



# Staged versus “one-time” multivessel intervention in elderly patients with non-ST-elevation acute coronary syndrome

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## Abstract

**Objective** To evaluate the clinical outcomes of “one-time” versus staged multivessel stenting in elderly ( $\geq 60$  years) patients with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) and multivessel disease (MVD). **Methods** We analyzed data of consecutive NSTEMI-ACS patients with multivessel percutaneous coronary intervention (PCI) who were enrolled in General Hospital of Shenyang Military Region between 2008 and 2012. A total of 1090 eligible patients aged  $\geq 60$  were further categorized into “one-time” group ( $n = 623$ ) and staged PCI group ( $n = 467$ ) according to intervention strategy. The primary endpoint was composite outcome of myocardial infarction (MI) or cardiac death during 3-year follow-up. **Results** The estimated 3-year composite rate of cardiac death or MI was 7.0% in the staged PCI group and 9.5% in the “one-time” group ( $P = 0.110$ ). Multivariate analysis confirmed the benefit of staged PCI on the primary events in the elderly (HR: 0.638, 95% CI: 0.408–0.998,  $P = 0.049$ ). In a propensity score matched cohort, staged PCI was associated with lower rates of primary events (6.1% vs. 10.4%,  $P = 0.046$ ) and MI (3.4% vs. 7.4%,  $P = 0.037$ ) at three years. In addition, there were reduced trends in the stent thrombosis at 30 days (0.3% vs. 1.4%,  $P = 0.177$ ) and at three years (1.1% vs. 2.4%,  $P = 0.199$ ) in the staged PCI group. There was no significant difference in the 3-year target vessel revascularization (15.5% vs. 14.4%,  $P = 0.746$ ). **Conclusions** In elderly NSTEMI-ACS patients with MVD, staged PCI might be an optimal strategy associated with reduced long-term cardiac death or MI compared with “one-time” PCI strategy, which needs further confirmation.

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**Keywords:** Multivessel revascularization; Non-ST-elevation acute coronary syndrome; Percutaneous coronary intervention

## 1 Introduction

The elderly comprise an increasing proportion of patients with non-ST-elevation acute coronary syndromes (NSTEMI-ACS),<sup>[1]</sup> and are more likely to have multivessel disease (MVD) compared with younger patients.<sup>[2]</sup> Percutaneous coronary intervention (PCI) is the most common method of revascularization in the elderly with MVD.<sup>[3,4]</sup> After culprit vessel revascularization, the interventional cardiologist is forced to decide whether to expand the procedure to the remaining significantly narrowed vessels or to end it. However, the optimal strategy for elderly NSTEMI-ACS patients with MVD has not been well established. Previous observa-

tional analyses suggested that in patients with NSTEMI-ACS, multivessel PCI which allowed a more complete treatment of other potentially unstable plaques was superior to culprit vessel only PCI in terms of repeat revascularization.<sup>[5,6]</sup> It remains unclear, however, whether the appropriate management for NSTEMI-ACS patients with MVD, especially for elderly patients, is staged PCI or “one-time” approach in the setting of culprit and non-culprit vessels revascularization. This study aimed to compare the clinical outcomes of the two different revascularization strategies in elderly NSTEMI-ACS patients.

## 2 Methods

### 2.1 Study population

This study was a retrospective, observational, non-randomized cohort study with prospective follow-up. Between 2008 and 2012, a total of 11,050 unselected patients treated with PCI were prospectively registered in the PCI database of General Hospital of Shenyang Military Region (China).

