Early reperfusion of the occluded infarct-related artery (IRA) using primary percutaneous coronary intervention (PCI) has been the primary goal of treatment for patients with acute ST-segment elevation myocardial infarction (STEMI). 1 Concomitant atherosclerosis in coronary arteries other than the IRA has been reported to be observed in 40–50% of patients with acute MI (AMI). 2 In addition, STEMI patients with multivessel disease (MVD) are at increased risk of major adverse cardiac events following primary PCI. 3 Although most interventional cardiologists believe that complete revascularization of ischemia-producing nonculprit obstructions provides better cardiovascular outcomes in STEMI patients with MVD, current guidelines do not recommend revascularization of nonculprit lesions unless complicated by hemodynamic instability. 3, 4 Should we only treat the culprit lesion or also treat obstructive nonculprit lesions?—and when?

In this issue of the Journal, Toyota et al 5 report that a staged PCI strategy for angiographically significant nonculprit lesions early reperfusion of the occluded infarct-related artery (IRA) using primary percutaneous coronary intervention (PCI) has been the primary goal of treatment for patients with acute ST-segment elevation myocardial infarction (STEMI). 1 Concomitant atherosclerosis in coronary arteries other than the IRA has been reported to be observed in 40–50% of patients with acute MI (AMI). 2 In addition, STEMI patients with multivessel disease (MVD) are at increased risk of major adverse cardiac events following primary PCI. 3 Although most interventional cardiologists believe that complete revascularization of ischemia-producing nonculprit obstructions provides better cardiovascular outcomes in STEMI patients with MVD, current guidelines do not recommend revascularization of nonculprit lesions unless complicated by hemodynamic instability. 3, 4 Should we only treat the culprit lesion or also treat obstructive nonculprit lesions?—and when?

How Should We Treat Myocardial Infarction Patients With Multivessel Disease?  
– Staged Revascularization? Or Stent Them All Acutely? –

Kenichi Tsujita, MD, PhD; Kenshi Yamanaga, MD; Koichi Kaikita, MD, PhD; Seiji Hokimoto, MD, PhD; Hisao Ogawa, MD, PhD

Table. Randomized Trials Comparing Complete Revascularization and Culprit-Only Revascularization in STEMI Patients With MVD

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Intervention</th>
<th>Timing for nonculprit lesion revascularization</th>
<th>1st endpoint</th>
<th>Place, time period</th>
<th>Outcome of 1st endpoint</th>
<th>HR for individual outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRAMI</td>
<td>Multicenter, single-blind, open-label</td>
<td>Preventive PCI (n=234) vs. no preventive PCI (n=231, IRA-only PCI)</td>
<td>Index procedure</td>
<td>Cardiac death/ nonfatal MI/ refractory angina</td>
<td>UK, 23 months (mean)</td>
<td>↓65%, preventive PCI better</td>
<td>0.34 (0.11–1.08) for cardiac death, 0.32 (0.13–0.75) for nonfatal MI, 0.35 (0.18–0.69) for refractory angina</td>
</tr>
<tr>
<td>CvLPRIT</td>
<td>Multicenter, open-label</td>
<td>In-hospital complete revascularization (n=150) vs. IRA-only revascularization (n=146)</td>
<td>Index procedure (2/3 patients) or staged within index hospitalization</td>
<td>All-cause death/ recurrent MI/HF/ ischemia-driven revascularization</td>
<td>UK, 12 months</td>
<td>↓53%, in-hospital complete revascularization better</td>
<td>0.32 (0.06–1.60) for all-cause death, 0.48 (0.09–2.62) for recurrent MI, 0.43 (0.13–1.39) for HF, 0.55 (0.22–1.39) for revascularization</td>
</tr>
<tr>
<td>DANAMI-3-PRIMULTI</td>
<td>Multicenter, open-label</td>
<td>Complete FFR-guided revascularization before discharge (n=314) vs. no further invasive intervention after primary PCI (n=313)</td>
<td>Staged within index hospitalization</td>
<td>All-cause death/ nonfatal MI/ ischemia-driven revascularization of lesions in non-IRA</td>
<td>Denmark, 12 months</td>
<td>↓44%, complete revascularization better</td>
<td>1.40 (0.63–3.00) for all-cause death, 0.94 (0.47–1.90) for nonfatal MI, 0.31 (0.18–0.53) for ischemia-driven revascularization</td>
</tr>
</tbody>
</table>

CvLPRIT, Complete Versus Lesion-only Primary PCI Pilot Study; DANAMI-3-PRIMULTI, Third Danish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction Primary PCI in Multivessel Disease; FFR, fractional flow reserve; HF, heart failure; HR, hazard ratio; IRA, infarct-related artery; MI, myocardial infarction; MVD, multivessel disease; PCI, percutaneous coronary intervention; PRAMI, Preventive Angioplasty in Acute Myocardial Infarction; STEMI, ST-segment elevation myocardial infarction.

The opinions expressed in this article are not necessarily those of the editors or of the Japanese Circulation Society.

