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Comparison of infarct-related artery *vs* multivessel revascularization in ST-segment elevation myocardial infarction with multivessel disease: Analysis from Korea Acute Myocardial Infarction Registry

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Abstract

Background: *Many ST-segment elevation myocardial infarction (STEMI) patients have multivessel disease. There is still controversy in treatment strategy in STEMI patients with multivessel disease. We compared clinical outcomes of multivessel revascularization with infarct-related artery (IRA) revascularization in STEMI patients.*

Methods: *The 1,644 STEMI patients with multivessel disease (1,106 in IRA group, 538 in multivessel group) who were received primary percutaneous coronary intervention (PCI) were analyzed from a nationwide Korea Acute Myocardial Infarction Registry. Primary endpoint was 12-month major adverse cardiac events (MACE, defined as death, myocardial infarction, and repeated revascularization). Secondary endpoints were 1-month MACE and each component, stent thrombosis during 12 month follow-up, and each components of the 12-month MACE.*

Results: *There were more patients with unfavorable baseline conditions in IRA group. 12-month MACE occurred in 165 (14.9%) patients in IRA group, 81 (15.1%) patients in multivessel group ($p = 0.953$). There were no statistical significance in the rate of 1-month MACE, each components of 1-month MACE, and stent thrombosis during 12 month follow-up. Each components of 12-month MACE were occurred similarly in both groups except for target lesion revascularization (2.4% in IRA group* vs *5.9% in multivessel group, $p < 0.0001$). After adjusting for confounding factors, multivessel revascularization was not associated with reduced 12-month MACE (OR 1.096, 95% CI 0.676–1.775, $p = 0.711$).*

Conclusions: *There were no significant differences in clinical outcomes between both groups except for high risk of target lesion revascularization in multivessel revascularization group.*
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Key words: myocardial infarction, coronary artery disease, percutaneous coronary intervention

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Introduction

About 50% of acute ST-segment elevation myocardial infarction (STEMI) patients have multivessel disease [1, 2]. STEMI patients with multivessel disease are at higher risk of heart failure and cardiogenic shock [1] and associated with two time's higher mortality during hospitalization and long--term follow-up [3, 4]. These patients show higher incidence of acute coronary syndrome and revascularization after initial intervention [5]. Recent guidelines recommend that PCI should not be performed in a non-infarct artery at the time of primary percutaneous coronary intervention (PCI) in patients without hemodynamic compromise [6]. These guidelines are based on experts' opinions, not on randomized controlled trials, which consider safety problems such as complications related to repeated intervention, low technical success rate, high incidence of coronary restenosis, and renal insufficiency following the use of contrast agents [7––9]. Nowadays, thanks to the technical improvements in the coronary intervention field, the introduction of noble drug-eluting stents, and the use of newer anti-platelet agents, active discussions regarding the safety of multivessel revascularization have been undertaken. However, in spite of the improvement of technology and procedural techniques, experts still prefers infarct-related artery (IRA) revascularization over multivessel revascularization. Because many studies consistently showed PCI of a non-infarct artery at the time of primary PCI in stable patients is associated with worse clinical outcomes [10–13]. There are still controversies, so we are still hesitating in deciding the extent of revascularization in acute STEMI setting.

Therefore, we compared the safety and efficacy of multivessel revascularization and IRA revascularization in the setting of primary PCI in Korean patients.

Methods

Study populations

From November 2005 to December 2007, a total of 1,644 patients from the Korea Acute Myocardial Infarction Registry (KAMIR) were enrolled in the present study. KAMIR is a prospective national multicenter observational registry carried out in about 50 tertiary hospitals in charge of primary PCI reflecting current practice of management, risk factors, and clinical outcomes in Korean patients with AMI. Included patients in our study were all diagnosed with STEMI as final diagnosis and they had multivessel coronary disease; coronary lesions of ≥ 50% stenosis in ≥ 2 epicardial coronary arteries, and they received primary PCI. All these patients had 12 month clinical follow up. A total of 1,644 patients were divided into two groups: IRA revascularization group (IRA group, n = 1,106, 67.3%) and multivessel revascularization group (multivessel group, n = 538, 32.7%) (Fig. 1). Mean age was 63.1 ± 11.8 and 73.8% were male. Mean follow up duration was 376.4 ± 62.1 days.

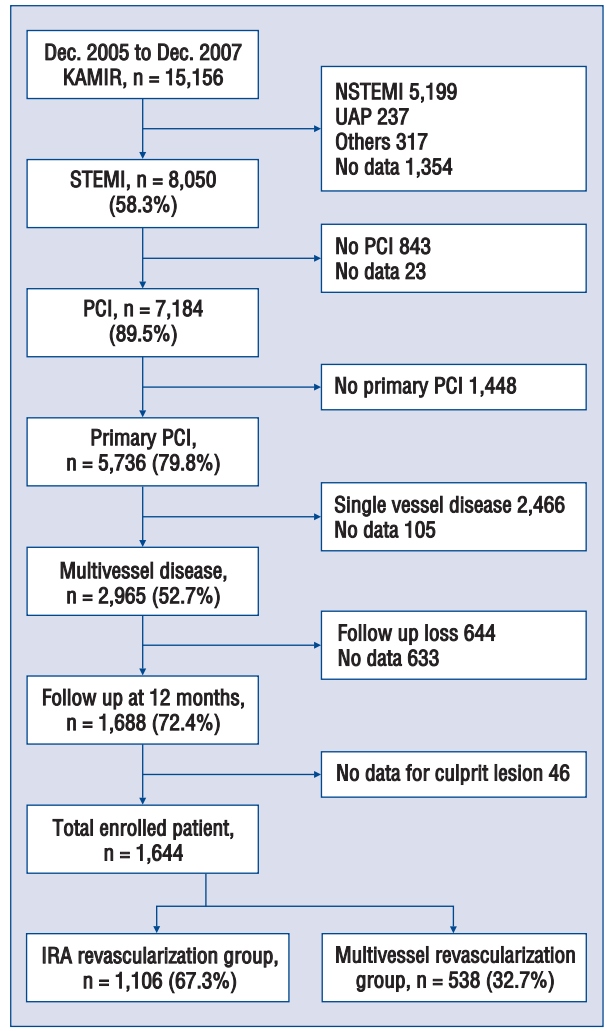

Figure 1. Study algorithm.

