Long-Term Safety and Efficacy of Staged Percutaneous Coronary Intervention for Patients with ST-Segment Elevation Myocardial Infarction and Multivessel Coronary Disease

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The relative benefit of staged percutaneous coronary intervention (PCI) versus culprit-only PCI in patients with ST-segment elevation myocardial infarction and multivessel coronary disease remains disputable. Therefore, we conducted this study to compare the long-term outcomes of staged complete revascularization and culprit-only PCI in this population. A total of 1,205 patients were treated with staged PCI (n = 576) or culprit-only PCI (n = 629) from January 2006 to December 2015 in our center. After propensity-score matching, 415 pairs of patients were identified, and postmatching absolute standardized differences were <10% for all covariates. The primary endpoint was major adverse cardiac and cerebrovascular event (MACCE), defined as a composite of all-cause death, myocardial infarction (MI), stroke, or unplanned revascularization. The mean follow-up duration was 5 years. Overall, staged complete revascularization was associated with lower risks of MACCE, MI, unplanned revascularization, and a composite of cardiac death, MI or stroke compared with culprit-only PCI in both overall population and propensity-matched cohorts. In Cox proportional hazards regression analysis, the strategy of staged PCI was consistently a significant predictor of lower incidences of MACCE, MI, unplanned revascularization and a composite of cardiac death, MI, or stroke. However, there was no difference in the risks of MACCE, MI and unplanned revascularization between the 2 approaches for diabetic patients. In conclusion, among patients with ST-segment elevation myocardial infarction and multivessel disease who underwent primary PCI, an approach of staged complete revascularization is superior to culprit-only PCI at 5-year follow-up. Nevertheless, the advantage of staged PCI is attenuated in diabetic patients. **(Am J Cardiol 2019;124:334−342)**

In patients with ST-segment elevation myocardial infarction (STEMI) who received primary percutaneous coronary intervention (PCI), about 50% have significant nonculprit lesions, and the outcome is worse compared with the case of patients with single-vessel disease.[1−4] However, the optimal management of nonculprit lesions for these patients is currently under debate. Although the results of some randomized controlled trials (RCTs)[5,6] and registries[7−10] have indicated support for a conservative approach, recent landmark RCTs have noted improved prognosis with immediate or staged complete revascularization in this setting.[11−14] Thus, the 2015 American College of Cardiology/American Heart Association (AHA) and 2017 European Society of Cardiology guidelines upgraded the recommendation for nonculprit lesions revascularization during primary PCI or as a staged procedure.[4,15] Nonetheless, due to the further complexity of immediate complete revascularization, most operators still prefer a culprit-only approach followed by staged complete PCI in China. Furthermore, despite the recent data and guidelines have been changed, the long-term relative safety and efficacy of staged versus culprit-only PCI has been seldom evaluated in this cohort (>5 years). Hence, this study was conducted to assess the long-term impact of staged complete revascularization for patients with STEMI and multivessel coronary disease undergoing primary PCI.

Methods

This was a retrospective cohort study, and patients with STEMI and multivessel coronary artery disease who underwent primary PCI within 12 hours from symptom onset at Beijing Anzhen Hospital between January 2006 and December 2015 were consecutively enrolled. Ethics approval for the study was obtained from the local ethical committee, and written informed consent was waived due

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to the retrospective enrollment. In addition, patient records were anonymized and deidentified before database merging and analysis. Multivessel disease was defined as the presence of ≥70 % angiographic stenosis in ≥1 nonculprit major coronary artery (with diameter ≥2.5 mm). Staged PCI was defined as PCI of significant nonculprit lesions scheduled during hospitalization and performed within 30 days after the primary PCI. We excluded patients with single vessel disease (n = 1,390), left main disease (≥50% diameter stenosis; n = 40) or a concomitant chronic total occlusion (n = 307). In addition, patients undergoing rescue PCI (n = 116), 1-time complete revascularization (n = 81), surgery (n = 97), medication treatment only (n = 34), or being dead before discharge (n = 16) were also not eligible.

All procedures were performed according to the current guidelines' recommendation and the operators' discretion.[4,15] After patients were discharged from the hospital, aspirin therapy was continued indefinitely (100 mg/day), clopidogrel (75 mg/day), or ticagrelor (180 mg/day) was administrated for ≥12 months. The culprit vessel was determined by the evaluation of electrocardiographic changes and the echocardiography as well as angiographic findings by the operators. The physicians and patients determined whether staged PCI of the significant nonculprit lesions should be conducted. Demographics, cardiovascular risk factors, clinical parameters, laboratory data, coronary angiographic, and procedural details were collected.

