EDITORIALS

A More COMPLETE Picture of Revascularization in STEMI

Lars Køber, M.D., and Thomas Engstrøm, M.D.

Up to half of patients presenting with acute ST-segment elevation myocardial infarction (STEMI) have multivessel coronary artery disease, and American College of Cardiology–American Heart Association–European Society of Cardiology guidelines have a class IIb recommendation for the treatment of nonculprit lesions.[1-4] Four intermediate-sized trials have shown that complete revascularization is safe and reduces the risk of repeat revascularization.[5-8] Until now, a general strategy of complete revascularization has not been shown to reduce the risk of hard outcomes, such as death and recurrent myocardial infarction. In addition, it has been suggested that identification of nonculprit lesions relevant for complete revascularization should be based on fractional flow reserve (FFR) measurements.

Mehta and colleagues now report in the *Journal* the results of the COMPLETE (Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early Percutaneous Coronary Intervention [PCI] for STEMI) trial, a large, randomized trial comparing complete revascularization with treatment of the culprit lesion only in patients presenting with STEMI.[9] A total of 4041 patients who had nonculprit lesions with at least 70% stenosis of the vessel diameter or an FFR measurement of 0.80 or less were randomly assigned, in a 1:1 ratio, to undergo either complete revascularization or treatment of the infarct-related artery only. Patients underwent randomization up to 72 hours after the index PCI procedure. Treatment of nonculprit lesions could be performed during the index admission or after discharge, a choice that was made by investigators before randomization. There was a low crossover rate (<5%) between the two treatment groups.

The risk of the first coprimary composite outcome (death from cardiovascular causes or recurrent myocardial infarction) was a quarter lower in the complete-revascularization group than in the culprit-lesion-only PCI group. This benefit was driven by a reduction in new myocardial infarction. Cardiovascular mortality was similar in the two groups (2.9% and 3.2%), as was all-cause mortality (4.8% and 5.2%). The risk of the second coprimary outcome, which included ischemia-driven revascularization in addition to the other two events, was 50% lower in the complete-revascularization group than in the culprit-lesion-only PCI group.

Among patients who were randomly assigned to undergo complete revascularization, one third had the second procedure after hospital discharge. Subgroup analyses that were based on the intended timing of the second procedure showed no interaction with the primary outcomes, which indicates that complete revascularization may be safely postponed until after hospital discharge in selected patients. The risk of adverse events (including stroke, major bleeding, and acute kidney injury) was similar in the two groups, which supports the safety of an additional procedure.

Comparing the COMPLETE trial with previous trials provides important information (Table 1). Although the patients in the COMPLETE trial had an age and sex distribution similar to that of the patients in the other trials, they had a lower yearly risk of the primary outcomes but still had more events than did the patients in all

Table 1. Comparison of the COMPLETE Trial with Previous Trials of Complete Revascularization.*

Variable	PRAMI	CvLPRIT	DANAMI-3–PRIMULTI	Compare-Acute	COMPLETE
No. of patients	465	296	627	885	4041
Mean age — yr	62	65	63	61	62
Male sex — %	78	81	81	77	80
Median follow-up — mo	23	12	27	12	36
Median time from randomization to second procedure — days	0 (same time as index procedure)	<2	2	0 (same time as index procedure)	1 (during admission); 23 (after discharge)†
FFR measurement of nonculprit lesions obtained	No	No	Yes	Yes	Yes (in <1% of patients)
Events with treatment of culprit lesion only — no./total no. of patients					
Death	16/231	10/146	11/313	10/590	106/2025
Cardiovascular death	10/231	7/146	9/313	6/590	64/2025
Myocardial infarction	20/231	4/146	16/313	28/590	160/2025
Revascularization	46/231	16/146	52/313	103/590	160/2025
Events with complete revascularization vs. treatment of culprit lesion only — hazard ratio (95% CI)					
Cardiovascular death or myocardial infarction	0.36 (0.18–0.73)	NA	0.80 (0.45–1.45)	NA	0.74 (0.60–0.91)
Death	NA	0.38 (0.12–1.20)	1.40 (0.63–3.00)	0.80 (0.25–2.56)	0.91 (0.69–1.20)

* Shown are data from the following trials: PRAMI (Preventive Angioplasty in Acute Myocardial Infarction),[5] CvLPRIT (Complete versus Lesion-Only Primary Percutaneous Coronary Intervention [PCI] Trial),[6] DANAMI-3–PRIMULTI (Third Danish Study of Optimal Acute Treatment of Patients with ST-Segment Elevation Myocardial Infarction [STEMI]: Primary PCI in Multivessel Disease),[7] Compare-Acute,[8] and COMPLETE (Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI).[9] CI denotes confidence interval, FFR fractional flow reserve, and NA not available in the publication.