The study was approved by the local bioethical committee and all patients gave their informed consent.

Definitions and coronary angiography

The diagnosis of AMI was based on clinical presentations, increased cardiac biomarkers (creatine kinase [CK]-MB, troponin-I or troponin-T), and 12-lead electrocardiographic findings. Among these patients, the diagnosis of STEMI was made

when their electrocardiogram shows ST-segment elevation of at least 1 mm in two or more contiguous limb leads or 2 mm in precordial leads.

The primary PCI was defined when it is performed in patients within 12 h of onset of STEMI. The culprit artery was determined with ECG, echocardiography and angiographic findings by each operator.

The definition of IRA revascularization is revascularization of only one culprit lesion in multivessel coronary disease during the index hospitalization. The definition of multievssel revascularization is revascularization for more than 2 coronary vessels including culprit artery during the index hospitalization periods. Total revascularization is defined as revascularization of whole diseased vessel during the index hospitalization. Left main lesion was more than 50% of diameter stenosis and left main complex lesion was left main lesion plus one or more epicardial coronary artery disease.

A successful PCI was documented by self-reporting of operator in each centers and traditionally accepted when defined to achieve angiographic success without associated in-hospital major clinical outcomes such as death, MI, cerebrovascular event and emergency coronary artery bypass grafting (CABG). Angiographic success was defined as the achievement of residual stenosis less than 50% and at least TIMI flow grade II after the treatment of IRA.

All patients received loading dose of 100 to 300 mg aspirin and 300 to 900 mg clopidogrel before the PCI. A 50 to 70 U/kg of unfractionated heparin was loaded before or during PCI and additional heparin was administered to patients to maintain activated clotting time at 250 to 300 s. After the procedure, 100 mg of aspirin and 75 mg of clopidogrel were prescribed daily. Glycoprotein (GP) IIb/IIIa inhibitor and thrombosuction were used to patients by the discretion of the operator.

Clinical endpoints

Baseline clinical and angiographic characteristics, procedural characteristics, laboratory findings, and medicational data were analyzed. Also, in-hospital complications including in-hospital mortality were analyzed. Primary clinical endpoint is cumulative major adverse cardiac event (MACE) during the 12-month follow up. MACE includes all cause death, myocardial infarction, and repeated revascularization; repeated PCI (re-PCI) and CABG. Re-PCI includes target lesion revascularization (TLR), target vessel revascularization (TVR), and non-target vessel revascularization (non-TVR).

Secondary endpoints are defined as MACE and each component during 1-month follow up, stent thrombosis during 12-month follow up, and each components of MACE during the 12-month follow up.

TLR was defined as re-PCI for restenosis or other complications of lesion which was treated segment from 5mm proximal and 5 mm distal to the stent. TVR was defined as repeated PCI for any segment of entire coronary artery proximal and distal to target lesion except for target lesion.

Statistical analysis

We analyzed data with SPSS ver. 18.0 (Statistical Package for the Social Sciences, SPSS Inc., USA). Continuous variables were demonstrated as mean ± standard deviation or median value. They were analyzed with student t-test. Nominal variables were demonstrated as percentage and analyzed with the χ^2 test or Fisher's exact test when appropriate. To compare cumulative 12 month MACE and event rates between both groups, Cox regression analysis was used. All variables which showed significances in univariate analysis ($p < 0.1$) for endpoints and the other variables that have been reported to be associated with prognosis of patients with AMI were included in adjusting Cox regression models. Included variables were age, gender, previous PCI history, previous hypertension history, initial left ventricular ejection fraction (LVEF) less than 40%, 3 vessel disease, Killip class III/IV, pre-TIMI flow grade 0, post-TIMI flow grade 3, current smoker, stent diameter implanted in the culprit vessel, implanted stent number per patient, successful PCI, defibrillation or cardioversion during the procedure, maximal CK-MB level, initial LDL level, prescription of cilostazol, clopidogrel, beta-blocker, statin, or ARB during the hospitalization, prescription of cilostazol at discharge, and whether carry out follow up coronary angiography or not. All analyses were 2-tailed and all variables were considered significant if p-value was less than 0.05.

Results

Baseline characteristics

Of the total 1,644 patients, 1,106 (67.3%) patients were IRA revascularization group and 538 (32.7%) patients were multivessel revascularization group. Mean age was 63.6 years in the IRA group and 62.1 years in multivessel group ($p = 0.014$). There was no significant difference in the rate of male between the two groups (72.3% *vs* 76.8%, $p = 0.055$). The patients in IRA group were older, more hypertensive, had more previous PCI history, and more previous aminosalicylic acid medication history. Also, at the initial laboratory findings,

the patients in the IRA group had higher peak CK-MB and lower LDL cholesterol level. Almost every patients in the study were administered aspirin and clopidogrel. The prescription rates of beta-blocker, angiotensin receptor blocker (ARB), statin, cilostazol, clopidogrel in hospitalization were higher in the multivessel group (Table 1). However, at the time of discharge, the prescription rates became similar except for cilostazol, which was more highly prescribed in multivessel group. Mean follow up duration was similar in both groups (374.9 *vs* 379.5 days, p = 0.168). Patients who had initial LVEF less than 40% were higher in the IRA group (72.5% *vs* 27.6%, p = 0.048).