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The database contained detailed information of clinical and angiographic characteristics, treatment strategies and clinical outcomes for all patients undergoing PCI. Patients were eligible if they were elderly ( $\geq 60$  years); admitted as NSTEMI-ACS and undergoing multivessel stenting (“one-time” or staged PCI). Patients were excluded if they: (1) had chronic total occlusion; (2) had technical failure, including staged PCI patients who had technical failure during the index PCI and scheduled for staging; (3) had malignant ventricular arrhythmia, haemodynamic instability or cardiac shock; (4) had an estimated glomerular filtration rate (eGFR)  $< 30$  mL/min per  $1.73\text{ m}^2$  or renal dialysis; (5) staged PCI patients who had major complication (i.e., no-reflow, acute stent thrombosis, coronary perforation) during the index intervention and (6) patients undergoing a staged PCI  $> 60$  days. The present study screened 1090 consecutive eligible patients. The trial was approved by the hospital ethics committee and all patients provided written informed consent.

## 2.2 Treatment

All patients were given loading doses of aspirin (300 mg) and clopidogrel (300–600 mg) before intervention, unless they had already received antiplatelet medication. The treatment strategy, stenting techniques and selection of stent type choice were all left to the operator’s discretion. Identification of the culprit vessel was undertaken by the operators, usually based on each patient’s ECG, echocardiogram, angiographic image and, if available, intravascular ultrasound (IVUS) and optical coherence tomography (OCT). A lesion was considered culprit on angiography if at least two of the following lesion morphological features suggestive of acute plaque rupture should be presented: plaque ulceration, intraluminal filling defects consistent with thrombus, plaque irregularity, dissection or impaired flow.<sup>[7–10]</sup> After PCI, lifelong use of aspirin was advised and clopidogrel was prescribed for 12 months.

## 2.3 Follow-up

All patients were followed up by outpatient visits or telephone interviews at 30 days, 6 months, 12 months, 24 months and 36 months after the index procedure. Follow-up duration was defined as the interval from the index procedure to the last telephone interview or hospital visit.

## 2.4 Outcomes and definitions

The primary outcome was the composite of cardiac death or myocardial infarction (MI) during 3-year follow-up. The secondary outcomes included contrast-induced acute kidney injury (CI-AKI), definite/probable stent thrombosis, 30-day composite rate of cardiac death or MI and the 3-year inci-

dences of cardiac death, MI and target vessel revascularization (TVR).

MVD was defined as the occurrence of a  $\geq 50\%$  stenosis of the left main coronary artery (left main disease) or a significant atherosclerotic coronary artery stenosis ( $\geq 70\%$  diameter stenosis) with additional significant stenosis ( $\geq 70\%$  diameter stenosis) of at least one other coronary artery assessed visually during coronary angiography.<sup>[11]</sup> Staged PCI was defined as PCI of the culprit lesion only with staged non-culprit PCI within 60 days. eGFR was calculated using the following equation for Chinese patients:  $\text{eGFR (mL/min per } 1.73\text{m}^2) = 175 \times (\text{serum creatinine})^{-1.234} \times (\text{age})^{-0.179} \times (0.79 \text{ if patient is female})$ .<sup>[12]</sup> Early invasive intervention is defined as coronary angiography performed within 24 h of hospital admission.<sup>[7]</sup> Delayed invasive intervention is defined as coronary angiography performed more than 24 h of hospital admission. Technical success was defined as balloon angioplasty or successful stent deployment at the desired position with visually estimated residual stenosis  $\leq 30\%$  followed by restoration of thrombolysis in myocardial infarction (TIMI) flow grade 3. All deaths were considered to be cardiac unless an unequivocal non-cardiovascular cause could be documented. MI followed the third universal definition of MI presented by the Third Global MI Task Force.<sup>[13]</sup> TVR was defined as any repeated PCI or coronary artery bypass grafting (CABG) of the initially treated coronary vessel. Complete revascularization was defined when no visually estimated stenosis  $\geq 50\%$  was found in the left main and no stenosis  $\geq 70\%$  was found in other major arteries and/or their major branches at discharge. CI-AKI was defined as an increase in serum creatinine (sCr) concentration  $\geq 0.5$  mg/dL (4.2 mmol/L) or 25% at 72 h after exposure to the contrast medium comparing baseline values. Stent thrombosis was classified as definite and probable according to the Academic Research Consortium definitions.<sup>[14]</sup>