Data for endpoints were obtained from hospital charts, clinical visit, and telephone interviews conducted by

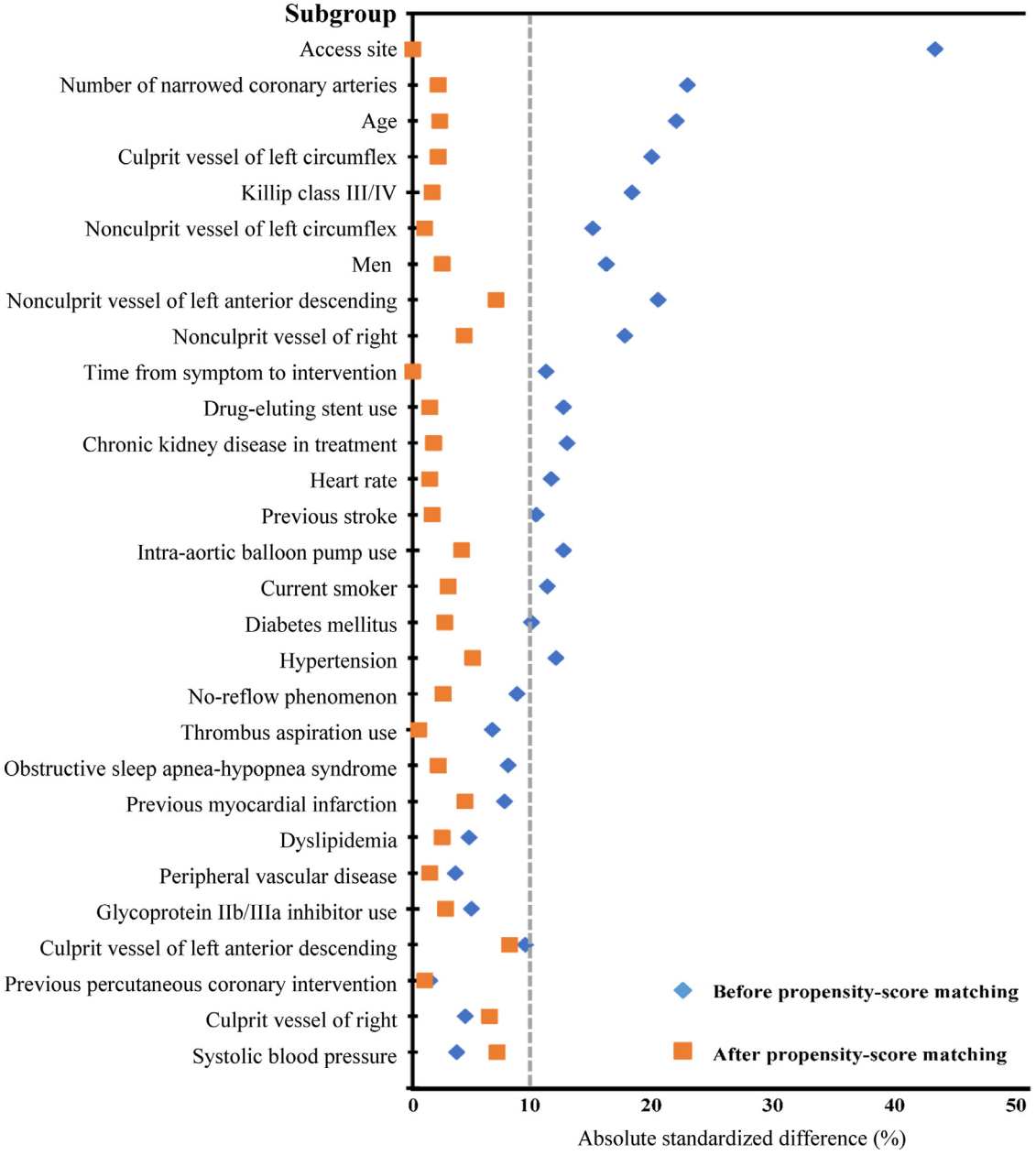

Figure 1. Absolute standardized differences before and after propensity-score matching.

Table 1
Baseline patient and angiographic characteristics before and after propensity-score matching analysis

