TAVR. We need to clarify how to properly follow-up TAVR patients and how to prevent such a catastrophic event after TAVR.

Finally, we are pleased that Professor Sondergaard highlighted the essential points of our work, and we appreciate his important comments.

Hidehiro Kaneko, MD
Michael Neuss, MD
Grit Tambor, MD
Frank Hoelschermann, MD
***Christian Butter, MD**
*Department of Cardiology
Heart Center Brandenburg
Department of Cardiology
Medical School Brandenburg
Ladeburger Straße 17
Bernau 16321
Germany
E-mail: c.butter@immanuel.de

http://dx.doi.org/10.1016/j.jcin.2016.11.039

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Neuss M, Kaneko H, Tambor G, Hoelschermann F, Butter C. Fatal thrombotic occlusion of left main trunk due to huge thrombus on prosthetic aortic valve after transcatheter aortic valve replacement. J Am Coll Cardiol Intv 2016;9:2257–8.

2. Makkar RR, Fontana G, Jilaihawi H, et al. Possible subclinical leaflet thrombosis in bioprosthetic aortic valves. N Engl J Med 2015;373:2015–24.

Treatment Strategies for Patients With ST-Segment Elevation Myocardial Infarction and Multivessel Disease

Is Staged PCI Truly the Best Option?

In a recent paper by Tarantini et al. (1), the authors performed a meta-analysis of studies evaluating the various strategies for the management of patients with ST-segment elevation myocardial infarction (STEMI) and multivessel disease. They demonstrated that staged multivessel percutaneous coronary intervention (PCI) was associated with a lower mortality as compared with infarct-related artery only PCI (IRA PCI) or multivessel PCI at the time of primary PCI (MV PPCI). In their analysis, the investigators categorized studies as "prospective" or "retrospective." By grouping the studies in this manner, they included some of the observational studies into the prospective category. Prospective randomized controlled trials (RCT) are generally regarded as a stronger source of evidence than prospective observational studies and are not often grouped together in meta-analyses. One way to synthesize evidence from various sources is to use a Bayesian cross-design meta-analysis, but it does not seem that the statistical methods the authors used employed such an approach. As such, we believe that the results of the analysis provide misleading information regarding the outcomes related to the various PCI strategies in patients with STEMI and multivessel disease.

Regarding the outcomes for patients undergoing IRA PCI versus MV PPCI, we feel that the nonrandomized studies should be excluded from this prospective analysis. We previously showed that there is a trend toward lower mortality with MV PPCI when results from the RCTs alone are pooled (2). In contrast, no difference in outcomes between IRA PCI or MV PPCI could be found using a Bayesian cross-design meta-analysis, which included both observational studies as well as RCTs (3).

We also noticed that the authors included all of the patients enrolled in the CvLPRIT (Complete versus Lesion-only Primary PCI) trial in the MV PPCI group. In the CvLPRIT trial, 97 patients (70%) underwent MV PPCI and the remaining 42 (30%) underwent staged multivessel PCI. There was a trend toward a worse outcome in the group of patients having a staged procedure as compared with those undergoing MV PPCI (4). It is possible that the inclusion of patients undergoing staged MV PCI, into the MV PPCI group biased the results of this analysis against MV PCCI.

Finally, regarding the comparison of MV PPCI with staged multivessel PCI, we disagree with the inclusion of the nonrandomized studies in this prospective grouping. At present, there are very few RCTs (with a very small number of patients) comparing these 2 approaches; therefore, we do not feel a valid comparison can be made using the pooled data from RCTs.

Although we are in agreement with the conclusions that a strategy of stage MV PCI may offer some advantages over a strategy of IRA PCI, and

theoretical advantages to MV PPCI, this opinion is based on clinical experience, but is not supported by the pooled results from the RCTs. The COMPLETE trial (Complete vs Culprit-Only Revascularization to Treat multi vessel Disease After Primary PCI for STEMI) (NCT01740479) will enroll 3900 patients to a strategy of staged MV PCI or an ischemia guided approach. We hope that this study will provide more definitive data regarding the potential advantages of staged MV PCI. Until there is more evidence to support one approach over another, physicians must use their clinical judgment to guide the treatment of patients with STEMI and multivessel disease.

*Jacqueline E. Tamis-Holland, MD
Eric Bates, MD
John Bittl, MD

*Mount Sinai Saint Luke's Hospital
Department of Cardiology
1111 Amsterdam Avenue
New York, New York 10025
E-mail: Jacqueline.tamis-holland@mountsinai.org

http://dx.doi.org/10.1016/j.jcin.2016.11.009

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Tarantini G, D'Amico G, Brener SJ, et al. Survival after varying revascularization strategies in patients with ST-segment elevation myocardial infarction and multivessel coronary artery disease: a pairwise and network meta-analysis. J Am Coll Cardiol Intv 2016;9:1765–76.

2. Bates ER, Tamis-Holland JR, Bittl JA, O'Gara PT, Levine GN. PCI strategies in patients with ST-segment elevation myocardial infarction and multivessel coronary artery disease. J Am Coll Cardiol 2016;68:1066–81.

3. Bittl JA, Tamis-Holland JE, Lang CD, et al. Outcomes after multivessel or culprit-vessel intervention for ST-elevation myocardial infarction in patients with multivessel coronary disease: a Bayesian cross-design meta-analysis. Cathet Cardiovasc Interv 2015;86 Suppl 1:S15–22.

4. 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.

REPLY: Treatment Strategies for Patients With ST-Segment Elevation Myocardial Infarction and Multivessel Disease

Is Staged PCI Truly the Best Option?

We thank Dr. Tamis-Holland and colleagues for their interest in our article (1).

We recognize that combining prospective observational studies with randomized controlled trials (RCTs) might be a limitation, but this was done to increase the statistical power of our observations. We acknowledge that this method might increase heterogeneity; thus, we performed a subgroup meta-analysis to explore the impact of the study type (i.e., retrospective vs. prospective) as a potential source of heterogeneity, as suggested by the *Cochran Handbook* (2). Moreover, although it might be interesting to group the studies as retrospective, observational prospective, and RCTs, we could not proceed in this way because of the low number of prospective studies included in the meta-analysis and the fact that at least 4 studies need to be included in each subgroup for meaningful results (3). In any case, we failed to find any heterogeneity in the subgroup of prospective studies. Finally, there are no prospective observational studies comparing infarct-related artery (IRA) percutaneous coronary intervention (PCI) versus staged PCI and single-stage multivessel (MV) PCI versus staged PCI; the study by Kornowski et al. (4) is a post hoc retrospective analysis from the HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trial.

We regret that the commentators did not note that we did perform a Bayesian analysis, besides the frequentist method, and it fully confirmed the latter. Applying the suggested cross-design meta-analysis, the significant impact of the IRA-only versus single-stage MV-PCI on long-term mortality is lost (**Figure 1**). However, a major drawback of this approach remains the low numbers of studies included in each group.

In the CvLPRIT trial (Complete Versus Lesion-Only Primary PCI Trial) (5), the choice of the strategy was not randomized, and none of the analyses used "as treated" methodology. Notwithstanding, the complete revascularization was recommended and performed during the index procedure in most patients, and thus, we decided to label this trial as single-stage MV-PCI strategy. As shown in **Figure 2**, reclassifying the latter trial as staged MV-PCI or removing it from the analysis (as suggested in the letter) does not change significantly the results of our analysis ($p = 0.005$ and $p = 0.0144$, respectively).

We thank the commentators again and agree with the need for prospective, randomized clinical trials addressing this important clinical dilemma.