replacement (TAVR) (1). Several of their points of merit further consideration.

Dr. Pollari and colleagues argue that calcific aortic stenosis and coronary atherosclerosis are unconnected entities with independent natural history. This statement remains controversial, with some prior studies suggesting that both conditions may share common pathophysiological and clinical features (2). Also, Dr. Pollari and colleagues pointed out that the incidence of ACS post-TAVR reported in our study may have been overestimated by the presence of myocardial injury post-TAVR occurring in the vicinity (≤30 days) of the procedure. Although we agree that cardiac troponin increase may persist up to 1 month following TAVR, particularly in patients treated by transapical approach (3), 30-day readmission for ACS occurred only in 3 patients (8.1% of the events occurring within the first year post-TAVR, 3.8% of the overall ACS). Of these, there were 2 episodes of type 2 non-ST-segment myocardial infarction in the setting of paroxysmal atrial fibrillation with new-onset troponin rise, and 1 episode of unstable angina. Hence, the overall rate of ACS would have remained similar even after excluding patients with early ACS. Furthermore, patients with <6-month follow-up were deliberately excluded to differentiate spontaneous ACS events (assessed in the study) from mechanical coronary obstruction or periprocedural myocardial injury.

Dr. Pollari and colleagues cast doubts on the potential protective role of TAVR on subsequent ACS. We believe this assumption may be related to a misconception because TAVR—or surgical aortic valve replacement—is not supposed to prevent ACS. Indeed, patients undergoing TAVR are often elderly and exhibit a high burden of cardiovascular risk factors, which increases the risk of coronary events. Dr. Pollari and colleagues also hypothesized that patients with lower pre-operative gradients may be less vulnerable to type 2 myocardial infarction due to less ventricular hypertrophy, compared with high-gradient patients. However, prior studies have suggested that patients with low-gradient aortic stenosis often have more advanced ventricular disease, with more pronounced concentric remodeling and myocardial fibrosis, compared with those with high gradient (4). Finally, no conclusions on the natural course of coronary disease should be drawn from comparing procedural aspects of patients undergoing percutaneous coronary intervention before and after TAVR, aside from potential difficulties—albeit not observed in our study—in coronary access post-TAVR. Upcoming data from ongoing randomized trials are anticipated to shed light on the optimal revascularization strategy for patients with coronary disease undergoing TAVR. Our study highlighted, for the first time, the relatively high incidence and poor prognosis of ACS post-TAVR. Further studies are needed to evaluate specific preventive measures and tailored management for this complex group of patients.

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REFERENCES

1. Vilalta V, Asmarats L, Ferreira-Neto AN, et al. Incidence, clinical characteristics, and impact of acute coronary syndrome following transcatheter aortic valve replacement. J Am Coll Cardiol Intv 2018;11:2523–33.

2. Milin AC, Vorobiof G, Aksoy O, Ardehali R. Insights into aortic sclerosis and its relationship with coronary artery disease. J Am Heart Assoc 2014;3. e001111.

3. Rodés-Cabau J, Gutiérrez M, Bagur R, et al. Incidence, predictive factors, and prognostic value of myocardial injury following uncomplicated transcatheter aortic valve implantation. J Am Coll Cardiol 2011;57:1988–99.

4. Herrmann S, Störk S, Niemann M, et al. Low-gradient aortic valve stenosis myocardial fibrosis and its influence on function and outcome. J Am Coll Cardiol 2011;58:402–12.

TO THE EDITOR

Will Pulmonary Artery Denervation Really Have a Place in the Armamentarium of the Pulmonary Hypertension Specialist?

Zhang et al. (1) reported significant improvements in hemodynamic and clinical outcomes after pulmonary artery denervation (PADN) in pulmonary hypertension (PH) due to left heart disease (PH-LHD). Several methodological issues should be mentioned.