Overall population	Staged revascularization	Culprit-only revascularization	p Value	Propensity-matched population		
Variable				Staged revascularization	Culprit-only revascularization	p Value
Age (years)	59 (50-66)	61 (53-69)	<0.0001	61 (52-68)	60 (51-68)	0.86
Men	476 (82.6%)	479 (76.2%)	0.006	326 (78.6%)	322 (77.6%)	0.74
Current smoker	327 (56.8%)	323 (51.4%)	0.06	213 (51.3%)	218 (52.5%)	0.73
Diabetes mellitus	164 (28.5%)	207 (32.9%)	0.10	134 (32.3%)	128 (30.8%)	0.65
Hypertension	335 (58.2%)	402 (63.9%)	0.04	266 (64.1%)	256 (61.7%)	0.47
Dyslipidemia	346 (60.1%)	364 (57.9%)	0.44	236 (56.9%)	241 (58.1%)	0.73
Previous myocardial infarction	26 (4.5%)	39 (6.2%)	0.20	21 (5.1%)	25 (6.0%)	0.54
Previous percutaneous coronary intervention	32 (5.6%)	38 (6.0%)	0.72	24 (5.8%)	25 (6.0%)	0.88
Previous stroke	47 (8.2%)	71 (11.3%)	0.07	40 (9.6%)	38 (9.2%)	0.81
Peripheral vascular disease	19 (3.3%)	17 (2.7%)	0.54	9 (2.2%)	10 (2.4%)	0.82
Chronic kidney disease in treatment	7 (1.2%)	19 (3.0%)	0.03	7 (1.7%)	8 (1.9%)	0.79
Obstructive sleep apnea-hypopnea syndrome	5 (0.9%)	11 (1.7%)	0.18	5 (1.2%)	4 (1.0%)	1.00
Heart rate (beats/min)	75 (67-85)	77 (70-86)	0.03	76 (68-85)	76 (69-86)	0.68
Systolic blood pressure (mmHg)	120 (110-130)	120 (108-130)	0.32	120 (110-130)	120 (105-130)	0.57
Peak troponin (μg/L)	68 (29-112)	70 (26-101)	0.10	72 (28-111)	68 (27-101)	0.17
Peak creatine kinase (U/L)	2058 (1103-3381)	2056 (1055-3382)	0.68	2055 (1065-3466)	1978 (1074-3367)	0.47
Peck creatine kinase myocardial band (U/L)	206 (111-305)	221 (103-302)	0.66	207 (110-302)	212 (97-302)	0.70
Low density lipoprotein cholesterol (mmol/L)	3.04 (2.45-3.57)	2.85 (2.39-3.44)	0.008	3.00 (2.41-3.57)	2.91 (2.42-3.45)	0.50
Estimated glomerular filtration rate (ml/min/1.73 m^2)	99.7 (91.0-107.0)	98.0 (88.7-105.5)	0.03	97.9 (89.3-106.4)	98.7 (89.3-106.4)	0.86
Uric acid (μmol/L)	320.8 (265.1-381.4)	325.8 (265.0-389.1)	0.71	320.5 (264.4-374.3)	323.9 (264.6-381.6)	0.79
Blood glucose (mmol/L)	7.90 (6.73-10.10)	8.35 (6.85-10.61)	0.04	8.20 (6.90-10.50)	8.27 (6.78-10.44)	0.83
Time from symptom to intervention(hours)	5 (3-7)	5 (3-8)	0.02	5 (3-8)	5 (3-8)	0.99
Location of myocardial infarction			0.41			0.52
Anterior	209 (36.3%)	251 (39.9%)		166 (40.0%)	150 (36.1%)	
Posterior	248 (43.1%)	251 (39.9%)		163 (39.3%)	172 (41.4%)	
Right ventricular	119 (20.7%)	127 (20.2%)		86 (20.7%)	93 (22.4%)	
Killip class III/IV	41 (7.1%)	79 (12.6%)	0.002	38 (9.2%)	40 (9.6%)	0.81
Radial artery access	153 (26.6%)	293 (46.6%)	<0.0001	148 (35.7%)	148 (35.7%)	1.00
No. narrowed coronary arteries			<0.0001			0.76
Two	368 (63.9%)	467 (74.2%)		291 (70.1%)	287 (69.2%)	
Three	208 (36.1%)	162 (25.8%)		124 (29.9%)	128 (30.8%)	
Culprit vessel			0.002			0.56
Left anterior descending	207 (35.9%)	256 (40.7%)		166 (40.0%)	151 (36.4%)	
Left circumflex	98 (17.0%)	64 (10.2%)		50 (12.0%)	52 (12.5%)	
Right	271 (47.0%)	309 (49.1%)		199 (48.0%)	212 (51.1%)	
Nonculprit artery						
Left anterior descending	292 (50.7%)	256 (40.7%)	0.001	180 (43.4%)	194 (46.7%)	0.33
Left circumflex	289 (50.2%)	361 (57.4%)	0.01	224 (54.0%)	223 (53.7%)	0.94
Right	204 (35.4%)	173 (27.5%)	0.003	135 (32.5%)	126 (30.4%)	0.50
Thrombus aspiration	399 (69.3%)	417 (66.3%)	0.27	276 (66.5%)	277 (66.7%)	0.94
No-reflow phenomenon*	48 (8.3%)	69 (11.0%)	0.12	38 (9.2%)	40 (9.6%)	0.81
Intra-aortic balloon pump use	68 (11.8%)	51 (8.1%)	0.03	38 (9.2%)	43 (10.4%)	0.56
Glycoprotein IIb/IIIa inhibitor use	157 (27.3%)	158 (25.1%)	0.40	100 (24.1%)	105 (25.3%)	0.69
Drug-eluting stent use	565 (98.1%)	604 (96.0%)	0.04	404 (97.3%)	405 (97.6%)	0.83
Type of stent			0.08			0.88
1st drug-eluting stent	445 (77.3%)	454 (72.2%)		314 (75.7%)	319 (76.9%)	
2nd drug-eluting stent	120 (20.8%)	150 (23.8%)		90 (21.7%)	86 (20.7%)	

(*continued*)

Table 1 (***Continued***)

Overall population	Staged revascularization	Culprit-only revascularization	p Value	Propensity-matched population		
Variable				Staged revascularization	Culprit-only revascularization	p Value
Bare-mental stent	1 (0.2%)	3 (0.5%)		1 (0.2%)	2 (0.5%)	
Percutaneous transluminal coronary angioplasty	10 (1.7%)	22 (3.5%)		10 (2.4%)	8 (1.9%)	
Medications at discharge						
Aspirin	576 (100%)	628 (99.8%)	1.00	415 (100%)	415 (100%)	1.00
P2Y12 receptor inhibitor	576 (100%)	629 (100%)	1.00	415 (100%)	415 (100%)	1.00
Angiotensin converting enzyme inhibitor/angiotensin receptor blocker	453 (78.6%)	433 (68.8%)	<0.0001	305 (73.5%)	300 (72.3%)	0.70
β-blockers	480 (83.3%)	544 (86.5%)	0.13	356 (85.8%)	351 (84.6%)	0.63
Statins	571 (99.1%)	625 (99.4%)	0.74	412 (99.3%)	411 (99.0%)	1.00
Nitrates	173 (30.0%)	164 (26.1%)	0.13	110 (26.5%)	115 (27.7%)	0.70

