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Culprit vessel only versus "one-week" staged percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction

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Abstract

Objective To explore the impact of a "one-week" staged multivessel percutaneous coronary intervention (PCI) versus culprit-only PCI on deaths and major adverse cardiac events (MACE). **Methods** We retrospectively analyzed 447 patients with multivessel disease who experienced a ST-segment elevation myocardial infarction (STEMI) within 12 h before undergoing PCI between July 26, 2008 and September 25, 2011. After completion of PCI in the infarct artery, 201 patients still in the hospital agreed to undergo PCI in non-infarct arteries with more than 70% stenosis for a "one-week" staged multivessel PCI. A total of 246 patients only received intervention for the culprit vessel. Follow-up ended on September 9, 2014. This study examined the differences in deaths from any cause (i.e., cardiac and noncardiac) and MACE between the two treatment groups. **Results** Compared to a culprit-only PCI treatment approach, the "one-week" staged multivessel PCI was strongly associated with greater benefits for 55-month all cause death [41 (16.7%) *vs*.13 (6.5%), $P = 0.004$] and MACE [82 (33.3%) *vs*. 40 (19.9%), $P = 0.002$] rates. In addition, there were significant differences in the number of myocardial infarctions [43 (17.5%) *vs*. 20 (10.0%), $P = 0.023$], coronary-artery bypass grafting [CABG; 20 (8.1%) *vs*. 6 (3.0%), $P = 0.021$], and PCI [31 (12.6%) *vs*. 12 (6.0%), $P = 0.018$]. Patients undergoing culprit-only PCI compared to "one-week" PCI had the same number of stent thrombosis events [7 (2.8%) *vs*. 3 (1.5%), $P = 0.522$]. **Conclusions** Compared to a culprit-only PCI treatment approach, "one-week" staged multi-vessel PCI was a safe and effective selection for STEMI and multi-vessel PCI.

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Keywords: ST-segment elevation myocardial infarction; Percutaneous coronary intervention; Multivessel revascularization

1 Introduction

Primary percutaneous coronary intervention (PCI) in acute ST-segment elevation myocardial infarction (STEMI) patients is a primary treatment because it has been shown to reduce the rate of death and major adverse cardiac events (MACE). Many STEMI patients have multivessel disease (MVD). Some researchers have suggested that multivessel coronary artery disease occurs in about 45%–60% of patients presenting with STEMI.[1] Previous studies have demonstrated that MVD in the setting of STEMI is an independent predictor of adverse outcomes.[2] Thus, non-culprit lesions, discovered at the time of STEMI, have been associated with worse long-term outcomes and revascularization of these non-culprit lesions may protect against future events. Recent treatment guidelines recommend infarct-related artery (IRA) revascularization, except for cases with hemodynamic instability, which can be managed with multivessel revascularization.[3] Short- and long-term mortality rates of acute STEMI patients with MVD are higher than those with single-vessel disease.[4-6] Some clinical trial data have indicated that, in patients with acute STEMI and MVD after undergoing infarct artery PCI, preventive PCI in non-infarct coronary arteries with major stenosis significantly reduced the risk of adverse cardiovascular events, as compared with PCI limited to the infarct artery in patients with STEMI and MVD. Whether multivessel intervention during the index primary PCI procedure is safe has been a matter of debate. We retrospectively analyzed deaths and MACE of patients undergoing a staged non-culprit PCI at "one-week" to explore the impact of "one-week" staged multivessel PCI versus culprit-only PCI.

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2 Methods

2.1 Study subjects

We retrospectively analyzed 447 multivessel diseased patients who were residents of the No.1 Hospital of Qinhuangdao (attached to Hebei Medical University) and experienced STEMI within 12 h before undergoing PCI between July 2008 and September 2011. After the completion of PCI in the infarct artery, 201 patients who were still in the hospital agreed to undergo PCI in non-infarct arteries with more than 70% stenosis for "one-week" staged multivessel PCI. A total of 246 patients received only treatment for the culprit vessel (culprit-only PCI). They were deemed to be eligible if the infarct artery had been treated successfully and there was 70% or more stenosis in one or more coronary arteries other than the infarct artery and the stenosis was deemed to be treatable by PCI. Patients were ineligible if they were in cardiogenic shock; had undergone previous coronary-artery bypass grafting (CABG); had only a non-infarct stenosis as a chronic total occlusion; had acute left main coronary artery occlusion; had the left main coronary anterior descending; and had circumflex branches ostial lesions, non-culprit vessel bifurcation lesions or thrombolytic therapy before PCI. Selection of the culprit vessel in similar conditions was evaluated by two operators. All patients gave written informed consent.

