6±6.4	63.6±6.1	0.9297
Laboratory tests after PCI						
Creatinine, μmol/L	80.1±18.7	80.9±16.6	0.2159	80.8±20.9	82.1±16.7	0.1744
eGFR, mL/min/1.73 m ²	86.0±15.7	85.6±15.6	0.5440	86.7±15.2	85.2±15.6	0.0502
Medication at discharge, n (%)						
Aspirin ^A	2,233 (98.8)	1,073 (99.4)	0.0990	780 (99.0)	783 (99.4)	0.4034
Clopidogrel ^A	2,252 (99.7)	1,077 (99.8)	0.5164	785 (99.6)	787 (99.9)	0.3167
Ticagrelor	7 (0.3)	2 (0.2)	0.5164	3 (0.4)	1 (0.1)	0.3167
β-blockers ^A	1,989 (88.0)	978 (90.6)	0.0259*	705 (89.5)	706 (89.6)	0.9344
ACEIs/ARBs	1,148 (50.8)	560 (51.9)	0.7249	407 (51.6)	407 (51.6)	1.0000
Calcium channel blockers	1,330 (58.9)	611 (56.6)	0.2179	461 (58.5)	453 (57.5)	0.6831
Nitrates	2,226 (98.5)	1,067 (98.9)	0.4139	775 (98.4)	779 (98.9)	0.3904
Statins ^A	2,159 (95.6)	1,048 (97.1)	0.0306*	754 (95.7)	767 (97.3)	0.0744

Data are expressed as mean±standard deviation, number (%). ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blockers; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MV-PCI, multivessel percutaneous coronary intervention; n, number; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; SV-PCI, single-vessel percutaneous coronary intervention. ^ARisk-adjusting variables selected for the multivariable Cox models. ^BRisk-adjusting variables selected for the propensity score analysis. *P values indicating statistical significance.

culprit lesion was identified according to the patient's electrocardiogram, non-invasive imaging manifestations, and coronary angiography records. For non-culprit lesions with percentage stenosis between 50% and 70%, a variety of factors will be taken into consideration to decide whether to treat such a lesion, including procedural aspects (i.e., intracoronary imaging to confirm lesion characteristics and stenotic severity, such as intravascular ultrasound (IVUS), optical coherence tomography (OCT); physiological assessment to investigate if the lesion leads to ischemia: fractional flow reserve (FFR)) and peri-procedural aspects (i.e., evaluation of patient baseline condition, assessment of bleeding risk if prolonged dual antiplatelet therapy is required, socioeconomic status).

Follow up

Follow-up data were collected by an independent group of clinical research coordinators via telephone interviews or

by outpatient visits at 1, 6, and 12 months and then once every year. All patients were advised to return for coronary angiography if indicated by symptoms or clinical evidence of myocardial ischemia.

Endpoints

The primary endpoint was major adverse cardiovascular and cerebrovascular events (MACCE) (the composite of all-cause death, cardiac death, MI, unplanned revascularization, or stroke) at the 2-year follow up. The secondary endpoints were the individual components of MACCE, in-stent thrombosis and bleeding. Bleeding was quantified according to Bleeding Academic Research Consortium Definition (BARC) criteria, including type 2, 3 and 5 in the analysis.¹⁹ Other outcomes included in-hospital mortality and contrast-induced acute kidney injury (CI-AKI). CI-AKI was defined as a rise in serum creatinine by ≥0.3 mg/dL (26.5 μmol/L) or a ≥50% elevation from baseline after PCI