* No-reflow phenomenon was defined as Thrombolysis In Myocardial Infarction flow grade ≤2 after primary percutaneous coronary intervention. Data were presented as median (interquartile range), mean (standard deviation), or n (%).

trained reviewers. To ensure that all patients had at least 2 years' follow-up information, the follow-up period was extended by May 31, 2018. The primary endpoint was major adverse cardiac and cerebrovascular event (MACCE), defined as a composite of all-cause death, myocardial infarction (MI), stroke, or unplanned revascularization. Secondary endpoints included all-cause death, cardiac death, MI, stroke, unplanned revascularization, and a composite of cardiac death, MI, or stroke. Deaths were classified as either cardiac or noncardiac. Cardiac death was defined as death due to suspected cardiac cause (e.g., MI, heart failure), and death due to undetermined cause. Diagnosis of MI was in compliance with the current guidelines.[16] Stoke was defined as new focal neurological deficit lasting >24 hours, confirmed by a neurologist based on imaging evidence.[17] Unplanned revascularization was repeat PCI or surgery of culprit or nonculprit vessels excluding staged PCI. All events were carefully verified and adjudicated by independent clinicians.

Continuous variables were expressed as mean (SD) or median (interquartile range) according to different distributions, and categorical variables were expressed as frequencies (percentages). Differences in various characteristics between the 2 groups were compared using Student's *t* test, Wilcoxon's rank sum test, Pearson's chi-square test, and Fisher's exact test, when appropriate. Cumulative incidence of clinical events was estimated using Kaplan-Meier curves, and differences were assessed with log-rank test. To identify predictors of long-term outcomes, the analysis of Cox proportional hazard model was conducted to provide adjusted HRs with 95% CIs.[18] Candidate adjustment variables are shown in supplementary Table 1. After forward stepwise selection with entry and exit criteria of p = 0.05 and 0.1 level, the variables summarized in supplementary Tables 2 to 8 were included in the final multivariable models for each endpoint.

To adjust the confounding from the real world, differences in long-term clinical outcome between the 2 groups in propensity-matched population were compared. Patients undergoing staged PCI were matched 1:1 with patients randomly selected from the culprit-only PCI group without replacement, on the basis of the nearest neighbor in terms of Mahalanobis distance with a caliper of 0.02. To estimate the propensity score, a logistic regression model was used including variables of age, gender, current smoker, diabetes, hypertension, dyslipidemia, previous MI, previous PCI, previous stroke, peripheral vascular disease, chronic kidney disease in treatment, obstructive sleep apnea-hypopnea syndrome, time from symptom to intervention, heart rate, systolic blood pressure, access site of PCI, Killip class, number of narrowed coronary arteries, culprit vessel of left anterior descending coronary artery, culprit vessel of left circumflex coronary artery, culprit vessel of right coronary artery, nonculprit vessel of left anterior descending coronary artery, nonculprit vessel of left circumflex coronary artery, nonculprit vessel of right coronary artery, use of drug-eluting stent, use of thrombus aspiration, use of intra-aortic balloon pump, no-reflow phenomenon, use of glycoprotein IIb/IIIa inhibitor, and use of aspirin, P2Y12 inhibitor, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β-blockers, statins, and nitrates during hospitalization.

Additionally, landmark analysis was undertaken according to a landmark point at 1.5 years, with the HRs calculated separately for events that occurred up to 1.5 years after primary PCI and ones that occurred between 1.5 years after primary PCI and the end of follow-up period. Furthermore, subgroup analysis of the primary endpoint of MACCE, and secondary endpoints of MI and unplanned revascularization were performed based on the following factors, including age (<65 and ≥65 years), gender, current smoker, diabetes, hypertension, access site, number of narrowed coronary arteries, and culprit vessel. All statistical analyses were conducted with SPSS 23.0 (IBM) and STATA 12.0 (StataCorp). A 2-sided p value of <0.05 was considered statistically significant.

Results

Among 3,286 patients who underwent primary PCI, 576 patients with STEMI and multivessel coronary disease

underwent staged complete revascularization, and 629 patients underwent culprit-only PCI, respectively. After propensity-score matching, 415 pairs of patients were identified (Supplementary Figure 1), and postmatching absolute standardized differences were <10% for all covariates (Figure 1). Table 1 shows the baseline patient and angiographic characteristics of the overall population and the propensity-matched cohorts. The mean follow-up period was 5.01 years.

The incidence of the primary endpoint of MACCE was significantly lower in the staged PCI group than that in the culprit-only PCI group (hazard ratio [HR] 0.72, 95% confidence interval [CI] 0.59 to 0.88), which was primarily caused by the lower risks of MI (HR 0.52, 95% CI 0.33 to 0.82) and unplanned revascularization (HR 0.74, 95% CI 0.58 to 0.94). In addition, staged PCI was also associated with lower risk of a composite of cardiac death, MI, or stroke compared with culprit-only PCI (HR 0.65, 95% CI 0.47 to 0.89) (Table 2 and Figure 2).