## 2.5 Statistical analysis

Continuous variables were demonstrated as mean  $\pm$  SD or median value [interquartile range (IQR)], and categorical variables as number and percentages. We compared categorical variables using Pearson Chi-square test or Fisher’s exact test when appropriate. We compared continuous variables using student’s unpaired *t*-test or the Mann-Whitney rank-sum test when appropriate. The influence of patient characteristics on selection of “one-time” procedure or a staged approach was examined by multivariate logistic regression. We adjusted all available variables listed in Table 1 and Table 2 except IVUS used, OCT used, length of hospital, medication at discharge and dual antiplatelet therapy (DAPT) duration. The cumulative incidences of clinical

events were estimated with the Kaplan-Meier method and compared by the log-rank test between the groups. Cox regression analysis was used to identify the independent predictors of primary events at three years. We adjusted all available variables listed in Table 1 and Table 2 except IVUS used, OCT used, length of hospital, medication at discharge and DAPT duration. The statistical approach for model building was forward stepwise variable selection, with a level for variable inclusion of  $P < 0.05$  and exit criterion was  $P > 0.10$ . In addition, the analysis was repeated in a propensity score matching using the same preselected variables that were included in the original Cox regression analysis above, with a difference of  $< 10\%$  regarded as acceptable. Matching was on a 1:1 basis and performed using nearest-neighbor matching. All statistical tests were 2-tailed and statistical analyses were conducted in SPSS V.18.0 software.

### 3 Results

#### 3.1 Patients and treatments

For the present analysis, “one-time” PCI was performed

in 57.2% (623/1090), and the remaining 42.8% (467/1090) had staged PCI [Of these, 83.9% (392/467) had staged non-culprit intervention during the same hospitalization and 16.1% (75/467) had planned staged non-culprit procedures after hospital discharge]. The median delay of the staged PCI was 5 days (IQR, 3–9 days). As noted in Tables 1 and 2, staged patients had higher prevalence of male, previous MI and triple-vessel disease. In addition, this group tended to have more stents implanted and longer hospital stay. The volume of contrast media utilized during the index procedure in the staged PCI group was smaller [(200 (200–300) mL vs. 200 (140–240) mL,  $P < 0.001$ ] though the total volume utilized in the initial procedure plus staged procedure was larger [400 (290–400) mL vs. 200 (200–300) mL,  $P < 0.001$ ]. Medications at discharge were similar between the groups. Most patients took dual antiplatelet treatment consistent with standard recommendation. The multivariate logistic regression model revealed that the patients with triple-vessel disease, accumulated contrast medium use  $> 300$  mL, or previous MI would be prone to undergo staged PCI.