Angiographic and procedural characteristics

The angiographic and procedural characteristics were described in the Table 2. In the IRA group, the incidence of 3 vessel disease was lower than multivessel disease (39.0% *vs* 44.4%, p = 0.035). There were more pre TIMI flow 0 patients and less post TIMI 3 patients in the IRA group and they were less treated with stenting and GP IIb/IIIa inhibitors. The number of stents which were implanted in the IRA group was small and the stent diameter was also small in that group. There were no significant differences in IRA, significance of lesion, length of stents implanted in target lesion, and procedural success rate. Almost every patients were implanted with drug-eluting stent (91.3% *vs* 89.0%, p = 0.160). Incidence of follow up angiography at 6–9 months was significantly higher in multivessel group (43.8% *vs* 52.8%, p < 0.0001).

Clinical endpoints

There was no significant difference in primary endpoint, the rate of cumulative MACE during the 12-month follow up [165 patients (14.9%) *vs* 81 patients (15.1%), p = 0.953] (Table 3). As one of our secondary endpoints, rates of each component of 12-month cumulative MACE were also similar between both groups, except for TLR, which showed higher rate in multivessel group (5.9% *vs* 2.4%, p < 0.0001). The rate of stent thrombosis was similar between both groups (0.9% *vs* 2.6%, p = 0.097).

The incidence of in-hospital mortality was similar in both groups (0.5% *vs* 0.4%, p = NS). There were no significant differences in rate of cardiogenic shock needing intra-aortic balloon pump insertion, cerebrovascular accident, new onset heart failure, major bleeding, or acute renal insufficiency between the two groups. But the rate of defibrillation/cardioversion due to ventricular tachycardia or fibrillation was lower in the multivessel group (4.5% *vs* 2.4%, p = 0.037) (Table 4).

The rate of 1 month MACE was also similar between two groups (35 [3.2%] *vs* 14 [2.6%] patients, p = 0.529) and the same for each components (Table 5).

Because there were significant differences in baseline characteristics, clinical status, and complications that occurred during hospitalization between both groups. We adjusted confounding factors such as age, gender, hypertension history, previous PCI history, previous medication history, pre- and post-TIMI flow grade, initial LVEF less than 40%, coronary disease extent, stent diameter, stenting, peak CK-MB and initial LDL cholesterol level, medication during hospitalization and at the time of discharge. Adjusted odds ratio of 12-month MACE calculated from multivariate logistic regression analysis was 1.085 (p = 0.757, 95% CI 0.647–1.817). There were no significant differences in odds ratio for death, MI, re-PCI, TLR, and non-TVR during 12 month follow up. The odds ratio of multivessel revascularization for TVR was 0.249 (95% CI 0.074–0.834, p = 0.024) with statistical significance. Cox regression analysis showed similar results (Table 6, Figs. 2, 3).

Discussion

The main result of our study was that multivessel revascularization showed similar clinical outcomes compared with IRA revascularization during the 12-month follow up. Although this study was an observational registry, it is worthy in that it analyzed a relatively large number of patients without strict exclusion criteria and reflecting recent treatment tendency. Results in this study are comparable with previous studies, so we think that our study qualifies as important evidence-based data.

Primary PCI in acute STEMI patients is a primary target of treatment, as it has reduced the rate of death and MACE. Of these acute STEMI patients, many have multivessel disease, for which recent treatment guidelines recommend IRA revascularization, except for the case of hemodynamic instability, which can be managed with multivessel revascularization [6]. The evidence for the recent guideline is level of C considering experts' opinions that IRA revascularization is better than multivessel revascularization in cost-effectiveness and safety.

Because short- and long-term mortality of acute STEMI patients with multivessel disease are higher than those with single-vessel disease [1, 3, 4], it seems that non-IRA revascularization at the

Table 1. Baseline clinical characteristics.

	Total (n = 1,644)	IRA revascularization (n = 1,106, 67.3%)	Multivessel revascularization (n = 538, 32.7%)	P
Age (years)	63.1±11.8	63.6±12.0	62.1±11.1	0.014
Male	1213 (73.8%)	800 (72.3%)	413 (76.8%)	0.055
Current smoker	747 (45.7%)	484 (44.0%)	263 (49.1%)	0.055
DM	484 (29.8%)	323 (29.6%)	161 (30.3%)	0.769
Hypertension	860 (52.8%)	604 (55.2%)	256 (47.9%)	0.005
Dyslipidemia	143 (9.9%)	103 (10.8%)	40 (8.1%)	0.106
Prev. MI	42 (2.6%)	29 (2.6%)	13 (2.4%)	0.804
Prev. PCI	76 (4.6%)	59 (5.3%)	17 (3.2%)	0.049
Prev. CABG	8 (0.5%)	7 (0.6%0	1 (0.2%)	0.286
Prev. CVA	99 (6.0%)	73 (6.6%)	26 (4.8%)	0.157
Family history of IHD	135 (8.9%)	81 (8.1%)	54 (10.6%)	0.103
Ant. wall in ECG	767 (46.7%)	505 (45.7%)	262 (48.7%)	0.247
Past medication-ASA	168 (10.2%)	133 (12.0%)	35 (6.5%)	0.001
Past medication-statin	81 (4.9%)	60 (5.4%)	21 (3.9%)	0.181
Killip class III/IV:	180 (11.2%)	126 (11.8%)	54 (10.1%)	0.323
I	1193 (74.3%)	782 (72.9%)	411 (77.0%)	0.081
II	232 (14.4%)	163 (15.2%)	69 (12.9%)	
III	91 (5.7%)	60 (5.6%)	31 (5.8%)	
IV	90 (5.6%)	67 (6.3%)	23 (4.3%)	
SBP < 90 mm Hg	112 (6.9%)	82 (7.5%)	30 (5.6%)	0.165
SBP [mm Hg]	126.3 ± 29.1	125.9 ± 29.4	127.3 ± 28.4	0.349
DBP [mm Hg]	78.3 ± 25.2	78.2 ± 28.6	78.5 ± 16.4	0.786
HR [bpm]	75.3 ± 19.5	75.4 ± 19.9	75.1 ± 18.5	0.815
Cr [mg/dL]	1.1 ± 0.9	1.1 ± 0.6	1.1 ± 1.2	0.888
Peak TnI [ng/mL]	63.9 ± 104.2	64.3 ± 100.7	63.1 ± 110.4	0.845
Peak CK-MB	182.7 ± 287.7	197.0 ± 321.0	153.37 ± 199.88	0.001
TC [mg/dL]	184.8 ± 44.0	183.7 ± 44.0	186.9 ± 44.1	0.171
TG [mg/dL]	128.9 ± 106.8	128.4 ± 105.6	129.8 ± 109.2	0.813
HDL-C [mg/dL]	43.7 ± 16.7	43.5 ± 19.0	44.0 ± 10.7	0.596
LDL-C [mg/dL]	118.9 ± 37.6	117.3 ± 36.5	122.1 ± 39.4	0.020
CRP [mg/dL]	0.8 (0.2–4.2)	0.5 (0.2–3.3)	0.5 (0.1–1.6)	0.538
BNP [pg/mL]	80 (17–327)	60.0 (18.0–277.3)	156.5 (26.5–327.8)	0.695
Medications:				
Aspirin	1632 (99.3%)	1095 (99.0%)	537 (99.8%)	0.118
Clopidogrel	1624 (98.8%)	1088 (98.4%)	536 (99.6%)	0.029
Cilostazol	593 (36.1%)	308 (27.8%)	285 (53.0%)	< 0.0001
Beta-blocker	1252 (76.2%)	812 (73.4%)	440 (81.8%)	< 0.0001
ACE-I	1174 (71.4%)	773 (69.9%)	401 (74.5%)	0.051
ARB	224 (13.6%)	137 (12.4%)	76 (16.2%)	0.036
Statin	1256 (76.4%)	816 (76.8%)	440 (81.8%)	< 0.0001
Discharge medication:				
Aspirin	1607 (97.7%)	1081 (97.7%)	526 (97.8%)	0.969
Clopidogrel	1593 (96.9%)	1070 (94.7%)	523 (97.2%)	0.608
Cilostazol	593 (36.1%)	308 (27.8%)	285 (53.0%)	< 0.0001
Beta-blocker	1235 (75.1%)	818 (74.0%)	417 (77.5%)	0.118
ACE-I	1130 (68.7%)	749 (67.7%)	381 (70.8%)	0.204
Statin	1261 (76.7%)	838 (75.8%)	423 (87.6%)	0.199
Follow up duration	374 (356–396)	370.5 (356.0–394.8)	358.5 (329.3–374.5)	0.017