Received December 16, 2015; accepted December 17, 2015; released online December 25, 2015

Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto (K.T., K.Y., K.K., S.H., H.O.); Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Suita (H.O.), Japan

Mailing address: Kenichi Tsujita, MD, PhD, Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan. E-mail: tsujita@kumamoto-u.ac.jp


All rights are reserved to the Japanese Circulation Society. For permissions, please e-mail: cj@j-circ.or.jp
was associated with lower 5-year mortality compared with a culprit-only PCI strategy in STEMI patients with MVD who underwent primary PCI, utilizing a large observational registry database of Japanese patients with AMI. The main result of the current analysis is important for the point that clinical benefit of complete revascularization by staged PCI has been confirmed in Japanese STEMI patients with MVD, especially pertaining to hard endpoints (all-cause death, cardiac death or MI).

Based on the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial\(^8\) in patients with STEMI complicated by cardiogenic shock, simultaneous complete revascularization has been recommended consistently. In contrast, in STEMI patients with MVD but without hemodynamic deterioration, acute multivessel PCI was not clinically beneficial and might be harmful.\(^7\) Recently, 3 randomized trials (Table) have tried to answer the clinical questions regarding optimal management of STEMI patients with obstructive nonculprit lesions.\(^5\)--\(^8\) In the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial,\(^9\) Wald et al found a 65% reduction in the primary composite endpoint of cardiac death, MI, or refractory angina within 23 months after complete revascularization of all obstructive (≥50% stenosis) nonculprit lesions during the index procedure. In the Complete versus Lesion-only Primary PCI Trial (CvLPRIT),\(^6\) Gershlick et al found a significant 53% reduction in the primary composite endpoint of all-cause mortality, recurrent MI, heart failure, or ischemia-driven repeat revascularization within 12 months of complete (either at the time of the index procedure or before hospital discharge) vs. culprit-lesion-only revascularization. Similar to the PRAMI and CvLPRIT, in the Third Danish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction Primary PCI in Multivessel Disease (DANAMI-3-PRIMULTI),\(^8\) the investigators showed a 44% reduction in the primary composite endpoint of death, MI or ischemia-driven revascularization within 12 months of a fractional flow reserve-guided complete revascularization strategy compared with culprit-only revascularization. Whereas all 3 randomized clinical trials demonstrated considerable clinical benefit of complete revascularization in STEMI patients with MVD undergoing primary PCI, none was powered for individual endpoints, especially for hard endpoints such as mortality. As shown in the Table, each individual component of the primary composite endpoint tended to be lower in patients assigned to complete revascularization; however, the between-group difference was not statistically significant. In contrast, the current analysis based on a large AMI registry data in Japan showed that adjusted risks for hard endpoints (“all-cause mortality” and “a composite of cardiac death or myocardial infarction”) were significantly lower in patients with staged PCI strategy than in patients with culprit-only strategy. However, both the above-mentioned randomized controlled trials and the current CREDO-Kyoto registry data consistently showed substantial clinical benefit from complete revascularization in STEMI patients with MVD.

How do we currently treat STEMI patients with MVD in real-world settings? And when should we revascularize the nonculprit lesions during the index hospitalization? In Japan, most interventional cardiologists have believed for a long time in the benefit and safety of culprit-only PCI during primary PCI unless there is hemodynamic instability, and have performed complete revascularization prior to discharge in a staged PCI fashion. For now, it seems that the staged PCI-oriented patient management scheme has provided us with safer index and staged PCI procedures (eg, lesion stabilization, procedure time, contrast exposure, and puncture site complication). The current analysis of the CREDO-Kyoto registry data supports such a patient management strategy for STEMI patients with MVD during the index hospitalization. In terms of the statistically robust superiority of the staged PCI against the culprit-only PCI, the large (≈4,000 patients) ongoing prospective randomized trial (Complete versus Culprit-only Revascularization to Treat Multi-vessel Disease After Primary PCI for STEMI (COMPLETE) trial) will provide more detailed evidence. Furthermore, we need additional randomized data to resolve the issue regarding the optimal timing of complete revascularization.

At this moment, obtaining evidence from prospective randomized studies and real-world registry data to support the complete revascularization strategy of recanalizing not only the culprit lesion but also nonculprit lesions, we should make good clinical judgements individually whether or not to treat nonculprit lesions during the index procedure. As even the nonculprit lesions have accelerated vulnerability in the acute phase of STEMI, postponing treatment of nonculprit lesions seems justified if the patient does not suffer from hemodynamic deterioration. In this situation, many clinical and lesion morphological factors should be considered when deciding if the nonculprit lesions should be treated during the index procedure or later. Finally, it must be clear that once the culprit lesion has been successfully recanalized, evaluating the clinical indication of nonculprit lesion PCI and undertaking effective preventive measures (optimal medical therapy) are equally important for the long-term benefit of the patient.\(^11\)\(^12\)

Disclosures
The authors declare no conflicts of interest.

References
Optimal PCI Strategy for STEMI Patients With MVD


