TABLE 1 Association Between Low DBP and Adverse Outcomes, After Further Adjustment for Heart Rate

	Cross-Sectional Analysis for Elevated hs-cTNT (≥14 ng/l)*			Prospective Proportional Hazards Analysis for Incident Outcomes†					
		Odds Ratio			CHD			Mortality	
Visit 2 Diastolic BP	n/N	(95% CI)	p Value	n/N	HR (95% CI)	p Value	n/N	HR (95% CI)	p Value
<60 mm Hg	39/1,087	2.47 (1.53–3.97)‡	<0.001‡	165/1,087	1.50 (1.20–1.86)‡	<0.001‡	345/1,087	1.41 (1.21–1.65)‡	<0.001‡
60–79 mm Hg	264/7,977	1.18 (0.89–1.55)	0.252	1,299/7,975	1.22 (1.07–1.39)	0.003	2,159/7,974	1.08 (0.98–1.20)	0.119
80–89 mm Hg	102/1,902	1.00 (reference)	—	350/1,902	1.00 (reference)	—	597/1,902	1.00 (reference)	—
≥90 mm Hg	50/599	0.72 (0.48–1.08)	0.111	129/599	0.89 (0.72–1.10)	0.288	238/599	1.01 (0.86–1.18)	0.921

Adjusted for age (years), race-center, gender, body mass index (kg/m^2), smoking (current; former; never), alcohol intake (current; former; never), hypertension medication use (yes, no), systolic blood pressure (BP), heart rate, diagnosed diabetes (yes, no), low-density lipoprotein cholesterol (mg/dl), high-density lipoprotein cholesterol (mg/dl), triglycerides (mg/dl), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate (ml/min/1.73m^2). *Logistic model for cross-sectional association between diastolic BP and baseline elevated high-sensitivity troponin T (hs-cTnT). †Cox model for prospective association between diastolic BP and incident events. ‡Significant values.

CHD = coronary heart disease; CI = confidence interval; HR = hazard ratio.

treated to a target of 85 mm Hg (6.8 pr 1,000 patient-years; relative risk: 1.22) (3).

Drs. Battista Danzi and Cuspidi suggest that heart rate may be an important factor in the association between low DBP and coronary ischemia. This important suggestion was also raised by Dr. Namasivayam and esteemed colleagues (4). While we do not have complex data such as systolic pressure-time loading, heart rate is available in the ARIC (Atherosclerosis Risk In Communities) study dataset. Thus, we performed additional analyses adding heart rate to our models. As can be seen in **Table 1**, the addition of heart rate did not appreciably alter our results, suggesting that the association between low DBP and adverse coronary outcomes is not mediated by heart rate.

Finally, the letter by Dr. Spence is a sobering reminder that, for some elderly patients, DBP measured by an arm cuff may actually be higher than central aortic DBP (the latter being the most relevant for coronary perfusion), a phenomenon that further helps to explain our results.

*John W. McEvoy, MB BCh BAO, MEHP, MHS
Yuan Chen, MS
Elizabeth Selvin, PhD, MPH

*Johns Hopkins Ciccarone Center for the Prevention of Heart Disease
Division of Cardiology
Johns Hopkins University School of Medicine
Welch Center for Prevention Epidemiology and Clinical Research at the Johns Hopkins Bloomberg School of Public Health
600 North Wolfe Street
Blalock 524C
Baltimore, Maryland 21287
E-mail: jmcevoy1@jhmi.edu

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Valve Thrombosis After Transcatheter Aortic Valve Replacement

Transcatheter aortic valve replacement (TAVR) is the standard of care for patients with severe aortic stenosis who are increased risk for open heart surgery. Currently more than 200,000 patients worldwide have received this therapy, and the majority of implanted valves have shown no evidence of structural degeneration with follow-up up to 5 years (1). However, recent reports of late structural degeneration including valve thrombosis (VT) at 8 years have raised safety concerns in light of the expansion of indications for use (2).

Given these considerations, we read with much interest the recent paper by Hannson et al. (3) assessing the VT using multidetector computed tomography. On multivariable analysis, a 29-mm transcatheter heart valve (THV) (relative risk: 2.89; 95% confidence interval: 1.44 to 5.80) and no post-

TAVR warfarin treatment (relative risk: 5.46; 95% CI: 1.68 to 17.70) independently predicted VT (3).

We congratulate the authors on conducting this well-conceptualized study; however, there remain limitations. They point out that a larger THV size is associated with VT but do not evaluate the THV procedures with sufficient granularity to provide a mechanistic understanding of why this may be so. There are >20 case reports on VT and at least 3 large registry-based studies that have looked at VT incidence after THV. On pathologic review, VT occurs in the NCC or RCC more commonly and often the coronary cusp that is far removed from the right and left coronary arteries (4). These observations and in vitro experiments may suggest that unphysiological flow states occur in aortic sinuses with crowding due to the native aortic valve leaflets (5). Additionally, the depth of implantation has been shown to be associated with TAVR-associated VT (2). A deeper implant may result in a constrained THV frame and result in relative immobility of the THV leaflet. Subsequent balloon post-dilation may result in valve injury without the complete THV expansion. Alternatively, if the annulus is large, there may be malcoaptation of the valve leaflets, creating a milieu for thrombus formation.

The authors' work is important and in keeping with the current research efforts that have reorientated from establishing the short-term safety and efficacy of THV to optimize the long-term patient outcomes. Their findings suggest that the optimal THV should be tailored to the specific patient anatomy, taking into account the interaction among the stent frame, native leaflets, sinus height and depth, and annulus and coronary location. Optimizing patient outcomes for the decades that follow a THV is required, particularly as we move to treat a younger patient subset.

*Femi Philip, MD
Howard Dinh, MD
John Ko, MD
Micheal I. Chow, MD
Joseph Huh, MD

*Interventional Cardiology
Cardiovascular Medicine
Kaiser Permanente Medical Group
3701 J Street
Suite 109
Sacramento, California 95816
E-mail: femi.philip@kp.org

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