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This study is not a completely sham-controlled study because sildenafil prescription became a discriminator of the true PADN versus the sham PADN procedure. It is difficult to understand the selection of sildenafil as a comparator arm. Pulmonary arterial hypertension (PAH) therapies including sildenafil have long been studied in PH-LHD with adverse clinical results (2,3). The use of PAH therapies is not recommended for PH-LHD according to the recent European Society of Cardiology/European Respiratory Society PH guidelines (4). A growing body of evidence indicates a potential role of left ventricular (LV) assist devices only to achieve reductions in pulmonary artery systolic pressure and pulmonary vascular resistance in PH-LHD. The investigators defined heart failure (HF) with preserved ejection fraction (EF) as LVEF ≥50% and HF with reduced EF as LVEF <50%. LVEF 40% to 49% (HF with mid-range EF) is a totally different entity. Only 65% to 70% of HF with reduced EF had received angiotensin-converting enzyme inhibitors/angiotensin receptor blockers/beta-blockers. A very limited time for the run-in period for stabilization was permitted. Optimization of medical therapy with angiotensin-converting enzyme inhibitors/angiotensin receptor blockers/beta-blockers/sacubitril has been missed in the follow-up. Sildenafil might have potentially increased the congestive state of the patients. Heart rate control should have had a huge impact on the results because one-half the patients had atrial fibrillation. It is unacceptable to give aspirin plus clopidogrel in the era of new oral anticoagulants. The heart rate would slow down after PADN. There is not any detailed information about the effects of PADN. Considering the PADN application site is in the vicinity of the superior cardiac plexus, the innervation of the heart might have been affected, and an eventual chronotropic effect would confound the results. The essential factors for the development of PH-LHD are LV end-diastolic pressure and functional mitral regurgitation, on which PADN may not have any possible effect. Better designed randomized studies are clearly needed to further define which patients might be most likely to respond to this innovative approach.

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REFERENCES

1. Zhang H, Zhang J, Chen M, et al. Pulmonary artery denervation significantly increases 6-min walk distance for patients with combined pre- and post-capillary pulmonary hypertension associated with left heart failure: the PADN-5 study. J Am Coll Cardiol Intv 2019;12:274–84.

2. Vachiéry JL, Delcroix M, Al-Hiti H, et al. Macitentan in pulmonary hypertension due to left ventricular dysfunction. Eur Respir J 2018;51:1701886.

3. Bermejo J, Yotti R, García-Orta R, et al. Sildenafil for improving outcomes in patients with corrected valvular heart disease and persistent pulmonary hypertension: a multicenter, double-blind, randomized clinical trial. Eur Heart J 2018;39:1255–64.

4. Galiè N, Humbert M, Vachiéry JL, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Eur Heart J 2016;37:67–119.

REPLY: Will Pulmonary Artery Denervation Really Have a Place in the Armamentarium of the Pulmonary Hypertension Specialist?

We thank Drs. Yaylali and Basarici for their interest in our paper (1) regarding the benefits of pulmonary artery denervation (PADN) for patients with combined pre- and post-capillary (Cpc) pulmonary hypertension (PH) due to left heart failure (LHF). Although we agree with Drs. Yaylali and Basarici that sildenafil is in general not recommended for LHF-PH by the European Society of Cardiology/European Respiratory Society guidelines, this does not mean that sildenafil is harmful to CpcPH. Obviously, CpcPH is completely different from the broad entity of LHF-PH. Additional published findings validate our unmoderated interpretation. First, from studies (2) on the comparison of sildenafil with placebo in patients with HF or isolated post-capillary PH, the controversial results may be due to the wider discrepancies in left ventricular ejection fraction (EF) values for defining HF with preserved EF (<35% vs. 50%), unknown percentage of CpcPH, follow-up duration (4 vs. 24 weeks), sample size (19 vs. 216 patients), dose of sildenafil (25 mg twice daily vs. 50 mg 3× a day) with or without titration, and the primary endpoints. A single-center registry study that included only 20 patients with CpcPH (defined as pulmonary vascular resistance >2.5 Woods units) by Urbanowicz et al. (3) reported a significant improvement of peak oxygen consumption (Vo_2), cardiac index, pulmonary vascular resistance, and mean pulmonary artery pressure after 12 months'