Table 2. Angiographic and Procedural Characteristics Stratified by PCI Strategy

Characteristics	All patients (n=3,338)			Matched patients (n=1,576)		
	SV-PCI (n=2,259)	MV-PCI (n=1,079)	P value	SV-PCI (n=788)	MV-PCI (n=788)	P value
SYNTAX score						
Pre-procedure ^B	11.2±7.7	15.2±7.8	<0.0001*	13.2±7.8	13.6±6.9	0.3854
0–22, n (%)	2,036 (90.7)	896 (83.2)	<0.0001*	688 (87.3)	706 (89.6)	0.3431
23–32, n (%)	181 (8.1)	154 (14.3)		86 (10.9)	72 (9.1)	
≥33, n (%)	27 (1.2)	27 (2.5)		14 (1.8)	10 (1.3)	
Post-procedure ^B	4.1±5.7	3.2±4.6	<0.0001*	3.3±4.7	3.5±5.0	0.4543
0–22, n (%)	2,203 (98.8)	1,069 (99.3)	0.3482	784 (99.5)	780 (99.0)	0.2464
23–32, n (%)	23 (1.0)	8 (0.7)		4 (0.5)	8 (1.0)	
≥33, n (%)	3 (0.1)	0		0	0	
Left main involvement,^{A,B} n (%)	159 (7.0)	102 (9.5)	0.0151*	67 (8.5)	64 (8.1)	0.7843
Lesion location, n (%)						
LAD+LCX ^A	445 (19.7)	179 (16.6)	0.0311*	152 (19.3)	145 (18.4)	0.6521
LAD+RCA ^A	531 (23.5)	125 (11.6)	<0.0001*	128 (16.2)	96 (12.2)	0.0210*
LCX+RCA ^A	219 (9.7)	89 (8.2)	0.1769	40 (5.1)	79 (10.0)	0.0002*
Tri-vessel disease ^B	1,064 (47.1)	686 (63.6)	<0.0001*	468 (59.4)	468 (59.4)	1.0000
Anatomical characteristics, n (%)						
Chronic total occlusion ^B	143 (6.3)	124 (11.5)	<0.0001*	72 (9.1)	76 (9.6)	0.7298
Heavy calcification ^{A,B}	60 (2.7)	54 (5.0)	0.0005*	33 (4.2)	35 (4.4)	0.8042
Bifurcation lesion ^{A,B}	358 (15.8)	302 (28.0)	<0.0001*	186 (23.6)	180 (22.8)	0.7204
Ostial lesion ^{A,B}	337 (14.9)	257 (23.8)	<0.0001*	164 (20.8)	163 (20.7)	0.9505
Puncture site, n (%)						
Radial artery	2,082 (92.2)	1,015 (94.1)	0.0468*	726 (92.1)	747 (94.8)	0.0323
Femoral artery	137 (6.1)	50 (4.6)	0.0927	53 (6.7)	31 (3.9)	0.0136
Other approaches	38 (1.7)	14 (1.3)	0.4013*	9 (1.1)	10 (1.3)	0.8175
IVUS use,^{A,B} n (%)	85 (3.8)	101 (9.4)	<0.0001*	49 (6.2)	59 (7.5)	0.3188
Number of stents	1.5±0.8	2.9±1.2	<0.0001*	1.7±0.9	2.7±1.1	<0.0001
Stent type						
BMS, n (%)	16 (0.7)	1 (0.1)	0.0194*	7 (0.9)	1 (0.1)	0.0334
DES, ^B n (%)	1,876 (83.0)	655 (60.7)	<0.0001*	559 (70.9)	558 (70.8)	0.9558

Data are expressed as mean±standard deviation, number (%). BMS, bare metal stent; DES, drug-eluting stent; IVUS, intravascular ultrasound; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery. Other abbreviations as in Table 1. ^ARisk-adjusting variables selected for the multivariable Cox models. ^BRisk-adjusting variables selected for the propensity score analysis. *P values indicating statistical significance.

Table 3. In Hospital and 2-Year Clinical Outcomes in the 2 Study Groups

	All patients (n=3,338)			Matched patients (n=1,576)		
	SV-PCI (n=2,259)	MV-PCI (n=1,079)	P value	SV-PCI (n=788)	MV-PCI (n=788)	P value
In-hospital outcomes, n (%)						
In-hospital mortality	1 (0.0)	1 (0.1)	0.5926	— ^B	—	—
Contrast-induced acute kidney injury	186 (8.2)	99 (9.2)	0.4903	69 (8.8)	71 (9.0)	0.9400
2-year clinical outcomes, n (%)						
MACCE	296 (13.1)	151 (14.0)	0.7349	119 (15.1)	117 (14.8)	0.8364
All-cause death	25 (1.1)	11 (1.0)	0.8019	10 (1.3)	11 (1.4)	0.8561
Cardiac death	13 (0.6)	6 (0.6)	0.8003	4 (0.5)	5 (0.6)	0.7622
Myocardial infarction	40 (1.8)	18 (1.7)	0.9280	14 (1.8)	12 (1.5)	0.8336
Unplanned revascularization	215 (9.5)	109 (10.1)	0.9535	91 (11.5)	83 (10.5)	0.4284
Stroke	35 (1.5)	24 (2.2)	0.1653	11 (1.4)	20 (2.5)	0.0918
In-stent thrombosis	19 (0.8)	9 (0.8)	0.7098	9 (1.1)	7 (0.9)	0.6527
Bleeding ^A	153 (6.8)	64 (5.9)	0.5200	52 (6.6)	51 (6.5)	0.8433

MACCE, major adverse cardiac and cerebrovascular events. Other abbreviations as in Table 1. ^ABleeding was quantified according to Bleeding Academic Research Consortium Definition (BARC) criteria, including types 2, 3 and 5 in the analysis. ^BNo event happened in matched patients.