**Table 1. Baseline characteristics.**

Characteristic	Unadjusted			Propensity score adjusted		
	One-time ( <i>n</i> = 623)	Staged PCI ( <i>n</i> = 467)	<i>P</i> value	One-time ( <i>n</i> = 291)	Staged PCI ( <i>n</i> = 291)	<i>P</i> value
Age, yrs	69 (64–74)	68 (64–74)	0.507	68 (64–74)	69 (64–74)	0.742
Male	369 (59.2%)	311 (66.6%)	0.013	190 (65.3%)	192 (66.0%)	0.861
BMI, kg/m <sup>2</sup>	24.7 ± 3.2	24.6 ± 2.9	0.601	24.7 ± 3.2	24.7 ± 3.1	0.926
Heart Rate, bpm	73.4 ± 11.1	73.5 ± 11.5	0.855	73.1 ± 10.8	72.9 ± 11.0	0.849
Atrial fibrillation	21 (3.4%)	19 (4.1%)	0.544	12 (4.1%)	9 (3.1%)	0.505
Risk factors						
Diabetes	202 (32.4%)	169 (36.2%)	0.194	103 (35.4%)	94 (32.3%)	0.430
Hypertension	416 (66.8%)	323 (69.2%)	0.403	198 (68.0%)	199 (68.4%)	0.929
Hyperlipidemia	257 (41.3%)	214 (45.8%)	0.132	131 (45.0%)	132 (45.4%)	0.934
PAD	16 (2.6%)	17 (3.6%)	0.307	11 (3.8%)	11 (3.8%)	1.000
Current smoker	238 (38.2%)	197 (42.2%)	0.184	123 (42.3%)	131 (45.0%)	0.504
Previous MI	89 (14.3%)	107 (22.9%)	$< 0.001$	61 (21.0%)	56 (19.2%)	0.605
Previous PCI	120 (19.3%)	101 (21.6%)	0.336	63 (21.6%)	54 (18.6%)	0.352
Previous CVD	51 (8.2%)	50 (10.7%)	0.156	29 (10.0%)	27 (9.3%)	0.779
Type of NSTEMI-ACS			0.273			0.841
UA	491 (78.8%)	355 (76.0%)		228 (78.4%)	226 (77.7%)	
NSTEMI	132 (21.2%)	112 (24.0%)		63 (21.6%)	65 (22.3%)	
Hb, g/dL	134.2 ± 17.0	133.1 ± 15.7	0.302	134.0 ± 17.6	132.9 ± 15.3	0.441
eGFR ≤ 60 mL/min per 1.73 m <sup>2</sup>	80 (12.8%)	64 (13.7%)	0.677	37 (12.7%)	37 (12.7%)	1.000
LVEF ≤ 40%	11 (1.8%)	9 (1.9%)	0.844	5 (1.7%)	6 (2.1%)	0.761

Data are presented as median (IQR), mean ± SD or *n* (%). ACS: acute coronary syndromes; BMI: body mass index; CVD: cerebrovascular disease; eGFR: estimated glomerular filtration rate; Hb: hemoglobin; IQR: interquartile range; LVEF: Left ventricular ejection fraction; MI: myocardial infarction; NSTEMI-ACS: non-ST-elevation acute coronary syndromes; NSTEMI: non-ST-elevation myocardial infarction; PCI: percutaneous coronary intervention; PAD: peripheral arterial disease; UA: unstable angina.