IRA — infarct-related artery; DM — diabetes mellitus; MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary artery bypass graft surgery; CVA — cerebrovascular accident; IHD — ischemic heart disease; ECG — electrocardiogram; ASA — aminosalicylic acid; SBP — systolic blood pressure; DBP — diastolic blood pressure; HR — heart rate; Cr — creatinine; TnI — troponin I; CK-MB — creatine kinase MB; TC — total cholesterol; TG — triglyceride; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol; CRP — C-reactive protein; BNP — B-type natriuretic peptide; ACE-I — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blocker

Table 2. Angiographic and procedural characteristics.

	Total (n = 1,644)	IRA revascularization (n = 1,106, 67.3%)	Multivessel revascularization (n = 538, 32.7%)	P
Disease extent:				
2VD	974 (59.2%)	675 (61.0%)	299 (55.6%)	0.035
3VD	670 (40.8%)	431 (39.0%)	239 (44.4%)	
Successful PCI	1583 (97.0%)	1058 (96.4%)	525 (98.1%)	0.061
Pre-TIMI 0:	903 (56.0%)	636 (58.8%)	267 (50.7%)	0.001
0	903 (56.0%)	636 (58.8%)	267 (50.3%)	0.003
1	140 (8.7%)	84 (7.8%)	56 (10.5%)	
2	241 (15.0%)	160 (14.8%)	81 (15.3%)	
3	328 (20.3%)	201 (18.6%)	127 (23.9%)	
Post-TIMI 3:	1496 (93.2%)	986 (91.8%)	510 (95.9%)	0.002
0	17 (1.1%)	15 (1.4%)	2 (0.4%)	0.009
1	10 (0.6%)	5 (0.5%)	5 (0.9%)	
2	83 (5.2%)	68 (6.3%)	15 (2.8%)	
3	1496 (93.2%)	986 (91.8%)	510 (95.9%)	
Culprit vessel:				
LM	22 (1.3%)	10 (0.9%)	12 (2.2%)	0.384
LAD	716 (43.6%)	488 (44.2%)	228 (42.4%)	
LCX	188 (11.4%)	112 (10.1%)	76 (14.1%)	
RCA	717 (43.6%)	495 (44.8%)	222 (41.3%)	
Type B2/C:	1277 (81.3%)	858 (82.3%)	419 (79.5%)	0.186
A	49 (3.1%)	31 (3.0%)	18 (3.4%)	0.006
B1	244 (15.5%)	154 (14.8%)	90 (17.1%)	
B2	414 (26.4%)	252 (24.2%)	162 (30.7%)	
C	863 (55.0%)	606 (58.1%)	257 (48.8%)	
Total revascularization	396 (24.1%)	0	396 (73.6%)	< 0.0001
PCI with stent:	1570 (95.9%)	1047 (95.1%)	523 (97.6%)	0.018
BMS	147 (9.5%)	90 (8.7%)	57 (11.0%)	0.160
DES	1402 (90.5%)	939 (91.3%)	463 (89.0%)	
Stent number/pt.	1.7 ± 0.9	1.4 ± 0.6	2.4 ± 1.0	< 0.0001
Stent length of IRA/pt. [mm]	25.6 ± 6.4	25.8 ± 6.4	25.4 ± 6.2	0.325
Stent diameter of IRA [mm]	3.19 ± 0.42	3.17 ± 0.43	3.23 ± 0.40	0.018
GP IIb/IIIa inhibitor	187 (27.8%)	102 (22.9%)	85 (37.6%)	< 0.0001
Initial LVEF < 40%	214/1535 (13.4%)	155/1021 (72.45)	59/514 (27.6%)	0.048
Follow-up coronary angiography	763 (46.7%)	481 (43.8%)	282 (52.8%)	< 0.001
Complications	248 (15.2%)	174 (15.9%)	74 (13.8%)	0.258
Days in CCU	3.4 ± 3.0	3.5 ± 3.29	3.38 ± 2.44	0.598