Figure 2. Cumulative incidence curves for the primary and secondary endpoints for patients undergoing SV-PCI and MV-PCI. (A–H) Cumulative incidence curves for (A) MACCE, (B) all-cause death, (C) cardiac death, (D) myocardial infarction, (E) unplanned revascularization, (F) stroke, (G) in-stent thrombosis, (H) bleeding. SV-PCI, single-vessel percutaneous coronary intervention; MV-PCI, multivessel percutaneous coronary intervention; MACCE, major adverse cardiac and cerebrovascular events.

Table 4. Cox Regression Analysis of SV-PCI/MV-PCI on 2-Year Clinical Outcomes

	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
All patients (n=3,338)				
MACCE	1.031 (0.854–1.246)	0.7482	0.967 (0.792–1.180)	0.7396
All-cause death	0.925 (0.481–1.779)	0.8128	1.085 (0.537–2.192)	0.8194
Cardiac death	1.110 (0.471–2.618)	0.8119	1.266 (0.515–3.117)	0.6071
Myocardial infarction	0.981 (0.588–1.636)	0.9412	1.023 (0.596–1.755)	0.9352
Unplanned revascularization	1.010 (0.806–1.265)	0.9334	0.924 (0.731–1.167)	0.5070
Stroke	1.396 (0.865–2.252)	0.1717	1.411 (0.854–2.332)	0.1792
In-stent thrombosis	1.138 (0.563–2.299)	0.7190	0.966 (0.462–2.019)	0.9267
Bleeding	0.911 (0.687–1.209)	0.5196	0.931 (0.693–1.251)	0.6366
Matched patients (n=1,576)				
MACCE	0.965 (0.753–1.236)	0.7772	1.000 (0.770–1.299)	1.0000
All-cause death	1.082 (0.477–2.452)	0.8507	1.000 (0.434–2.307)	1.0000
Cardiac death	1.184 (0.361–3.880)	0.7802	1.000 (0.290–3.454)	1.0000
Myocardial infarction	0.929 (0.459–1.878)	0.8367	0.750 (0.355–1.585)	0.4513
Unplanned revascularization	0.884 (0.659–1.184)	0.4076	0.917 (0.673–1.249)	0.5815
Stroke	1.772 (0.897–3.497)	0.0994	1.909 (0.920–3.959)	0.0824
In-stent thrombosis	0.810 (0.336–1.955)	0.6395	0.636 (0.247–1.642)	0.3499
Bleeding	0.963 (0.662–1.399)	0.8416	0.906 (0.613–1.338)	0.6193
Weighted				
MACCE	–	–	0.979 (0.808–1.185)	0.8258
All-cause death	–	–	1.235 (0.641–2.380)	0.5274
Cardiac death	–	–	1.331 (0.566–3.128)	0.5118
Myocardial infarction	–	–	0.974 (0.565–1.679)	0.9240
Unplanned revascularization	–	–	0.925 (0.738–1.160)	0.5011
Stroke	–	–	1.347 (0.815–2.227)	0.2455
In-stent thrombosis	–	–	1.131 (0.544–2.353)	0.7412
Bleeding ^A	–	–	0.906 (0.672–1.221)	0.5163

CI, confidence interval; HR, hazard ratio. Other abbreviations as in Tables 1,3. ^ABleeding was quantified according to BARC criteria, including types 2, 3 and 5 in the analysis.

during hospital stay.²⁰ Endpoint events were adjudicated by 2 independent cardiologists, and disagreement was resolved by consensus.

Statistical Analysis

Categorical variables are shown as numbers and percentages. Continuous variables are expressed as mean±standard deviations. Statistical differences were assessed by using the Student's t-test or the Mann-Whitney U-test for continuous variables, and by Pearson's chi-square test or Fisher's exact test for categorical variables. Cumulative incidences of clinical events were calculated using the Kaplan-Meier method, and comparisons were made with the log-rank test. Cox proportional hazards regression analyses were performed to estimate the hazard ratios (HRs) for PCI strategy comparisons and their 95% confidence intervals (CIs). We justified for age, sex, and 21 clinically relevant risk-adjusting variables that changed the unadjusted HR by at least 10 percent when added to multivariable Cox regression models. Proportional hazards assumption was evaluated by testing the significance of an interaction term of the PCI strategy and follow-up time, and by computing cumulative incidence plots. The time-dependent Cox regression model was applied when the proportional hazards assumption was violated. Subgroup analyses were performed using a few preselected risk factors of interest (age, gender, presence of diabetes, left ventricular

ejection fraction, pre-procedure synergy between PCI with taxus and cardiac surgery (SYNTAX) score, and presence of left main disease) to analyze interactions between PCI strategy and the selected factors for the outcomes.