**Table 2. Treatment and procedure related characteristics.**

Characteristic	Unadjusted			Propensity score adjusted		
	One-time (n = 623)	Staged PCI (n = 467)	P value	One-time (n = 291)	Staged PCI (n = 291)	P value
Timing of invasive strategy			0.488			0.589
Early PCI	199 (31.9%)	140 (30.0%)		92 (31.6%)	86 (29.6%)	
Delayed PCI	424 (68.1%)	327 (70.0%)		199 (68.4%)	205 (70.4%)	
Disease extent			< 0.001			0.447
2-vessel disease	348 (55.9%)	139 (29.8%)		122 (41.9%)	113 (38.8%)	
3-vessel disease	275 (44.1%)	328 (70.2%)		169 (58.1%)	178 (61.2%)	
Left main disease	74 (11.9%)	73 (15.6%)	0.073	43 (14.8%)	44 (15.1%)	0.907
Temporary pacemaker used	3 (0.5%)	4 (0.9%)	0.443	2 (0.7%)	3 (1.0%)	0.653
IVUS used	21 (3.4%)	10 (2.1%)	0.227	9 (3.1%)	8 (2.7%)	0.806
OCT used	4 (0.6%)	2 (0.4%)	0.953	2 (0.7%)	2 (0.7%)	1.000
Stent numbers per patient	3 (2–4)	4 (3–5)	< 0.001	3 (3–4)	4 (3–4)	0.508
Total stent length, mm	72 (54–96)	116 (85–144)	< 0.001	94 (72–124)	95 (74–125)	0.766
Complete revascularization	404 (64.8%)	293 (62.7%)	0.474	173 (59.5%)	181 (62.2%)	0.497
Contrast volume, mL						
Initial procedure	200 (200–300)	200 (140–240)	< 0.001	230 (200–300)	180 (120–240)	< 0.001
Staged procedure	–	165 (130–200)	–	–	180 (120–200)	–
Total	200 (200–300)	400 (290–400)	< 0.001	230 (200–300)	400 (270–400)	< 0.001
Total volume > 300 mL	92 (14.8%)	341 (73.0%)	< 0.001	55 (18.9%)	204 (70.1%)	< 0.001
Length of hospital, days	6 (4–8)	10 (8–14)	< 0.001	6 (5–9)	11 (8–14)	< 0.001
Medications at discharge						
Aspirin	614 (98.6%)	462 (98.9%)	0.587	289 (99.3%)	289 (99.3%)	1.000
Clopidogrel	621 (99.7%)	465 (99.6%)	0.772	289 (99.3%)	290 (99.7%)	1.000
ACE inhibitor/ARB	422 (67.7%)	320 (68.5%)	0.783	195 (67.0%)	196 (67.4%)	0.930
β-blockers	485 (77.8%)	369 (79.0%)	0.644	226 (77.7%)	225 (77.3%)	0.921
Statins	511 (82.0%)	397 (85.0%)	0.191	245 (84.2%)	247 (84.9%)	0.819
Calcium blocker	72 (11.6%)	58 (12.4%)	0.664	39 (13.4%)	36 (12.4%)	0.711
DAPT duration, days			0.371			0.547
< 180	32 (5.1%)	21 (4.5%)		14 (4.8%)	12 (4.1%)	
180–360	65 (10.4%)	38 (8.1%)		31 (10.7%)	24 (8.2%)	
> 360	526 (84.4%)	408 (87.4%)		246 (84.5%)	255 (87.6%)	

Data are presented as median value (interquartile range) or n (%). ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; DAPT: dual antiplatelet therapy; IVUS: intravascular ultrasound; OCT: optical coherence tomography; PCI: percutaneous coronary intervention.

### 3.2 Clinical outcomes

Of the 1090 patients, 25 (2.3%) lost to follow-up while 1070 (98.2%) were followed up for at least two years and 948 (87.0%) were followed up for three years. There were 57 and 30 composite end points, 31 and 18 cardiac deaths, 35 and 18 MI in the “one-time” and staged PCI group during follow-up. As noted in Table 3 and Figure 1A, the estimated 30-day composite rate of cardiac death or MI was 1.3% for staged PCI and 1.9% for “one-time” PCI ( $P = 0.410$ ). The estimated 3-year composite event rate was 7.0%

in staged PCI group compared with 9.5% in “one-time” PCI group ( $P = 0.110$ ). In addition, no significant differences in the CI-AKI (2.8% vs. 2.9%,  $P = 0.917$ ), the 3-year rates of cardiac death (4.2% vs. 5.9%,  $P = 0.304$ ), MI (4.2% vs. 5.9%,  $P = 0.185$ ), definite/probable ST (1.1% vs. 1.9%,  $P = 0.258$ ) and TVR (16.4% vs. 14.3%,  $P = 0.081$ ) were observed.

