Neuss et al. (1) related their case report to HALT and stated that HALT is a phenomenon particularly found after TAVR with the Portico valve. However, HALT causes neither symptoms nor an increased transvalvular gradient, and increased risk of thromboembolic events and impaired leaflet durability is speculative. Furthermore, HALT has been described in both surgical and transcatheter bioprosthetic aortic valves with no statistically significant differences in the frequency between brands.

In the reported case, there was no confirmation of HALT by CT scan or transesophageal echocardiography. Furthermore, there was a normal gradient across the aortic valve, which would be expected in thrombosis with a clinically relevant impact on valve function.

The U.S. Food and Drug Association has reviewed data currently available on HALT and has not recommended a change in current antithrombotic therapy for TAVR patients. Instead, antithrombotic therapy decisions should be tailored for each patient with careful consideration of their specific risk/benefit profile.

The unsubstantiated association between this unfortunate rare case and HALT could spread unsupported alarm. A more thorough evaluation of all potential contributors, for example, atrial fibrillation, coagulopathies, age, and sex of the patient, should be undertaken before linking the event to an otherwise subclinical observation.

*Lars Sondergaard, MD, DMSc

*The Heart Center, Rigshospitalet
Blegdamsvej 9
Copenhagen 2100
Denmark
E-mail: drsondergaard@gmail.com

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REPLY: Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

We thank Prof. Sondergaard for his interest in our work (1) and appreciate his profound and insightful comments regarding this important topic. Our work was published recently in *JACC: Cardiovascular Interventions* and reported a case of fatal thrombotic occlusion of the left main trunk due to a large thrombus developing on the transcatheter heart valve (THV).

As Prof. Sondergaard mentioned, the association between hypoattenuated leaflet thickening (HALT) on computed tomography (CT) after bioprosthetic aortic valve and the incidence of adverse clinical outcomes such as a thromboembolic event has not yet been established. However, it also has not been concluded that HALT does not contribute to the development of thromboembolic events. Hence, it is quite important to clarify the pathological role of HALT in further studies.

Additionally, we completely agree with Prof. Sondergaard that HALT is not a phenomenon that is found only after transcatheter aortic valve replacement (TAVR) using a Portico valve (St. Jude Medical, St. Paul, Minnesota). As Makkar et al. (2) reported, this phenomenon could occur after TAVR using other THVs and after surgical aortic valve replacement. Therefore, this phenomenon is currently attracting clinical interest, and we need to elucidate its significance and establish the optimal antithrombotic strategy.

As Prof. Sondergaard mentioned, transthoracic echocardiography showed normal valve function of the implanted Portico with a large thrombus. However, this echocardiography was performed in the emergency department for the purpose of a quick check during a hemodynamically unstable state due to left main trunk occlusion. Therefore, it might be difficult to completely deny the increased transvalvular gradient. Additionally, this patient did not undergo CT examination after TAVR. Therefore, the presence of HALT cannot be excluded.

The clinical background of this patient is also important. Except for age (81 years, which is not surprising for patients undergoing TAVR), this patient had no factors (such as atrial fibrillation, coagulopathies, or history of thromboembolism) that made him/her prone to the development of a thromboembolic event. As described in our work, the clinical course after TAVR of this patient was good. Therefore, it was difficult to predict this event 2 years after

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

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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