2.2 Definitions

The diagnosis of acute myocardial infarction (AMI) was based on clinical presentation, increased levels of cardiac biomarkers (i.e., creatine kinase-MB and troponin-I), and 12-lead electrocardiographic findings. Among these patients, a diagnosis of STEMI was made when an electrocardiogram showed ST-segment elevation of at least 1 mm in two or more contiguous limb leads or 2 mm in precordial leads. The definition of culprit-only PCI is revascularization of only one culprit lesion in multivessel coronary disease during the index hospitalization. The definition of "one-week" staged multivessel PCI is revascularization in patients with acute STEMI and MVD after undergoing infarct artery PCI and staged PCI in non-infarct coronary arteries with major stenosis at one week during the index hospitalization period.

All patients received a loading dose of 100 mg to 300 mg aspirin and 300 mg to 600 mg clopidogrel before PCI. A dose of 50 U/kg to 70 U/kg unfractionated heparin was loaded before or during PCI and additional heparin was administered to patients to maintain their activated clotting time at 250 s to 300 s. After the procedure, 100 mg of aspirin and 75 mg of clopidogrel were prescribed daily. Glycoprotein (GP) IIb/IIIa inhibitors were given to patients by the discretion of the physician. We examined the differences in death from all cause (i.e., cardiac and noncardiac) between the two treatment groups at the 55-month follow-up. Additionally, the following results were analyzed: major adverse cardiac events defined as nonfatal MI requiring hospitalization (excluding peri-procedural MI), death from all cause, and target vessel revascularization. Target vessel revascularization (TVR) was defined as any re-intervention including CABG or PCI to treat a luminal stenosis occurring in the same coronary vessel. The ST-segment resolution rate of < 50% was defined as imperfect ST segment resolution.

2.3 Follow-up

Clinical follow up was performed every three months and then yearly, usually at clinic visits but sometimes during telephone calls with patients. The follow-up period ended on September 30, 2014. The median follow-up was 55 months. At each visit, researchers recorded information including the date of death and MACE (as ensured by hospital records).

2.4 Statistical analysis

Continuous variables are expressed as mean ± SD or as median values and were analyzed with independent sample *t* tests. Nominal variables are presented as percentages and were analyzed with a chi-square test or Fisher's exact test when appropriate. Cox proportional hazards regression was performed to determine the independent predictors of all cause death at 55 months. Results are displayed using Kaplan-Meier plots and were compared with a log-rank test. All analyses were two-tailed and all variables were considered significant if the *P*-value was < 0.05. All statistical analyses were performed using SPSS12.0 (SPSS Inc., Chicago, USA).

3 Results

Of the 1,610 STEMI patients in the cardiac care unit of the No.1 Hospital of Qinhuangdao between July 26, 2008 and September 25, 2011, 447 patients (30.2%) with multivessel CAD underwent PCI of the IRA, while 246 patients underwent only culprit vessel revascularization at the time of primary PCI, and the remainder of patients who were still in the hospital underwent "one-week" staged multivessel PCI. Eighteen patients in the "one-week" staged multivessel PCI group and 15 in the group receiving culprit-only PCI were lost to follow-up. The baseline characteristics of the patients were similar in the two groups (Table 1).

The angiographic and PCI data are shown in Table 2. The number of stents that were implanted in the culprit-only

Table 1. Baseline characteristics.