IRA — infarct related artery; VD — vessel disease; PCI — percutaneous coronary intervention; TIMI — thrombolysis in myocardial infarction; LM — left main; LAD — left anterior descending artery; LCX — left circumflex artery; RCA — right coronary artery; BMS — bare metal stent; DES — drug-eluting stent; GP IIb/IIIa inhibitor — glycoprotein IIb/IIIa inhibitor; LVEF — left ventricular ejection fraction; CCU — coronary care unit

same time as primary PCI would maximize recovery of whole ventricular function by improving myocardial perfusion, thereby producing better clinical outcomes. Actually, it is known that vulnerable plaque distribution is generally not limited only to IRA in acute coronary syndrome, accounting for the recurrence of angina pectoris, acute coronary syndrome, and need for re-PCI of non-IRA [5, 14]. This supposition is supported by the fact that the introduction of drug-eluting stents has reduced restenosis of lesions and need for re-PCI [15], and by the fact that clinical results of multivessel revascularization have been improved with these technical development and use of a variety of GP IIb/IIIa inhibitors [16–18].

Table 3. Twelve month cumulative major adverse cardiac events and stent thrombosis.

	Total (n = 1,644)	IRA revascularization (n = 1,106, 67.3%)	Multivessel revascularization (n = 538, 32.7%)	P
12-month MACE	246 (15.0%)	165 (14.9%)	81 (15.1%)	0.953
Death	34 (2.1%)	25 (2.3%)	9 (1.7%)	0.429
Cardiac death	23 (1.4%)	15 (1.4%)	8 (1.5%)	0.836
Non-cardiac death	11 (0.7%)	10 (0.9%)	1 (0.2%)	0.115
MI	11 (0.7%)	7 (0.6%)	4 (0.7%)	0.799
Repeated PCI	195 (11.9%)	129 (11.7%)	66 (12.3%)	0.732
TLR	59 (3.6%)	27 (2.4%)	32 (5.9%)	< 0.0001
TVR	27 (1.6%)	21 (1.9%)	6 (1.1%)	0.239
Non-TVR	109 (6.6%)	81 (7.3%)	28 (5.2%)	0.103
CABG	6 (0.4%)	4 (0.4%)	2 (0.4%)	0.976
Stent thrombosis	10 (1.5%)	4 (0.9%)	6 (2.6%)	0.097

MACE — major adverse cardiovascular event; MI — myocardial infarction; PCI — percutaneous coronary intervention; TLR — target lesion revascularization; TVR — target vessel revascularization; non-TVR — non-target vessel revascularization; CABG — coronary artery bypass graft; NS — non-specific

Table 4. In-hospital outcomes.

	Total (n = 1,644)	IRA revascularization (n = 1,106, 67.3%)	Multivessel revascularization (n = 538, 32.7%)	P
In-hospital mortality:	8 (0.5%)	6 (0.5%)	2 (0.4%)	NS
Cardiac	8	6	2	NS
Non-cardiac	0	0	0	NS
Complications:	248 (15.2%)	174 (15.9%)	74 (13.8%)	0.258
IABP	78 (4.7%)	51 (4.6%)	27 (5.0%)	0.715
CVA	7 (0.4%)	7 (0.6%)	0	0.104
Acute renal failure	4 (0.2%)	3 (0.3%)	1 (0.2%)	NS
Defib/cardioversion due to VT or VFib	63 (3.8%)	50 (4.5%)	13 (2.4%)	0.037
Major bleeding	3 (0.2%)	2 (0.2%)	1 (0.2%)	NS
New onset HF	11 (0.7%)	10 (0.9%)	1 (0.2%)	0.115

IRA — infarct related artery; IABP — intra-aortic balloon pump; CVA — cerebrovascular accident; Defib — defibrillation; VT — ventricular tachycardia; VFib — ventricular fibrillation; HF — heart failure

Table 5. One month major adverse cardiac events.

	Total (n = 1,644)	IRA revascularization (n = 1,106, 67.3%)	Multivessel revascularization (n = 538, 32.7%)	P
One-month MACE	49 (3.0%)	35 (3.2%)	14 (2.6%)	0.529
Death	12 (0.7%)	7 (0.6%)	5 (0.9%)	0.543
Cardiac death	12 (0.7%)	7 (0.6%)	5 (0.9%)	0.543
Non-cardiac death	0	0	0	0
MI	7 (0.4%)	4 (0.4%)	3 (0.6%)	0.689
Repeated PCI	26 (1.6%)	22 (2.0%)	4 (0.7%)	0.057
TLR	2 (0.1%)	1 (0.1%)	1 (0.2%)	0.548
TVR	1 (0.1%)	1 (0.1%)	0	NS
TLR/TVR	3 (0.2%)	2 (0.2%)	1 (0.2%)	NS
Non-TVR	22 (1.3%)	19 (1.7%)	3 (0.6%)	0.066
CABG	2 (0.1%)	0	2 (0.4%)	0.107

MACE — major adverse cardiovascular event; MI — myocardial infarction; PCI — percutaneous coronary intervention; TLR — target lesion revascularization; TVR — target vessel revascularization; non-TVR — non-target vessel revascularization; CABG — coronary artery bypass graft; NS — non-specific

Table 6. Odds ratio (OR) for 12 month clinical outcomes with multivessel revascularization.

