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Editorial

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Can Local Treatment Alter the Prognosis of Acute Myocardial Infarction Patients With Multivessel Disease and Diabetes?

Seung Hun Lee, MD, PhD[1], and Chang-Wook Nam, MD, PhD[2]

[1]Division of Cardiology, Department of Internal Medicine, Chonnam National University Hospital, Chonnam National University Medical School, Gwangju, Korea
[2]Division of Cardiology, Department of Internal Medicine, Cardiovascular Center, Keimyung University Dongsan Hospital, Daegu, Korea

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Correspondence to
Chang-Wook Nam, MD, PhD
Division of Cardiology, Department of Internal Medicine, Cardiovascular Center, Keimyung University Dongsan Hospital, 1035, Dalgubeol-daero, Dalseo-gu, Daegu 42601, Korea.
Email: ncwcv@dsmc.or.kr

ORCID iDs
Seung Hun Lee
https://orcid.org/0000-0002-2337-7826
Chang-Wook Nam
https://orcid.org/0000-0002-3370-5774

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In patients with acute myocardial infarction (AMI), percutaneous coronary intervention (PCI) for an infarct-related artery (IRA) is necessary to restore coronary blood flow. Approximately half of AMI patients have a concomitant multivessel disease (MVD) and a poor prognosis than others. For patients with MVD, the remaining issue is whether to revascularize the non-IRAs after successful PCI for IRA. A decade ago, the 2013 American guideline recommended the selective PCI for non-IRAs, in the case of patients had symptoms of myocardial ischemia (*Class I*, *Level of Evidence: C*) or abnormality on non-invasive testing (*Class IIa*, *Level of Evidence: B*). In the last decade, the clinical benefits of angiography- or physiology-guided complete revascularization (CR) compared with culprit-only (termed incomplete revascularization, IR) PCI for AMI patients with MVD were repeatedly evaluated in the landmark randomized clinical trials PRAMI, CvLPRIT, DANAMI-3-PRIMULTI, COMPARE-ACUTE, and COMPLETE (**Table 1**).[1-7] In addition, results of the FRAME-AMI study provided evidence that physiology-guided CR might be more beneficial for reducing clinical events than angiography-guided CR at a median follow-up of 3.5 years (physiology-guided CR 7.4% vs. angiography-guided CR 19.7%; hazard ratio [HR], 0.43; 95% confidence interval [CI], 0.25–075; p=0.003).[8] Based on these data, the latest 2023 European guideline endorsed CR as Class I (*Level of Evidence: A*) for ST-segment elevation AMI and Class IIa (*Level of Evidence: C*) for non-ST-segment elevation AMI. This conclusion left other issues such as angiography versus physiology-guided CR and immediate *versus* staged CR as the main issues in AMI patients with MVD.

Recently, new data have emerged for evaluating the clinical benefits of CR for patients with AMI and MVD (**Table 1**). In the FIRE trial, physiology-guided CR was compared with culprit-only PCI for 1,445 older patients (≥75 years) with AMI and MVD. CR reduced the primary outcome, a composite of death, MI, stroke, or ischemia-driven revascularization, compared to culprit-only PCI at 1-year follow-up (CR 15.7% vs. culprit-only 21.0%; HR, 0.73; 95% CI, 0.57–0.93; p=0.01).[6] On the other hand, the FULL REVASC trial showed negative results of physiology-guided CR compared with culprit-only PCI.[7] Among 1,542 patients with AMI and MVD, fractional flow reserve-guided CR was not significantly different from culprit-only PCI in terms of reducing adverse events, a composite of death, MI, or unplanned revascularization (CR 19.0% vs. culprit-only 20.4%; HR, 0.93; 95% CI, 0.74–1.17; p=0.53). Although the study population and methodology were somewhat different, the results were

Table 1. Summary of major clinical trials comparing the complete versus culprit-only revascularization for AMI with multivessel disease