	Culprit-only PCI (n = 246)	Staged multi-vessel PCI (n = 201)	P Value
Age, yrs	60.6 ± 11.3	61.3 ± 9.6	0.989
Male, n (%)	187 (56.5)	144 (43.5)	0.294
BMI, kg/m^2	29.4 ± 5.4	29.6 ± 4.7	0.718
Smoking history, n (%)	142 (51.8)	132 (48.2)	0.096
Hypertension, n (%)	134 (52.3)	122 (47.7)	0.166
Family history of CHD, n (%)	56 (56.6)	43 (43.4)	0.650
Diabetes mellitus, n (%)	55 (57.3)	41 (42.7)	0.655
History of MI, n (%)	16 (57.1)	12 (42.9)	0.817
History of CHF, n (%)	56 (54.3)	80(45.7)	0.799
SBP, mmHg	122.5 ± 23.7	120.8 ± 27.1	0.464
Cr, μmol/L	88.4 ± 36.5	84.8 ± 31.1	0.273
WBC, 10^9/L	10.8 ± 3.8	10.4 ± 3.1	0.247
Peak CK-MB, mmol/L	1940.5 ± 150.7	2248.3 ± 182.9	0.065
Peak cTnI, ng/mL	28. 9 ± 5.5	36.5 ± 6.9	0.201
TC, mg/dL	108.1 ± 89.9	111.5 ± 98.9	0.702
HDL-C, mg/dL	39.3 ± 8.4	39.8 ± 11.9	0.602
LDL-C, mg/dL	118.0 ± 32.0	116.0 ± 34.0	0.580

Data are presented as mean ± SD or n (%). CHF: Congestive heart failure; CK-MB: creatine kinase-MB; Cr: creatinine; cTnI: cardiac troponin I; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; MI: myocardial infarction; SBP: systolic blood pressure; TC: total cholesterol; WBC: White blood cells.

Table 2. Angiographic data and PCI.

	Culprit-only PCI (n = 246)	Staged multi-vessel PCI (n = 201)	P Value
Infarct-related artery			
Left anterior descending artery	127 (51.6)	111 (55.2)	0.448
Left circumflex artery	35 (14.2)	22 (11.4)	0.420
Right coronary artery	84 (34.1)	66 (32.8)	0.770
Extent of multi-vessel disease			
Two-vessel disease	162 (65.9)	116 (57.7)	0.077
Three-vessel disease	84 (34.1)	85 (42.3)	0.077
Imperfect ST segment resolution	67 (27.2)	52 (26.0)	0.769
Stent number	1.26 ± 0.5	2.24 ± 0.6	0.000
Drug-eluting stent	201 (100)	246 (100)	1.000
Stent type			
Firebird	151 (61.6)	116 (58.0)	0.350
Excel	86 (35.1)	72 (36.0)	
Cypher	8 (3.3)	12 (6)	
Intra-aortic balloon pump	22 (9.0)	11 (5.5)	0.159

Data are presented as mean ± SD or n (%). PCI: percutaneous coronary intervention.

PCI group was small compared to the "one-week" staged multivessel PCI group (1.26 ± 0.5 *vs*. 2.24 ± 0.6, $P < 0.001$). There were no significant differences in the extent of multi-vessel disease, including two-vessel disease [162 (65.9%) *vs*. 116 (57.7%), $P = 0.077$] and three-vessel disease [84 (34.1%) *vs*. 66 (42.3%), $P = 0.077$]. In addition, there were also no differences in the infarct-related artery and imperfect ST-segment resolutions [67 (27.2%) *vs*. 52 (26.0%), $P = 0.769$]. All the patients were implanted with drug-eluting stents [246 (100%) *vs*. 201 (100%), $P = 1.000$].

Table 3 summarizes the MACE and death data through the 55 months of follow-up for both groups. Compared to a culprit-only PCI treatment approach, "one-week" staged multivessel PCI was strongly associated with greater benefits for 55-month all cause death, MI, PCI and CABG. The rate of MACE at 55 months was different between the two groups of patients [82 (33.3%) *vs*. 40 (19.9%), $P = 0.002$]. In addition, there were significant differences for all cause death [41 (16.7%) *vs*. 13 (6.5%)], $P = 0.004$], MI [43 (17.5%) *vs*.20 (10.0%), $P = 0.023$], CABG [20 (8.1%) *vs*. 6 (3.0%), $P = 0.021$] and PCI [31 (12.6%) *vs*. 12 (6.0%), $P = 0.018$]. Patients undergoing culprit-only PCI compared to "one-week" staged multivessel PCI also had the same number of stent thrombosis events [7 (2.8%) *vs*. 3 (1.5%), $P = 0.522$], with more stent thrombosis events within the first month after STEMI.

The Kaplan–Meier analysis showed that the risk reduction of MACE (Figure 1A) and all cause death (Figure 1B) in the "one-week" staged multivessel PCI group was evident within 55 months after the procedure and was maintained thereafter.