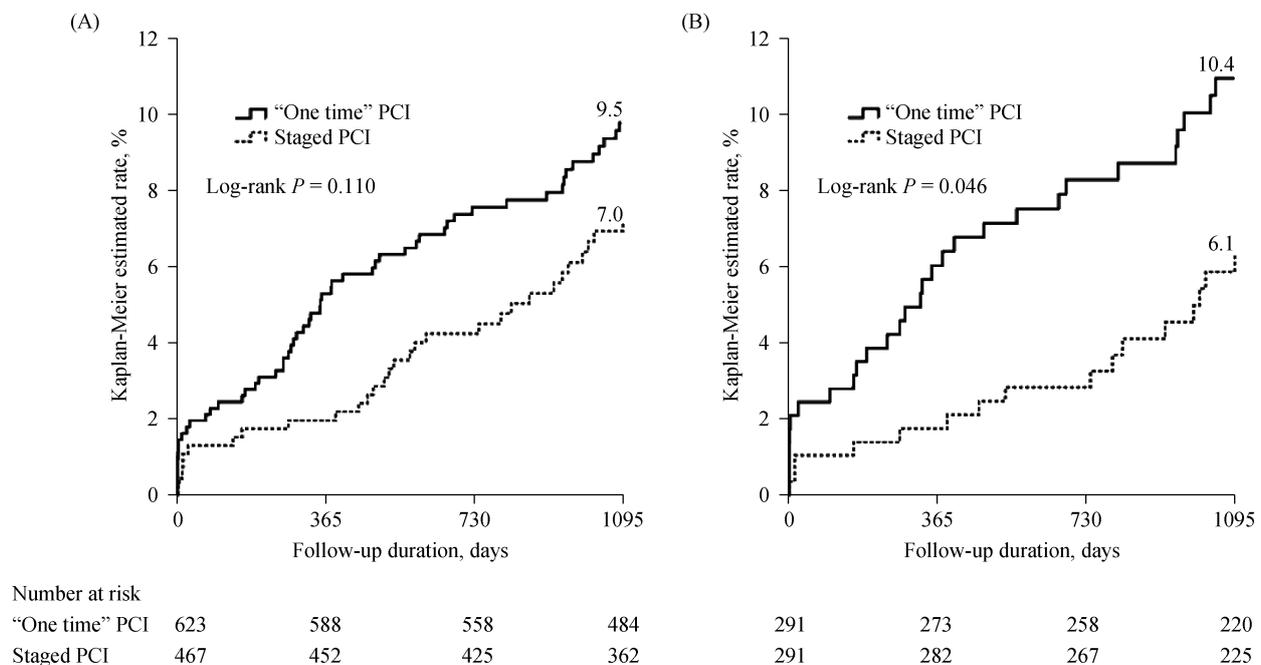
### 3.3 Multivariable analysis

In multivariable model after adjusting, the staged versus “one-time” multivessel PCI strategy was an independent predictor of reduced composite of MI or cardiac death at

**Table 3. Clinical outcomes for unadjusted and adjusted populations.**

Outcomes	Unadjusted			Propensity score adjusted		
	One-time ( <i>n</i> = 623)	Staged PCI ( <i>n</i> = 467)	<i>P</i> value	One-time ( <i>n</i> = 291)	Staged PCI ( <i>n</i> = 291)	<i>P</i> value
CI-AKI	18 (2.9%)	13 (2.8%)	0.917	10 (3.4%)	8 (2.8%)	0.632
30 days						
Cardiac death or MI	12 (1.9%)	6 (1.3%)	0.410	7 (2.4%)	3 (1.0%)	0.201
Cardiac death	3 (0.5%)	2 (0.4%)	0.899	2 (0.7%)	1 (0.3%)	0.563
MI	11 (1.8%)	5 (1.1%)	0.338	6 (2.1%)	2 (0.7%)	0.152
Definite/probable ST	8 (1.3%)	3 (0.6%)	0.293	4 (1.4%)	1 (0.3%)	0.177
TVR	8 (1.3%)	5 (1.1%)	0.745	4 (1.4%)	2 (0.7%)	0.408
Three years						
Cardiac death or MI	57 (9.5%)	30 (7.0%)	0.110	29 (10.4%)	16 (6.1%)	0.046
Cardiac death	31 (5.9%)	18 (4.2%)	0.304	13 (5.2%)	8 (3.2%)	0.228
MI	35 (5.9%)	18 (4.2%)	0.185	20 (7.4%)	9 (3.4%)	0.037
Definite/probable ST	12 (1.9%)	5 (1.1%)	0.258	7 (2.4%)	3 (1.1%)	0.199
TVR	76 (14.3%)	74 (16.4%)	0.081	39 (14.4%)	42 (15.5%)	0.746

Data are presented as *n* (%). CI-AKI: contrast-induced acute kidney injury; MI: myocardial infarction; PCI: percutaneous coronary intervention; ST: stent thrombosis; TVR: target vessel revascularization.