12 month clinical outcomes	Unadjusted OR (95% confidence interval)	P	Adjusted OR (95% confidence interval)	P
Death	0.734 (0.340–1.584)	0.431	1.198 (0.333–4.317)	0.782
MI	1.174 (0.342–4.027)	0.799	1.474 (0.400–5.433)	0.560
Re-PCI	1.057 (0.770–1.450)	0.732	1.025 (0.716–1.468)	0.892
TLR	2.253 (1.495–4.256)	0.001	1.903 (0.728–4.974)	0.189
TVR	0.582 (0.230–1.450)	0.245	0.249 (0.074–0.834)	0.024
Non-TVR	0.693 (0.445–1.079)	0.105	1.144 (0.563–2.328)	0.710
CABG	1.026 (0.187–5.620)	0.976	–	–
12 month MACE	1.009 (0.756–1.346)	0.953	1.085 (0.647–1.817)	0.757

MI — myocardial infarction; PCI — percutaneous coronary intervention; TLR — target lesion revascularization; TVR — target vessel revascularization; non-TVR — non-target vessel revascularization; CABG — coronary artery bypass graft; MACE — major adverse cardiovascular event

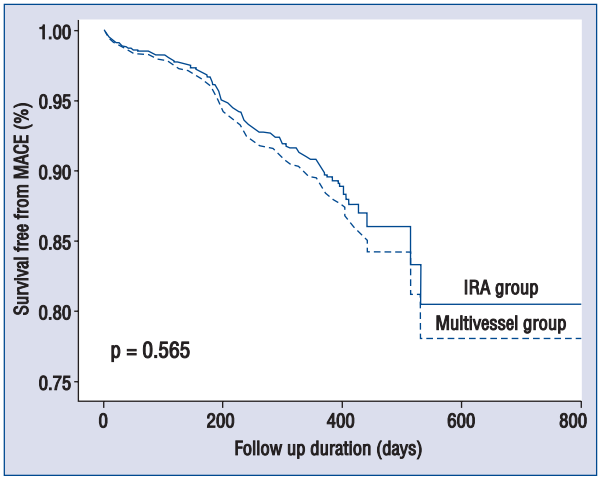

Figure 2. Twelve month survival free from major adverse cardiovascular event (MACE) in multivessel and infarct-related artery (IRA) revascularization groups.

On the other hand, the severity of non-target lesion might be more exaggerated than it really is because of vasoconstriction due to increased blood level of catecholamine, which commonly happens in the setting of acute myocardial infarction [19]. And it can be a more severe problem, especially when lesion severity is measured by bare eyesight and not by quantitative coronary angiographic methods. One randomized controlled trial compared procedures according to bare eyesight and fractional flow reserve (FFR), and it revealed that more procedures were done and the rates of MACE were higher in patients whose procedures were guided by bare eyesight than by FFR [20]. Therefore, it can also be said that IRA revascularization might be a suitable option due to the risk of overestimation of intermediate coronary lesions such a hypercoagulable status, as in acute coronary syndrome.

Previous studies have represented a variety of conclusions: some reported that IRA revascularization is better [8, 21], some reported that both strategies are similar in clinical outcomes [22–23], and some concluded that multivessel revascularization is more beneficial than IRA revascularization [24––26]. Even recently, two meta-analyses reported different conclusions. A meta-analysis by Navarese et al. [27] that included two RCTs and eight non-randomized controlled trials not considering staged revascularization showed results that multivessel revascularization reduced re-PCI, but did not reduce death or myocardial infarction. Another meta-analysis by Sethi et al. [28] that included two RCTs and nine non-randomized controlled trials reported that there were no significant differences in rates of MACE or long-term mortality between the two strategies, but it excluded all cardiogenic shock patients.

Because our study is a multicenter observational registry with no strict inclusion and exclusion criteria, selection bias might be inherent. Actually, there were more unfavorable factors in the IRA group compared with multivessel group. There were more patients with hypertension and previous PCI history, as well as older patients and more women in the IRA revascularization group. Patients in the IRA revascularization group had higher rate of pre-TIMI 0 flow initially, and lower rate of post-TIMI 3 flow grade. They used less GP IIb/IIIa inhibitors and had lower LVEF initially. This might be presumed to be because the operators chose IRA revascularization for patients who arrived with unfavorable clinical and angiographic conditions to minimize procedure time and procedure-related complications including reperfusion arrhythmia. However, after adjusting all of these confounding factors, there was no statistical significance in