4 Discussion

In our study, 447 (30.2%) patients had MVD. Corpus, *et al*.[7] reported that STEMI patients with MVD had higher 1-year rates of adverse cardiac outcomes, compared to those

Table 3. Adverse events at 55-month follow-up.

	Culprit- only PCI (n = 246)	Staged multivessel PCI (n = 201)	P Value
Death, all cause	41 (16.7)	13 (6.5)	0.004
MI	43 (17.5)	20 (10.0)	0.023
Repeated revascularization			
PCI	31 (12.6)	12 (6.0)	0.018
CABG	20 (8.1)	6 (3.0)	0.021
MACE	82 (33.3)	40 (19.9)	0.002
Stent thrombosis	7 (2.8)	3 (1.5)	0.522

Data are presented as n (%). CABG: coronary-artery bypass grafting; MACE: major adverse cardiovascular event; MI: myocardial infarction; PCI: percutaneous coronary intervention.

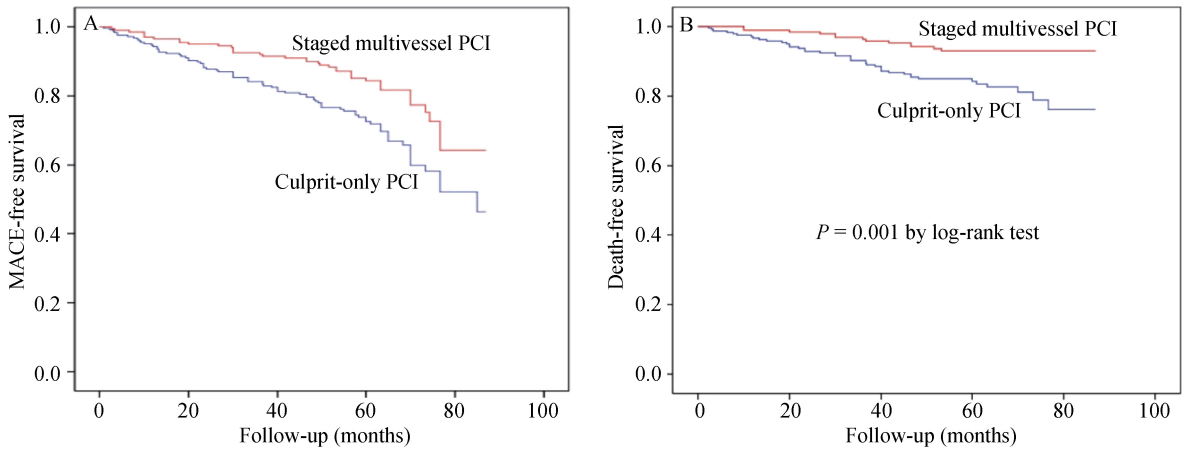

Figure 1. The Kaplan–Meier analysis showed that the risk reduction of MACE (A) and all cause death (B). MACE: major adverse cardiac events; PCI: percutaneous coronary intervention.

with single-vessel disease. However, guidelines recommend only IRA intervention during primary percutaneous coronary intervention (PPCI), except in patients with hemodynamic instability.[8,9] Staged PCI in patients with MVD and with no hemodynamic compromise is an independent predictor of survival, and more frequent ischemic events have been reported in direct versus staged revascularization of STEMI patients with multivessel disease.[10,11]

Recently, the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial[12] indicated that preventive PCI in non-infarct coronary arteries with major stenosis significantly reduced the risk of adverse cardiovascular events, as compared with PCI limited to the infarct artery. In patients with STEMI and multivessel disease, it seems that non-IRA revascularization at the same time as primary PCI maximizes recovery of whole ventricular function by improving myocardial perfusion, thereby producing better clinical outcomes. In addition, Complete Versus Lesion-Only Primary PCI Trial (CVLPRIT) study results showed that patients undergoing multivessel revascularization had lower mortality rates and 12 month MACE incidence rates compared to subjects who had culprit-only PPCI.[13] Qarawani, *et al*.[14] showed that multivessel revascularization during AMI is safe and feasible.