**Figure 1. Kaplan-Meier assessment for the composite end points of cardiac death or MI for unadjusted (A) and propensity score matched patients (B).** MI: myocardial infarction; PCI: percutaneous coronary intervention.

three years [hazards ratio (HR): 0.638, 95% confidence interval (CI): 0.408–0.998, *P* = 0.049]. Additional variables that were independently correlated with primary events during 3-year follow-up were shown in Table 4.

### 3.4 Propensity-matched analysis

After generating a propensity score, 291 of the 467 pa-

tients who underwent staged PCI were matched with a patient respectively who underwent “one-time” PCI. There were no differences in preselected variables between the propensity-matched cohorts (Table 1 and Table 2). As noted in Table 3, Figure 1B, the composite rate of cardiac death or MI at 30 days did not differ significantly between the two study groups, but it presented a trend in favor of staged PCI

**Table 4. Multivariable predictors of clinical events at three years.**

Predictors	HR (95% CI)	P value
Staged PCI ( <i>vs.</i> “one time”)	0.638 (0.408–0.998)	0.049
Previous MI	1.691 (1.049–2.726)	0.031
Previous CVD	1.875 (1.064–3.307)	0.030
Age, yrs	1.035 (1.002–1.069)	0.038
Hb, g/dL	0.980 (0.967–0.993)	0.002
eGFR $\leq$ 60 mL/min per 1.73m <sup>2</sup>	1.956 (1.197–3.194)	0.007
Temporary pacemaker used	6.621 (2.008–21.827)	0.002

EGFR: estimated glomerular filtration rate; CVD: cerebrovascular disease; Hb: hemoglobin; HR: hazards ratio; MI: myocardial infarction; PCI: percutaneous coronary intervention.

approach (1.0% *vs.* 2.4%,  $P = 0.201$ ). The incidence of definite/probable ST at 30 days also tended to be lower in the staged PCI group (0.3% *vs.* 1.4%,  $P = 0.177$ ). At three years, staged PCI was associated with lower composite rate of primary events (6.1% *vs.* 10.4%,  $P = 0.046$ ) and lower MI (3.4% *vs.* 7.4%,  $P = 0.037$ ). In addition, no significant differences in the CI-AKI (2.8% *vs.* 3.4%,  $P = 0.632$ ), the 3-year rates of cardiac death (3.2% *vs.* 5.2%,  $P = 0.228$ ) and TVR (15.5% *vs.* 14.4%,  $P = 0.746$ ) were observed.

## 4 Discussion

This study showed that, in elderly NSTEMI-ACS patients with MVD, staged PCI resulted in lower composite of cardiac death or MI despite a lack of impact on TVR. In addition, in our registry, there was a reduced trend of stent thrombosis in elderly patients who underwent staged PCI. To our knowledge, this is the first study to examine the efficacy of staged PCI versus “one-time” multivessel PCI in elderly NSTEMI-ACS patients with MVD.

Elderly patients with NSTEMI-ACS benefit from interventional therapies combined with optimal medical therapies.<sup>[15]</sup> However, with respect to clinical outcomes, periprocedural complications of intervention as well as the long-term ischemic risk remain higher in elderly NSTEMI-ACS patients with multivessel PCI than in younger patients.<sup>[4]</sup> For elderly people who tend to have poor condition and concomitant comorbidities, multivessel coronary artery disease is a critical issue that requires physicians to consider appropriate treatment strategies.