After the potential confounders were adjusted, staged complete PCI remained associated with a decreased risk of the primary endpoint of MACCE (HR 0.72, 95% CI 0.59 to 0.88) (Table 2). Other independent predictors for MACCE were previous stroke (HR 1.55, 95% CI 1.16 to 2.08) and chronic kidney disease in treatment (HR 2.19, 95% CI 1.30 to 3.68) (Supplementary Table 2). Furthermore, treatment with staged PCI was also a significant predictor of lower MI (HR 0.49, 95% CI 0.31 to 0.78), unplanned revascularization (HR 0.67, 95% CI 0.53 to 0.86), and a composite of cardiac death, MI, or stroke (HR 0.71, 95% CI 0.51 to 0.98).

Results of propensity-score matching analysis with respect to the primary endpoint of MACCE (HR 0.70, 95% CI 0.55 to 0.89) as well as the secondary endpoints of MI (HR 0.48, 95% CI 0.27 to 0.84), unplanned revascularization (HR 0.66, 95% CI 0.49 to 0.88), and a composite of cardiac death, MI, or stroke (HR 0.66, 95% CI 0.45 to 0.97) were concordant with the major analysis of the overall population (Table 2 and Figure 3). There was no significant difference in the risks of all-cause death, cardiac death, and stroke between the 2 groups.

According to the landmark analysis, there was no relation between the treatment and time (within 1.5 years vs subsequent period) with respect to all endpoints for both overall population (Supplementary Figure 2) and propensity-matched cohorts (Supplementary Figure 3) except cardiac death. The approach of staged PCI tended to be associated with lower incidences of MACCE, MI, unplanned revascularization, and a composite of cardiac death, MI, or stroke from 1.5 years after primary PCI to the end of follow-up period in both overall population and propensity-matched cohorts. Of note, cardiac mortality was significantly lower in the staged PCI group than that in the culprit-only PCI group up to 1.5 years in the overall population ($p_{interaction}$ =0.04), whereas no difference was found between the two groups regarding cardiac mortality up to 1.5 years in the propensity-matched cohorts ($p_{interaction}$ =0.20).

Subgroup analyses were performed based on important baseline information for propensity-matched population and formal testing for interactions indicated that results of the comparison of MACCE (Figure 4), MI (Supplementary Figure 4), and unplanned revascularization (Supplementary

Table 2
Five-year outcomes in overall population and propensity-matched population

Clinical endpoint	No. patients with event (overall)		Crude hazard ratio (95% confidence interval)	Adjusted hazard ratio (95% confidence interval)	No. patients with event (matched)		Hazard ratio (95% confidence interval)
	Staged revascularization	Culprit-only revascularization			Staged revascularization	Culprit-only revascularization	
Major adverse cardiac and cerebrovascular event	193 (33.5%)	216 (34.3%)	0.72 (0.59-0.88)	0.72 (0.59-0.88)	127 (30.6%)	143 (34.5%)	0.70 (0.55-0.89)
Cardiac death/myocardial infarction/stroke	70 (12.2%)	87 (13.8%)	0.65 (0.47-0.89)	0.71 (0.51-0.98)	49 (11.8%)	60 (14.5%)	0.66 (0.45-0.97)
All-cause death	55 (9.5%)	57 (9.1%)	0.78 (0.54-1.14)	1.04 (0.71-1.52)	39 (9.4%)	35 (8.4%)	0.94 (0.59-1.48)
Cardiac death	28 (4.9%)	28 (4.5%)	0.82 (0.48-1.39)	1.29 (0.74-2.22)	22 (5.3%)	17 (4.1%)	1.08 (0.57-2.04)
Myocardial infarction	31 (5.4%)	49 (7.8%)	0.52 (0.33-0.82)	0.49 (0.31-0.78)	19 (4.6%)	33 (8.0%)	0.48 (0.27-0.84)
Stroke	13 (2.3%)	18 (2.9%)	0.62 (0.30-1.26)	0.64 (0.31-1.31)	9 (2.2%)	16 (3.9%)	0.48 (0.21-1.09)
Unplanned revascularization	125 (21.7%)	150 (23.8%)	0.74 (0.58-0.94)	0.67 (0.53-0.86)	78 (18.8%)	100 (24.1%)	0.66 (0.49-0.88)

Data were presented as n (%).