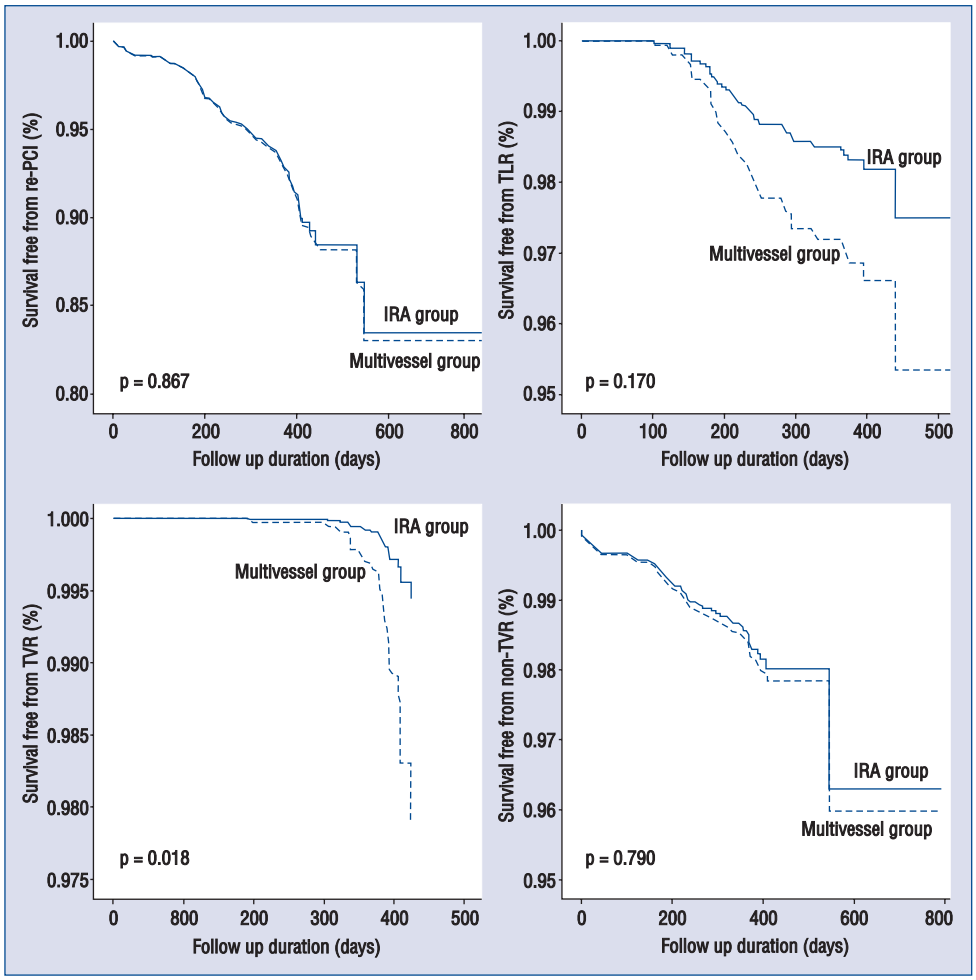

Figure 3. Twelve month survival free from re-percutaneous coronary intervention (PCI), target lesion revascularization (TLR), target vessel revascularization (TVR), and non-TVR in multivessel and infarct-related artery (IRA) revascularization groups.

12 month MACE. These results reflect that recent technical improvement and the aid of adjuvant medical treatment augmented the benefits of multivessel revascularization in this study.

More recently, there were many studies comparing the effects of staged PCI with IRA and multivessel revascularization. An analysis from HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trial by Kornowski et al. [13] compared one time multivessel PCI *vs* staged PCI and resulted that multivessel PCI might be associated with hazard for mortality and stent thrombosis. Hannan et al. [29] analyzed 3,521 STEMI patients as treatment strategy of culprit vessel PCI during the index procedure, staged PCI during the index admission, and staged PCI after the index procedure but within 60 days with propensity matching analysis. The results showed that there were no statistical differences in clinical outcomes between culprit vessel PCI during the index procedure group and staged PCI during the index admission. And patients underwent staged multivessel revascularization after the index procedure but within 60 days showed significantly lower mortality rates at 12 month follow up. That study supports the recent guidelines and suggests staged PCI after the index procedure. In addition to that, recently a meta-analysis including Hannan's study by Vlaar et al. [12] revealed that multivessel revascularization at the index procedure should be deferred and PCI for the significant non-culprit lesion should be done at planned staged procedures.

In this study, we could not classify multivessel revascularization at the index procedure and staged PCI at the index hospitalization. Also, there exists the possibility that staged PCI after the index hospitalization might be counted as non-TVR.

So, the incidence of non-TVR in the IRA group might be over-estimated. That's why there was no benefit of reducing non-TVR in the multivessel group in this study. Although multivessel revascularization group includes staged PCI during the index admission in this study, on the assumption that the effect of staged PCI during the index admission is equal to that of IRA revascularization, our results presents that multivessel revascularization might be equally safe and beneficial compared with IRA revascularization. Because in-hospital outcomes in this study show that there are no significant differences in total complications, acute renal failure, major bleeding, etc. On the contrary, there was more defibrillation/cardioversion due to ventricular tachycardia or ventricular fibrillation. An analysis of effect of multivessel over IRA revascularization in NSTEMI patients by Kim et al. [30] from KAMIR registry, which was conducted in our country as same procedural environment with this study presented that the beneficial effect of multivessel revascularization. In the acute myocardial infarction setting including STEMI and NSTEMI, to know what is the exact culprit artery is very challenging thing. Sometimes suboptimal results after PCI comes from not only complications related to procedures but also from such a confusing situations not knowing the exact culprit artery. So we think that with aid of functional examination of culprit artery and technical, medicational improvements in the procedural field, complications and limitations of multivessel revascularization would be overwhelmed.

Regarding limitations of our study, first there is selection bias because of the characteristics of our study. Second, as our study was based on observational registry, technical aspects and criteria of clinical outcomes were not standardized, especially in determining IRA. Third, we did not consider staged revascularization due to limitation of data.

Conclusions

Summarizing the results of our study, there were no significant differences between IRA revascularization and multivessel revascularization in the rates of 12-month MACE, and each components except for high rate of TVR in the multivessel group. Also, there were no statistical differences in in-hospital mortality and composite of complications, 1-month MACE and each component. Our conclusion is that our results support current guidelines that recommend IRA revascularization in hemodynamic stable STEMI patients in the setting of primary PCI. In addition to that, we cautiously suggest that multivessel revascularization might be equally safe and beneficial compared with IRA revascularization especially done by experienced interventional cardiologist and in the case of multiple culprit lesion is suspected.

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References

1. Muller DW, Topol EJ, Ellis SG, Sigmon KN, Lee K, Califf RM. Multivessel coronary artery disease: a key predictor of short-term prognosis after reperfusion therapy for acute myocardial infarction (TAMI) Study Group. Am Heart J, 1991; 121: 1042–1049.
2. Jaski BE, Cohen JD, Trausch J et al. Outcome of urgent percutaneous transluminal coronary angioplasty in acute myocardial infarction: Comparison of single-vessel versus multivessel coronary artery disease. Am Heart J, 1992; 124: 1427–1433.
3. Sorajja P, Gersh BJ, Cox DA et al. Impact of multivessel disease on reperfusion success and clinical outcomes in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. Eur Heart J, 2007; 28: 1709–1716.
4. Parodi G, Memisha G, Valenti R et al. Five year outcome after primary coronary intervention for acute ST elevation myocardial infarction: Results from a single centre experience. Heart, 2005; 91: 1541–1544.
5. Goldstein JA, Demetriou D, Grines CL, Pica M, Shoukfeh M, O'Neill WW. Multiple complex coronary plaques in patients with acute myocardial infarction. N Engl J Med, 2000; 343: 915–922.
6. Kushner FG, Hand M, Smith SC Jr. et al. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update). A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol, 2009; 54: 2205–2241.