Propensity-score matching (PSM) and inverse probability of treatment weighting (IPTW) were undertaken as sensitivity analyses. The propensity score was generated by logistic regression analysis with 22 baseline variables related to PCI strategy and/or the outcome variables (Table 1 and Table 2). The patients in the 2 groups were matched in a 1:1 manner using a greedy matching strategy algorithm, with a caliper width equal to 0.02 of the standard deviation of the logit of the propensity score. The propensity score and (1-propensity score) were used to calculate the inverse-probability-weighting weights of SV-PCI and MV-PCI.

Two-tailed P values of <0.05 were considered to be statistically significant. PSM was conducted with the R statistical software version 3.4.0 (www.r-project.org). The other analyses were conducted with SPSS version 22.0 (IBM, Armonk, NY, USA).

Results

Patient Characteristics

Among the 3,338 patients included in the study, 2,259 (67.7%) underwent SV-PCI whereas 1,079 (22.3%) underwent MV-PCI. Two-year follow up was available for all

Figure 3. Subgroup analysis on MACCE between SV-PCI and MV-PCI. *P value for interaction in each subgroup analysis for adjusted HRs. n, number; pts, patients; MACCE, major adverse cardiac and cerebrovascular events; SV-PCI, single-vessel percutaneous coronary intervention; MV-PCI, multivessel percutaneous coronary intervention; LVEF, left ventricular ejection fraction; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery; HR, hazard ratio.

patients with a median follow-up duration of 2.1 (IQR: 2.1–2.1 and range: 0–2.1) years. The baseline characteristics were mostly comparable between the 2 groups before PSM, except that MV-PCI patients were more likely to present with non-ST-segment elevation myocardial infarction, had higher body mass index, a lower rate of prior PCI, with β -blockers and statins more frequently prescribed at discharge ($P<0.05$) (Table 1). Angiographic and procedural characteristics were significantly different between the 2 groups in several aspects before PSM. Patients in the MV-PCI group had higher pre-procedure SYNTAX scores and lower post-procedure SYNTAX scores (Table 2). Patients with MV-PCI were more likely to have complex anatomical characteristics, reflected by higher rates of tri-vessel disease, chronic total occlusion, bifurcation lesion, and ostial lesion compared with the SV-PCI group (Table 2). Higher rates of IVUS use were seen in the MV-PCI group (Table 2). Patients who underwent MV-PCI had more stents implanted; however, the percentage of drug-eluting stent (DES) implantation was significantly lower (Table 2).

Clinical Outcomes

In terms of in-hospital clinical outcomes, no significant difference was observed for the incidence of CI-AKI and mortality (all $P>0.05$) (Table 3).

The analysis of 2-year MACCE showed no significant difference between the 2 groups (SV-PCI: $n=296$ [13.1%] vs. MV-PCI: $n=151$ [14.0%], $P=0.735$; unadjusted HR=1.031;

95% CI: 0.854–1.246), and the risk of the primary outcome measure remained neutral after adjustment (adjusted HR=0.967; 95% CI: 0.792–1.180) (Figure 2, Table 3 and Table 4). The cumulative incidences and the risks of the secondary outcome measures at 2 years were not significantly different between the 2 groups before and after adjustment (Figure 2, Table 3 and Table 4).

Subgroup Analysis

For subgroup analyses including age, gender, presence of diabetes, left ventricular ejection fraction, pre-procedure SYNTAX score, and presence of left main disease, there was no significant interaction between each subgroup factor and the effect of PCI strategy in terms of MACCE (all P for interaction >0.05) (Figure 3).

Sensitivity Analysis

The PSM analysis showed consistent results with the analysis based on all patients; that is, that there were no significant differences in the primary and secondary outcome measures between the SV-PCI group and the MV-PCI group. Overall, 788 MV-PCI patients were propensity matched with SV-PCI patients at a 1:1 ratio. After PSM, most characteristics became more comparable between the 2 groups (Table 1 and Table 2). Risk of 2-year primary and secondary endpoints were similar between the groups before and after adjustment ($P>0.05$) (Supplementary Figure, Table 3). IPTW analysis revealed similar results (Table 3).