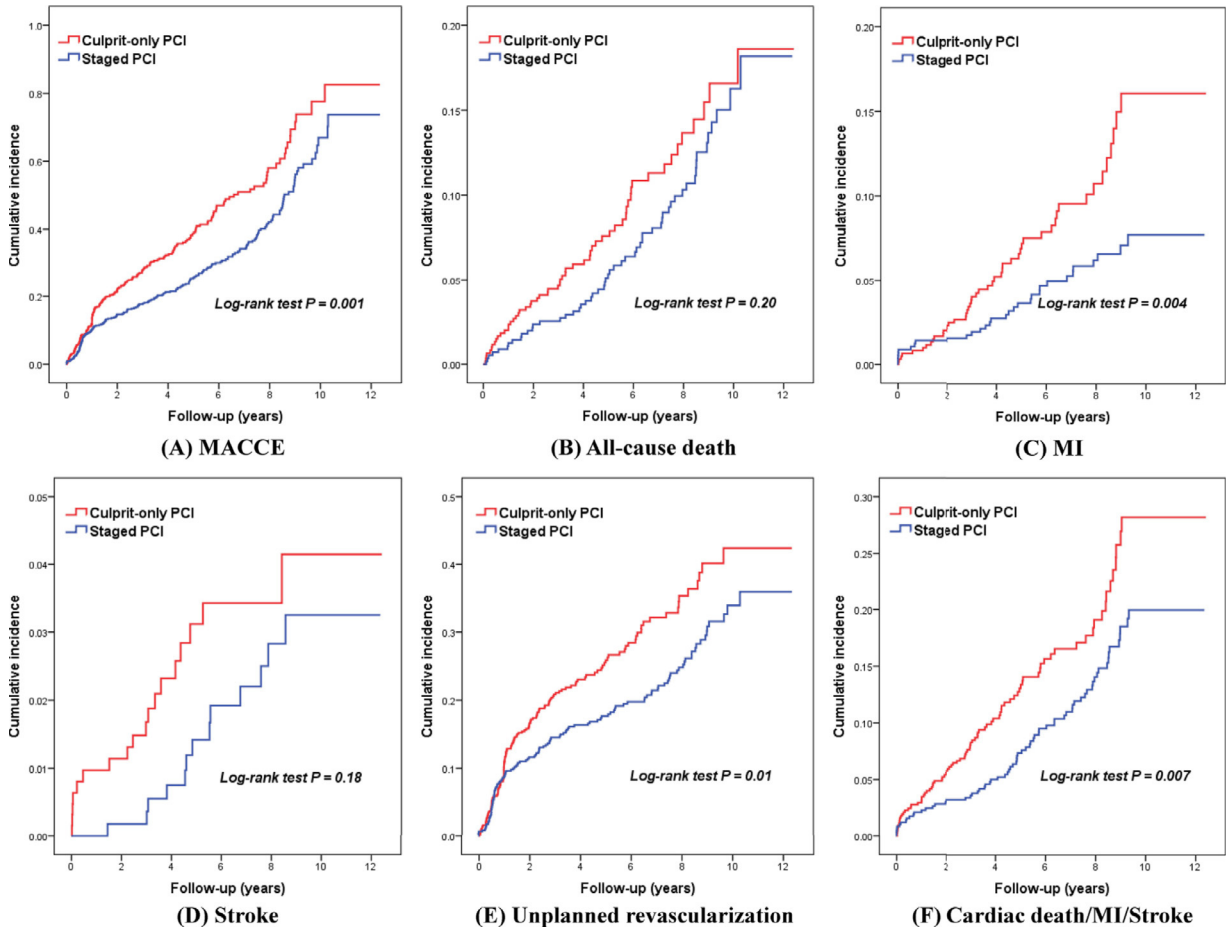

Figure 2. Kaplan-Meier event rate curves of clinical outcomes in overall population. MACCE = major adverse cardiac and cerebrovascular event; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Figure 5) between the 2 groups were consistent across most subgroups. However, among patients with diabetes mellitus, risks of MACCE (HR 0.98, 95% CI 0.65 to 1.48; $p_{interaction} = 0.049$), MI (HR 1.25, 95% CI 0.47 to 3.27; $P_{interaction}=0.02$) and unplanned revascularization (HR 1.04, 95% CI 0.63 to 1.74; $p_{interaction} =0.03$) with staged PCI were similar to those with culprit-only PCI. Additionally, the benefit of staged PCI regarding MI (HR 0.16, 95% CI 0.05 to 0.54; $p_{interaction} = 0.03$) was more pronounced among patients with 3-vessel disease.

Discussion

During the study period of 10 years, 48% patients with STEMI and multivessel disease underwent staged complete revascularization in our center. This study indicated that staged PCI was associated with lower incidences of MACCE in both overall population and propensity-matched cohorts, which was largely caused by lower risks of MI and unplanned revascularization. Furthermore, risk of a composite of cardiac death, MI, or stroke was significantly lower for patients who underwent staged PCI than those undergoing culprit-only PCI. There was no difference in the incidences of MACCE, MI and unplanned revascularization between diabetic patients undergoing the 2 treatment strategies.