7. Shishehbor MH, Topol EJ, Mukherjee D et al.; TARGET Investigators. Outcome of multivessel coronary intervention in the contemporary percutaneous revascularization era. Am J Cardiol, 2006; 97: 1585–1590.
8. Ijsselmuiden AJ, Ezechiels J, Westendorp IC et al. Complete versus culprit vessel percutaneous coronary intervention in multivessel disease: A randomized comparison. Am Heart J, 2004; 148: 467–474.
9. Marenzi G, Assanelli E, Campodonico J et al. Contrast volume during primary percutaneous coronary intervention and subsequent contrast-induced nephropathy and mortality. Ann Intern Med, 2009; 150: 170–177.
10. Toma M, Buller CE, Westerhout CM et al.; APEX-AMI Investigators. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: Insights from the APEX-AMI trial. Eur Heart J, 2010; 31: 1701–1707.
11. Politi L, Sgura F, Rossi R et al. Multivessel coronary disease in ST-elevation myocardial infarction: three different revascularization strategies and long-term outcomes. Heart, 2010; 96: 662–667.
12. Vlaar PJ, Mahmoud KD, Holmes DR Jr. et al. Culprit vessel only versus multivessel and staged percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction. J Am Coll Cardiol, 2011; 58: 692–703.
13. Kornowski R, Mehran R, Dangas G, et al.; HORIZONS-AMI Trial Investigators. Prognostic impact of staged versus "one--time" multivessel percutaneous intervention in acute myocardial infarction. J Am Coll Cardiol, 2011; 58: 704–711.
14. Ambrose JA. In search of the "vulnerable plaque": Can it be localized and will focal regional therapy ever be an option for cardiac prevention? J Am Coll Cardiol, 2008; 51: 1539–1542.
15. Kukreja N, Onuma Y, Garcia-Garcia HM et al.; Interventional Cardioglogist of the Thorax-center(2000–2005). Three-year survival following multivessel percutaneous coronary intervention with bare-metal or drug-eluting stents in unselected patients. Am J Cardiol, 2009; 103: 203–211.
16. De Luca G, Suryapranata H, Stone GW et al. Abciximab as adjunctive therapy to reperfusion in acute ST-segment elevation myocardial infarction: a meta-analysis of randomized trials. JAMA, 2005; 293: 1759–1765.
17. De Luca G, Suryapranata H, Stone GW et al. Coronary stenting versus balloon angioplasty for acute myocardial infarction: A meta-regression analysis of randomized trials. Int J Cardiol, 2008; 126: 37–44.
18. De Luca G, Gibson CM, Bellandi F et al. Early glycoprotein IIb-IIIa inhibitors in primary angioplasty(EGYPT) cooperation: An individual patient data meta-analysis. Heart, 2008; 94: 1548––1558.
19. Hanratty CG, Koyama Y, Rasmussen HH, Nelson GI, Hansen PS, Ward MR. Exaggeration of nonculprit stenosis severity during acute myocardial infarction: Implications for immediate multivessel revascularization. J Am Coll Cardiol, 2002; 40: 911–916.
20. Tonino PA, De Bruyne B, Pijls NH et al.; FAME Study Investigators. Fractional flow reserve versus angioplasty for guiding percutaneous coronary intervention. N Engl J Med, 2009; 360: 213–224.
21. Roe MT, Cura FA, Joski PS et al. Initial experience with multivessel coronary intervention during mechanical reperfusion for acute myocardial infarction. Am J Cardiol, 2001; 88: 170––173.
22. Di Mario C, Mara S, Flavio A et al. Single vs. multivessel treatment during primary angioplasty: results of the multicentre randomized HEpacoat for culprit or multivessel stenting for Acute Myocardial Infarction (HELP AMI) study. Int J Cardiovasc Int, 2004; 6: 128–133.
23. Chen LY, Lennon RJ, Grantham JA et al. In-hospital and long--term outcomes of multivessel percutaneous coronary revascularization after acute myocardial infarction. Am J Cardiol, 2005; 95: 349–354.
24. Qarawani D, Nahir M, Abbound M, Hazanov Y, Hasin Y. Culprit only versus complete coronary revascularization during primary PCI. Int J Cardiol, 2008; 123: 288–292.
25. Brener SJ, Milford-Beland S, Roe MT, Bhatt DL, Weintraub WS, Brindis RG. Culprit-only or multivessel revascularization in patients with acute coronary syndromes: an American College of Cardiology National Cardiovascular Database Registry report. Am Heart J, 2008; 155: 140–146.
26. Kong JA, Chou ET, Minutello RM, Wong SC, Hong MK. Safety of single versus multi-vessel angioplasty for patients with acute myocardial infarction and multi-vessel coronary artery disease: Report from the New York State Angioplasty Registry. Coron Artery Dis, 2006; 17: 71–75.
27. Navarese EP, De Servi S, Buffon A, Suryapranata H, De Luca G. Clinical impact of simultaneous complete revascularization vs. culprit only primary angioplasty in patients with ST-elevation myocardial infarction and multivessel disease: A meta-analysis. J Thromb Thrombolysis, 2011; 31: 217–225.
28. Sethi A, Bahekar A, Bhuriya R, Singh S, Ahmed A, Khosla S. Complete versus culprit only revascularization in acute ST elevation myocardial infarction: A meta-analysis. Catheter Cardiovasc Interv, 2011; 77: 163–170.
29. Hannan EL, Samadashvili Z, Walford G et al. Culprit vessel percutaneous coronary intervention versus multivessel and staged percutaneous coronary intervention for ST-segment elevation myocardial infarction patients with multivessel disease. J Am Coll Cardiol Cardiovasc Interv, 2010; 3: 22–31.
30. Kim MC, Jeong MH, Ahn Y et al. What is optimal revascularization strategy in patients with multivessel coronary artery disease in non-ST-elevation myocardial infarction? Multivessel or culprit-only revascularization. Int J Cardiol, 2011; 153: 148–153.