† Investigators specified before randomization whether they intended to perform the second procedure during the index hospitalization or after hospital discharge. Among the patients who underwent complete revascularization, the intended timing of the second procedure was during the index hospitalization for 1285 patients and after hospital discharge for 596 patients.

the other trials together, a finding that shows the importance of having properly sized trials with long-term follow-up.

Is functional assessment with FFR of nonculprit lesions unnecessary? In the COMPLETE trial, almost all nonculprit lesions were treated on the basis of angiographic findings, but nearly 60% of the lesions had at least 80% stenosis of the vessel diameter on visual estimation and 38% were in the left anterior descending coronary artery. Thus, most lesions were angiographically significant, and FFR may still have an important role in diagnosing lesions of intermediate severity.

Should the results of the COMPLETE trial, in combination with the results of previous randomized trials, change the guidelines to support complete revascularization in all patients with STEMI and multivessel disease? Patients participating in trials are different from sicker patients seen in the clinical setting, and extrapolation of the results to patients with a greater risk of complications may not be safe. Among patients in the COMPLETE trial, the mean SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score — a score used to predict the risk associated with revascularization by taking into account the complexity of coronary artery disease, with scores ranging from 0 (no disease) to more than 50 (multiple very complex lesions) — was relatively low, conferring an increased chance of successful revascularization. More complex nonculprit lesions (associated with higher SYNTAX scores) may be different physiologically and may

be less suitable for routine treatment. Also, some patients may benefit more from firm adherence to high-potency dual antiplatelet therapy with either prasugrel or ticagrelor. In the COMPLETE trial, one quarter of the patients received clopidogrel, which may not be the most effective therapy in patients with acute coronary syndromes.[10]

Should the consistent lack of benefit with respect to all-cause mortality discourage the strategy of routine complete revascularization? Since this strategy appears to be safe and reduces the risk of the composite outcome of cardiovascular death or recurrent myocardial infarction, as well as the risk of future revascularization, it appears to be appropriate to recommend complete revascularization for patients similar to those included in the COMPLETE trial. We hope that the investigators will be able to obtain data from longer follow-up in order to evaluate whether the tendency toward a small reduction in all-cause mortality becomes significant over time. Better selection of high-risk patients may also refine the determination of who is most likely to benefit from complete revascularization. Regardless, in light of the results of the well-planned and well-executed trial by Mehta et al., the guidelines should recommend a strategy of full revascularization in patients with STEMI and multivessel disease, at least in those who have suitable nonculprit lesions.

Disclosure forms provided by the authors are available with the full text of this editorial at NEJM.org.

From the Department of Cardiology, Rigshospitalet, University of Copenhagen, Copenhagen.

This editorial was published on September 1, 2019, at NEJM.org.

1. Kelbaek H, Terkelsen CJ, Helqvist S, et al. Randomized comparison of distal protection versus conventional treatment in primary percutaneous coronary intervention: the Drug Elution and Distal Protection in ST-Elevation Myocardial Infarction (DEDICATION) trial. J Am Coll Cardiol 2008;51:899-905.
2. Rasoul S, Ottervanger JP, de Boer MJ, et al. Predictors of 30-day and 1-year mortality after primary percutaneous coronary intervention for ST-elevation myocardial infarction. Coron Artery Dis 2009;20:415-21.
3. Neumann F-J, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;40:87-165.
4. Levine GN, Bates ER, Blankenship JC, et al. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation 2016;133:1135-47.
5. Wald DS, Morris JK, Wald NJ, et al. Randomized trial of preventive angioplasty in myocardial infarction. N Engl J Med 2013;369:1115-23.
6. Gershlick AH, Khan JN, Kelly DJ, et al. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. J Am Coll Cardiol 2015;65:963-72.
7. Engstrøm T, Kelbæk H, Helqvist S, et al. Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3–PRIMULTI): an open-label, randomised controlled trial. Lancet 2015;386:665-71.
8. Smits PC, Abdel-Wahab M, Neumann FJ, et al. Fractional flow reserve–guided multivessel angioplasty in myocardial infarction. N Engl J Med 2017;376:1234-44.
9. Mehta SR, Wood DA, Storey RF, et al. Complete revascularization with multivessel PCI for myocardial infarction. N Engl J Med 2019;381:1411-21.
10. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009;361:1045-57.

DOI: 10.1056/NEJMe1910898

A Metabolic Vulnerability of Vision

Henna Tyynismaa, Ph.D.

New therapies targeting metabolic vulnerabilities of specific tumor types have created wide interest in recent years. Through research now reported in the *Journal* by Gantner et al.,[1] metabolic precision therapy may become possible in patients with a rare eye disease, macular telangiectasia type 2, which leads to a progressive loss of central vision in both eyes in middle-aged or older persons.[2]

The macula is the small area in the back of the eye that is responsible for high-resolution (i.e., sharp) vision. In the center of the macula is the fovea, which has the highest density of cone photoreceptor cells and thus, as compared with