Discussion

This is a large retrospective cohort study. The main finding of our study is that the cumulative incidences and adjusted risks of 2-year MACCE and secondary outcome measures showed no significant difference between patients treated with MV-PCI vs. SV-PCI.

Our finding is consistent with the results of some previous studies.^{8,11–13} Admittedly, MV-PCI at one time can achieve more complete revascularization, avoid additional risks and reduce costs from otherwise multistage procedures for NSTEMI-ACS patients with MV-CAD. Nevertheless, one-stage MV-PCI has been reported to be associated with an elevated risk of complications, including stent thrombosis (possibly due to hypercoagulable status associated with acute coronary syndrome and increased number or length of stents), inflammatory burden (mainly due to increased damage to coronary artery epithelium and increased vascular exposure to stent polymers) and contrast-induced nephropathy (due to increased amount of contrast use).¹⁰ However, we did not observe an increased risk of CI-AKI in our study. Furthermore, treating non-infarction related artery and implanting more stents may cause additional myocardial injury related to the procedure.²¹ Owing to the lack of powerful evidence favoring MV-PCI in terms of hard clinical endpoints, the optimal PCI strategy for multivessel lesions in the setting of NSTEMI-ACS remains controversial.

Contrary to our findings, some studies found that MV-PCI was associated with lower mortality,^{5,6,17,18} and some reported that MV-PCI reduced unplanned repeat revascularization.^{4,14–16} The possible explanations are listed as follows. First, the low-risk population of the study led to relatively low event rates at follow up in both groups, resulting in no significant difference in 2-year MACCE between the 2 groups. Second, operators were more likely to perform MV-PCI in higher-risk patients, which may offset its benefits. Third, although patients in the MV-PCI group had more lesions treated than those in the SV-PCI group, not all of them received complete revascularization, thus, the difference in prognosis between groups was not significant.

Moreover, the proportion of DES among all the implanted stents exceeded 99%, which is much higher than in other similar studies. A DES reduces restenosis by approximately 50–70% in comparison with BMS, and the new-generation DES performs even better, especially in reducing late and very late stent thrombosis,^{22,23} leading to a lower rate of unplanned revascularization. In addition, thanks to the expertise of our interventionalists and the application of IVUS to guide the treatment of complex lesions, accurate pinpointing of the culprit vessel was achieved. Evidence from several meta-analyses suggested better outcomes with IVUS-guided PCI in terms of reduced restenosis and repeat revascularization, regardless of stent type.^{24–27} This enabled patients who underwent culprit-only SV-PCI to have a better chance of getting the correct unstable lesion solved at the initial procedure. Therefore, lesions scheduled to be intervened in future planned procedures are more frequently stable plaques, resulting in reduced unplanned repeat revascularization for the SV-PCI group.

To the best of our knowledge, most studies in this field started before 2005,^{6–8,11,13–17} and some had enrolled patients for 10 years,^{5,6,15,16} which may limit their generalizability.

Contemporary practice has changed significantly in the past decades, with an increase in the use of a radial approach, DESs, and IVUS, leading to better clinical outcomes with PCI. Compared to these studies, our research provides more valuable evidence for current clinical practice.

Potential limitations of our study warrant discussion. First, this is an observational study. Although we used extensive adjustments and PSM to minimize potential confounders, there remain unmeasured residual confounders. Second, our study was conducted in a specialized cardiovascular hospital, and most of the patients were younger, had less severe comorbidities and were in a better clinical status than those in previous similar studies, thus, the incidence of MACCE was relatively low. This could limit the generalizability of our findings. Third, our data were not able to provide information on whether patients in the MV-PCI group received complete revascularization. Fourth, although intravascular imaging and physiological assessment have been used in patients as per standard protocol, these data are not available in our database. Finally, we are unable to adjust for the confounding effect of lesion location and severity of non-culprit lesions, as we cannot pinpoint the culprit lesion location for MV-PCI patients based on the available data.

Conclusions

In NSTEMI-ACS patients with MV-CAD, multivessel PCI in the index procedure is not superior to SV-PCI on the culprit vessel. Future randomized controlled trials are needed to validate the effect of multivessel PCI, especially function-guided complete revascularization, in the setting of current standard clinical practice.

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Disclosures

The authors declare that there are no conflicts of interest.

IRB Information

Institutional Review Board of Fuwai Hospital (No. 2013-449) approved this study.

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
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