The management of nonculprit lesions in STEMI has been the subject of extensive debate for 2 decades. Based on previous RCTs and observational studies, culprit-only PCI was recommended in patients with STEMI and multivessel disease. However, results of the recent large RCTs have challenged this concept. The Preventative Angioplasty in Myocardial Infarction, Complete Versus culprit-Lesion only PRimary PCI Trial, The Third DANish Study of Optimal Acute Treatment of Patients with STEMI−PRImary PCI in MULTIvessel Disease, and Compare-Acute trials suggested significant benefit of immediate or complete revascularization compared with culprit-only PCI.[11−14] Thus, the recommendation for nonculprit lesions PCI during primary PCI or as a staged procedure has been upgraded to class IIb in the 2015 American College of Cardiology/American Heart Association guideline, whereas the revascularization of nonculprit lesions before discharge received a class IIa recommendation in the 2017 European Society of Cardiology guideline for the treatment of STEMI.[4,15] In clinical scenarios, due to the complexity of immediate complete revascularization, most operators in China still prefer a culprit-only approach followed by staged complete revascularization. However, the relative benefit of staged PCI versus culprit-only PCI in patients with STEMI and multivessel disease has been rarely assessed during long-term follow-up. Thus, it is necessary to evaluate the long-term

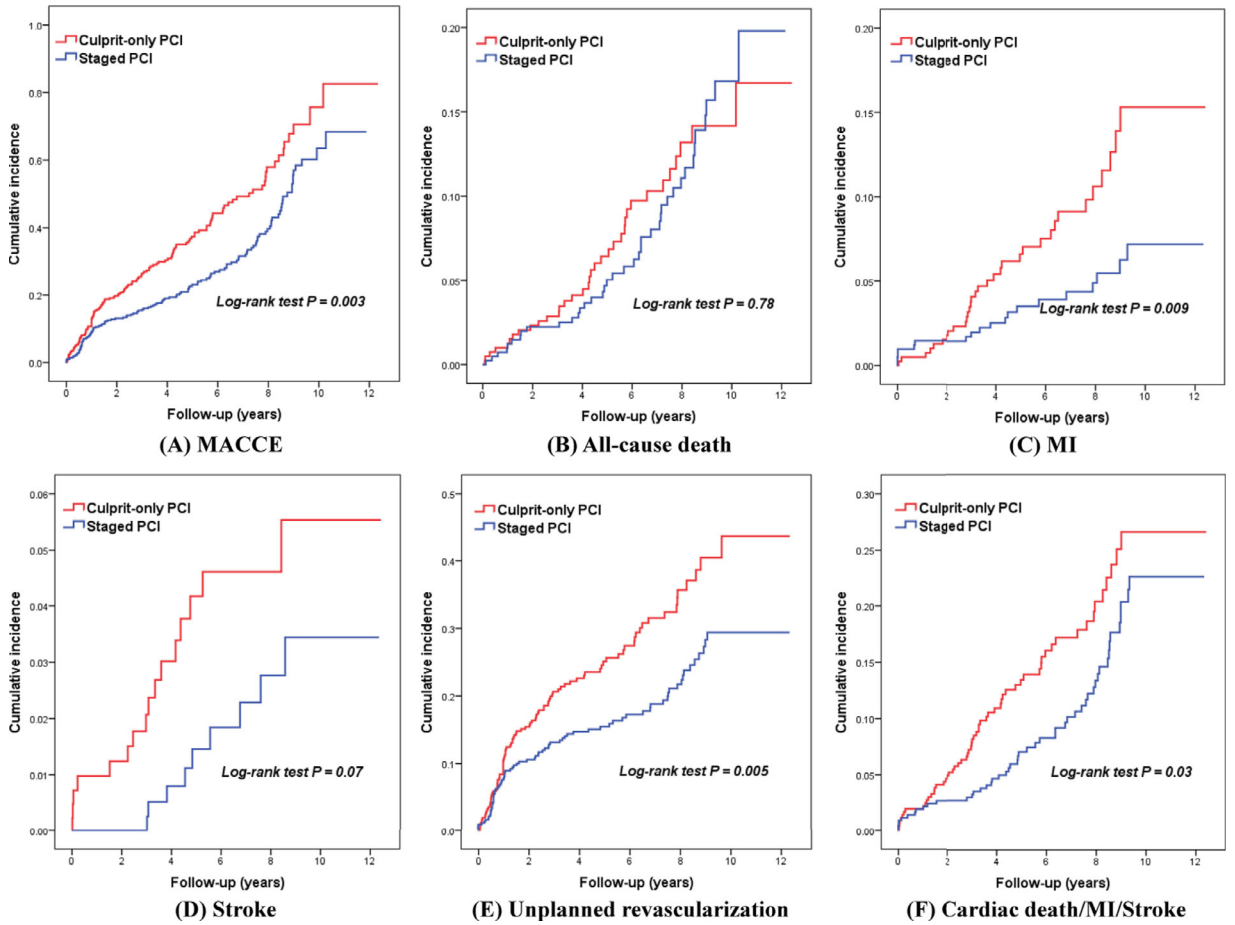

Figure 3. Kaplan-Meier event rate curves of clinical outcomes in propensity-matched population. MACCE = major adverse cardiac and cerebrovascular event; MI = myocardial infarction; PCI = percutaneous coronary intervention.

safety and efficacy of staged complete revascularization in this population.