Study (year)	Study population	Intervention	Primary end point	Follow-up duration (years)	Main findings
PRAMI (2013)[1]	465 STEMI	Angiography-guided CR vs. culprit-only PCI	Cardiac death, non-fatal MI, and refractory angina	2 (median)	9% vs. 23% (HR, 0.35; 95% CI, 0.21–0.58; p<0.001)
CvLPRIT (2015)[2]	296 STEMI	Angiography-guided CR vs. culprit-only PCI	All-cause death, recurrent MI, HF, and ischemia-driven revascularization	1	10% vs. 21.2% (HR, 0.45; 95% CI, 0.24–0.84; p=0.009)
DAMANI-3-PRIMULTI(2015)[3]	627 STEMI	FFR-guided CR vs. culprit-only PCI	All-cause death, non-fatal MI, and ischemia-driven revascularization	2 (median)	13% vs. 22% (HR, 0.56; 95% CI, 0.38–0.83; p=0.004)
COMPARE-ACUTE (2017)[4]	885 STEMI	FFR-guided CR vs. culprit-only PCI	All-cause death, non-fatal MI, revascularization, and cerebrovascular events	1	7.8% vs. 20.5% (HR, 0.35; 95% CI, 0.22–0.55; p<0.001)
COMPLETE (2019)[5]	4,041 STEMI	Angiography-guided CR vs. culprit-only PCI	1. Cardiac death or MI	3 (median)	1. 7.8% vs. 10.5% (HR, 0.74; 95% CI, 0.60–0.91; p=0.004)
			2. Cardiac death, MI, or ischemia-driven revascularization		2. 8.9% vs. 16.7% (HR, 0.51; 95% CI, 0.43–0.61; p<0.001)
FIRE (2023)[6]	1,445 STEMI (≥75 years)	Physiology-guided CR vs. culprit-only PCI	All-cause death, MI, stroke, or ischemia-driven revascularization	1	15.7% vs. 21.0% (HR, 0.73; 95% CI, 0.57–0.93; p=0.01)
FULL REVASC (2024)[7]	1,542 STEMI or very-high-risk NSTEMI	FFR-guided CR vs. culprit-only PCI	All-cause death, MI, or unplanned revascularization	4.8 (median)	19.0% vs. 20.4% (HR, 0.93; 95% CI, 0.74–1.17; p=0.53)

CI = confidence interval; CR = complete revascularization; FFR = fractional flow reserve; HR = hazard ratio; MI = myocardial infarction; NSTEMI = non-ST segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions

Writing - original draft: Nam CW, Lee SH; Writing - review & editing: Nam CW.

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contradictory. Whether these 2 discrepant results will again become a controversy for CR remains unknown?

In this issue of the *Korean Circulation Journal*, Kang et al.[9] analyzed tremendous data regarding the dedicated drug-eluting stents registry and reported the clinical effects of CR in diabetic AMI patients with MVD. The authors selected 2,150 AMI patients and classified the study population based on CR versus IR and the presence of diabetes. Notably, CR significantly reduced 3-year adverse events only in the non-diabetic AMI patients (CR 11.7% vs. IR 23.2%; adjusted HR, 0.52; 95% CI, 0.36–0.75), but not in diabetic AMI patients (CR 24.3% vs. IR 27.8%; adjusted HR, 0.86; 95% CI, 0.60–1.25). The target lesion failure (TLF), a composite of cardiac death, target vessel-related MI, and target lesion revascularization, for CR was comparable to that of IR among diabetic patients (CR 13.0% vs. 16.1%; adjusted HR, 0.88; 95% CI, 0.54–1.44). Conversely, CR was associated with a decreased risk of TLF compared with IR in non-diabetic patients (CR 5.3% vs. IR 10.4%; adjusted HR, 0.40; 95% CI, 0.23–0.70). The authors explained the differing prognostic effects of CR to be based on the presence of diabetes and the problems originating from more frequent stenting in the CR group. Because the stent is a local treatment and leaving metal in the vessel is an ongoing problem, local treatment cannot alleviate diffuse atherosclerosis in diabetic patients.

The present investigators are congratulated for providing valuable data highlighting the importance of underlying co-morbidity. However, some of the results should be interpreted with caution and future studies are warranted. First, as the authors pointed out, this study was a retrospective analysis of patient-pooled level data from multiple drug-eluting stents registries. Therefore, an inherent risk of selection bias and unintentional confounders existed. Although the authors adjusted for confounders with various statistical methods, the limitation of the current analysis was evident, and the findings could not be clearly concluded. Furthermore, because the patients were not randomized to CR or IR, the reason for IR might be heterogeneous. For example, some lesions were not optimal candidates for PCI or operator preferences were not for CR during the acute phase. Second, given that the study period was a decade ago, a significant difference should have been observed

compared with contemporary practice for diabetes and AMI, including medical treatment such as potent $P2Y_{12}$ inhibitors or sodium-glucose cotransporter-2 inhibitors, PCI strategy, and devices. Third, we already know that the previous concept of angiographical CR was not sufficient for post-PCI optimization based on intravascular imaging or functional CR using physiologic assessment.[8)10-12)] Furthermore, a recent sub-study of RENOVATE-COMPLEX-PCI emphasized the clinical benefits of intravascular imaging-optimized stent implantation for the patients with acute coronary syndrome (optimized 6.5% vs. unoptimized 14.1%; HR, 0.49; 95% CI, 0.27–0.87; p=0.02).[12)] Fourth, the majority of the study population presented with non-ST segment elevation AMI (approximately 56%). In the aforementioned clinical trials, the focus was on ST-segment elevation AMI, and randomized studies for non-ST segment elevation AMI are scarce. Although the sub-study of the COMPLETE trial showed consistent positive results of CR irrespective of diabetic status,[5)] future studies should validate the results of the present study.

In summary, the clinical benefit of CR for AMI with MVD might differ depending on the presence of diabetes. The main goal of disease treatment is to heal the myocardium and not just vessels. Finally, because stenting is only a "local" treatment, the necessity of this procedure for diabetic non-IRA lesions should be cautiously considered.

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