Complete revascularization resulted in an improved acute clinical course. These data support a policy of complete revascularization during primary PCI for STEMI. However, Jeger, *et al*.[15] showed that a strategy of multivessel revascularization should be pursued, notwithstanding the timing of complete revascularization. To avoid the potential risks of simultaneous multivessel PCI, a strategy of staged complete revascularization appears to be the best choice. An analysis of the large-scale, contemporary and prospective international Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial strongly suggested that a deferred angioplasty strategy for non-culprit lesions should remain the standard approach for patients with STEMI and MVD undergoing primary PPCI. Actually, a longer and more complex procedure performed in highly unstable conditions with an extremely prothrombotic and inflammatory milieu could itself increase the risks.[16] In addition, the severity of non-IRA may be more exaggerated than it really is because of vasoconstriction due to increased blood levels of catecholamine, which commonly happens in the setting of AMI.[17] Varani, *et al*.[18] reported that, after exclusion of patients with hemodynamic compromise on admission, no mortality differences were found between the subgroups of MVD patients treated either with acute multivessel PCI or with a staged strategy.

The results of our study showed that "one-week" staged multivessel PCI showed differences in clinical outcomes compared with culprit-only PCI during the 55-month follow-up. There were no significant differences in the extent of MVD, number of infarct-related arteries, and imperfect ST-segment resolution. We limited differences due to selection bias by excluding patients with clinical features that could interfere with indications, timing, and completeness of revascularization. Compared to the culprit-only PCI treatment approach, "one-week" staged multivessel PCI was strongly associated with greater benefits for 55-month all cause death, MI, PCI and CABG. A culprit-only PCI strategy was independently associated with high all cause deaths (HR: 3.119, 95% CI: 1.586–6.135; P = 0.001) and MACE (HR: 1.952, 95% CI: 1.311–2.906; P = 0.001) at 55 months. The analysis of the HORIZONS-AMI trial showed that staged versus single PCI was also an independent predictor for improved MACE at 30 days and one year. Manari, *et*

al.[19] showed that acute multivessel PCI was associated with increased adjusted short-term mortality as compared to staged revascularization. Their findings supported performing culprit-only PPCI in STEMI patients with MVD without hemodynamic compromise, followed by a staged PCI of non-culprit significant lesions. Hannan, *et al*.[20] analyzed 3,521 STEMI patients with a treatment strategy of culprit-only PCI during the index procedure and staged PCI during the index admission. They found that patients underwent staged multivessel revascularization after the index procedure but within 60 days, showed significantly lower mortality rates at the 12-month follow-up. In addition, the same study demonstrated that STEMI patients undergoing complete anatomical revascularization within 60 days of PPCI had lower mortality rates than subjects who had incomplete revascularization. The results of these studies are consistent with our study.

In our study, "one-week" staged multivessel PCI in non-culprit coronary arteries with stenosis > 70% was selected. The degree of stenosis in non-culprit lesions in STEMI was completely different compared to patients with stable coronary artery disease. The "pro-inflammatory environment" can contribute to subsequent adverse events. Actually, in acute coronary syndrome it is known that vulnerable plaque distribution is generally not limited to only culprit lesions, but accounts for acute coronary syndrome and the recurrence of angina pectoris. Therefore, non-culprit lesions may not be stable. Our study supported the current guidelines that recommend consideration of multivessel PCI during STEMI in patients with cardiogenic shock in the presence of multiple, critical stenosis, or highly unstable lesions. Our findings indicated that, for STEMI patients with MVD, "one-week" staged multivessel PCI after the index procedure reduced the rates of death and MACE to comparable results for those with culprit-only PCI. We also paid close attention to the recent studies that have shown "one-time" multivessel revascularization might be safe and beneficial. However, randomized controlled trials between "one-time" multivessel revascularization and "one-week" staged multivessel PCI have not been performed. Further research is needed to answer these questions.

4.1 Limitations

First, our study was a retrospective, non-randomized trial and selection bias may have existed. Second, fractional flow reserve evaluation was not used at the time of the study.[21] Third, the study is not a nationwide registry study, but was based on data from only a single center. Finally, although we conducted our analysis by adjusting all possible confounding factors, however other potential confounding factors were possibly associated with clinical outcomes.

4.2 Conclusions

Compared to a culprit-only PCI treatment approach, "one-week" staged multivessel PCI is a safe and effective selection for STEMI and multivessel coronary artery disease.

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