Compared to patients with stable coronary artery disease, STEMI patients are more likely to have typical vulnerable plaques, with a large amount of necrotic core and thin-cap fibroatheroma.[19] In theory, intervening of the nonculprit disease may cause no-reflow phenomenon, iatrogenic small MI, coronary reserve reduction, and increased risk of renal disease. Conversely, early revascularization of nonculprit lesions can reduce ischemic burden, stabilize vulnerable plaque, thus reducing the incidence of ischemic events.[20]

In the present study, due to differences in MI and unplanned revascularization between the 2 therapeutic approaches, staged PCI was significantly associated with lower risk of 5-year adverse events versus culprit-only PCI. Obviously, due to its ability of reducing ischemic burden and stabilizing vulnerable plaques, the benefits of complete revascularization outweigh its risks. Coincidentally, the benefit of staged PCI we observed is similar to the previous study conducted by Toyota et al.[21] Nevertheless, the advantage of staged PCI over culprit-only PCI regard as 5-year mortality did not exist in propensity-matched population and the advantage of stage PCI over culprit-only PCI regard as the lower risks of cardiac death, MI, and stroke diminished after adjusting for confounders in that study. In our study, patients who underwent staged PCI consistently had lower incidences of MACCE, MI, unplanned revascularization, and a composite of cardiac death, MI, or stroke than those undergoing culprit-only PCI in overall population, propensity-matched population, and multivariable adjusted analysis, indicating the result is reliable.

Another important finding of our study is that staged complete revascularization loses its advantage in patients with diabetes. In clinical practice, compared with nondiabetic patients, diabetic patients are always more associated with complex diseases with characteristics of smaller vessel size, longer lesion length, and greater plaque burden. Furthermore, the morbidity and mortality are also higher in diabetic patients undergoing PCI, even with the advent of novel-generation drug-eluting stents, diabetes mellitus remains a risk factor for restenosis and stent thrombosis.[22,23] Therefore, the predicted benefits of staged PCI of the nonculprit lesions were less pronounced in diabetics compared with nondiabetics.

Several limitations cannot be ignored that presented in our study. First, the study is nonrandomized. Despite the use of multivariable adjusted analysis and propensity-matched analysis, it was impossible to control all confounding factors and eliminate the selection bias. Actually, sick patients are less likely to undergo staged PCI unless they have refractory angina due to nonculprit lesions. Second,

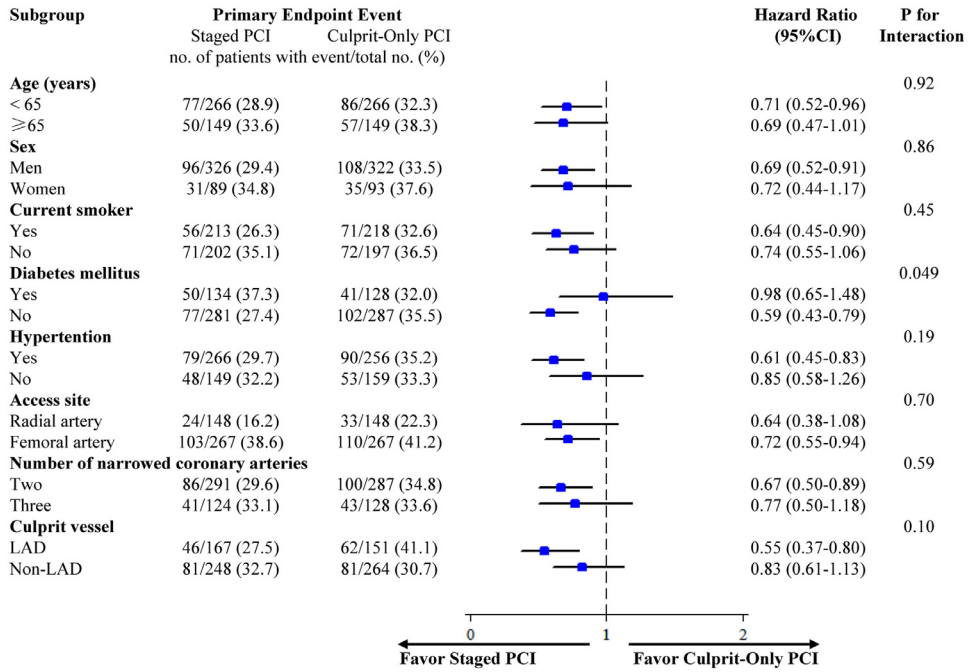

Figure 4. Subgroup analysis for major adverse cardiac and cerebrovascular event in propensity-matched population. CI = confidence interval; LAD = left anterior descending coronary artery; PCI = percutaneous coronary intervention.

participants were collected across a 10-year time span. During this time, PCI was subject to change in stent type, interventional techniques as well as antiplatelet therapies, influencing the results. Third, our study did not suggest the optimal timing of nonculprit lesions PCI, i.e., immediate and staged complete revascularization, for only 81 patients underwent 1-time multivessel PCI during the study period. In addition, as recommended in the guideline,[4] most patients undergoing immediate complete revascularization are complicated with cardiogenic shock. Yet severe systolic dysfunction may mask the effect of treatment strategies on prognosis. Fourth, for most patients, the significance of nonculprit lesions was assessed on angiography other than ischemia testing like fractional flow reserve or noninvasive physiological stress test.

In conclusion, among patients with STEMI and multivessel disease, an approach of 30-day staged complete revascularization after primary PCI is superior to culprit-only PCI with respect to lower incidences of MACCE, MI, unplanned revascularization, and a composite of cardiac death, MI, or stroke at 5-year follow-up. However, the advantage of staged PCI is attenuated in patients with diabetes. Thus, further large scale RCTs are warranted to compare immediate versus staged complete revascularization in this population.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary materials

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