Although more and more data have suggested a benefit for multivessel PCI during the index admission in patients with STEMI and MVD,<sup>[16–20]</sup> not much data exist on the revascularization strategy for NSTEMI-ACS patients with MVD, especially elderly patients. Some observational studies showed that routine PCI of non-culprit arteries in

NSTEMI-ACS might be of benefit and raised questions about the timing of non-culprit arteries revascularization.<sup>[5,6]</sup> Hannan, *et al.*<sup>[21]</sup> analyzed the cohort of NSTEMI-ACS patients (5193 patients in total) and explored the “one-time” complete revascularization in the index hospitalization versus PCI of the culprit lesion only with staged non-culprit PCI for complete revascularization in a subsequent admission. At three years, there was no significant difference in all-cause mortality between the two groups. However, data for other clinical endpoints such as cardiac death, MI, and TVR after procedure were not available in the study. Moreover, the staged PCI group did not include the patients who underwent staged PCI during the index hospitalization. To date, we are not aware of any evidence to evaluate the effect of revascularization, *i.e.*, culprit-only versus multivessel revascularization and one-time versus staged multivessel revascularization, in elderly patients with NSTEMI-ACS and MVD.

In the absence of evidence comparing multivessel PCI with staged PCI approach for NSTEMI-ACS patients, the clinical practice is mixed among various choices. A published American survey reported that for NSTEMI-ACS patients with MVD, 42% of cardiologists would opt for treatment of both culprit lesion and non-culprit lesions at initial setting, 37% would treat non-culprit arteries in a staged procedure and 14% would opt for treatment of the culprit lesion only at initial setting and subsequent medical therapy without coronary revascularization unless the patient developed persistent ischemia or symptoms.<sup>[22]</sup>

We found that staged PCI is associated with the reduced short- and long-term ischemic risks in the elderly NSTEMI-ACS patients. The reasons may be multifactorial and partially explained as follows. Any PCI procedure is challenging to the elderly.<sup>[23,24]</sup> Compared to the young, elderly patients have higher prevalence of complex coronary lesions, extensive coronary atherosclerosis, comorbidities and physiological impairment.<sup>[23,24]</sup> “One-time” PCI treatment for the elderly presenting with NSTEMI-ACS may increase risks for procedural complications, longer procedural time and stent thrombosis in a heightened thrombotic and inflammatory state.<sup>[25–28]</sup> On the contrary, PCI on the culprit lesion only and staged non-culprit PCI at a later date with the optimal medical treatment provides stabilization of the elderly patients and allows heart team to reassess the clinical and angiographic state. An analysis of 1726 patients with an average age of 62.6 enrolled in the multicenter German Cypher Stent Registry database showed that management of > 1 lesion during the same intervention was identified as an independent predictor of the combined endpoint of death from any cause, myocardial infarction, stroke or TVR after

PCI.<sup>[29]</sup> Taken together, staged PCI should be considered as a preferred strategy in elderly patients.

Our study has several limitations. First, the choices of one-time or staged PCI were not based on a randomization but at physicians' discretion, which resulted in obvious selection bias. Attempts were made in order to minimize the effects of selection bias, such as eliminating patients with clinical characteristics that made them clearly inappropriate for "one-time" procedure [i.e., severe renal dysfunction (eGFR < 30 mL/min per 1.73m<sup>2</sup>), technical failure or major complications during the first part of a staged procedure], analyzing data with multivariate regression and propensity score matching. However, results should still be interpreted with caution due to potential bias. Second, the experience and technique of the operator was very important, but very difficult to measure. Third, the study was not sufficiently powered to compare the incidences of stent thrombosis and the composite of cardiac death or MI at 30 days between groups because these rates were low. Fourth, we had underestimated the incidence of MI since follow-up angiography and routine cardiac biomarkers surveillance was not mandatory. Last, the study was not a multicenter study, but a single center study.

In conclusion, staged PCI might be an optimal strategy, associated with reduced cardiac death or MI, for elderly NSTEMI-ACS patients with MVD, compared with one-time PCI strategy after adjustment, which needs further confirmation by large randomized trials.

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