Blood Pressure, Arterial Load, and Survival After Transcatheter Aortic Valve Replacement

Reducing the Gradient Is Only Part of the Picture

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Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of symptomatic severe aortic stenosis (AS) across a spectrum of older patients whose surgical risk ranges from intermediate to prohibitive. The impressive results achieved in randomized controlled trials[1–3] have provided the basis for ongoing or planned investigations in low surgical risk[4] and asymptomatic patients.[5] Presently, TAVR is offered at >500 medical centers in the United States[6] and the annual number of TAVR procedures has surpassed that for isolated surgical aortic valve replacement.[6,7]

See Article by Lindman et al

Increasing confidence in the expanded use of TAVR relates, in part, to the iterative improvements seen in patient selection, imaging, device and delivery system design, anesthetic management, postprocedural care, multidisciplinary team dynamics, and institutional benchmarking against national performance standards. Serial reductions in the major complications of in-hospital death, stroke, perivalvular regurgitation, and heart block have occurred although a more complete longitudinal assessment of prosthetic valve thrombosis, durability, quality of life, and survival is needed. The expectations of patients, families, referring physicians and payers are high—sometimes unrealistically so. On completion of a technically successful procedure, there is usually a collective sigh of relief and the anticipation that the associated reduction in the magnitude of aortic valve obstruction will alone translate into clinical benefit. Experience has shown, however, that several patient-related factors that impact prognosis may not be improved, a reality that accentuates the importance of appropriate case selection. Until recently, relatively little attention has been paid to postprocedural physiological changes that may also bear on longer-term outcomes.

In this issue of *Circulation: Cardiovascular Imaging*, Lindman et al[8] explore the relationships among post-TAVR systolic blood pressure (SBP) and arterial load and survival in a cohort of 2141 prohibitive- or high-surgical risk patients enrolled in the PARTNER I trial (Placement of Aortic Transcatheter Valve; NCT 00530894) or continued access registry. Lower SBP (100–129 versus 130–170 mm Hg) and higher total and pulsatile (but not resistive) arterial load were associated with an increased 30-day to 1-year all-cause mortality. Standard calculations for noninvasive estimation of total (indexed arterial elastance), pulsatile (pulse pressure, indexed systemic arterial compliance), and resistive (indexed systemic vascular resistance) arterial loads were utilized. All-cause mortality was highest for those patients with low SBP and low systemic arterial compliance (Figure 1[8]). Lower SBP was associated with higher rates of myocardial infarction, more severe angina, lower left ventricular ejection fraction, inability to complete a 6-minute walk test and worse quality of life. Lower (<60 mm Hg) diastolic blood pressure was also associated with an increased rate of all-cause mortality. Interpretation of the findings should account for the high prevalence of pre-TAVR comorbidities known to affect vascular function in an elderly patient cohort (mean age, 84 years), including hypertension (92%), diabetes mellitus (37%), peripheral artery disease (42%), and chronic kidney disease (17%).

The observations on the deleterious effects of low SBP after TAVR were contrary to the authors' original hypothesis, not readily explained by alterations in left coronary perfusion pressure (which would be more dependent on diastolic blood pressure) and at odds with the increasingly accepted management strategy in which the intensity of SBP lowering is matched to the estimated risk of adverse cardiovascular outcomes, as reflected in the results of the SPRINT (Systolic Blood Pressure Intervention Trial; NCT 01206062),[9] even for patients aged >75 years.[10] However, SPRINT did not include patients with symptomatic heart failure (as would be expected for all patients in the PARTNER I cohort), left ventricular ejection fraction <35%, prior stroke (26% of PARTNER I patients had stroke or transient ischemic attack in the preceding 6–12 months) or diabetes mellitus. The observational nature of the current study raises the possibility that the association of low SBP after TAVR with 30-day to 1-year all-cause mortality risk may reflect reverse causality or residual confounding.[11] In the latter regard, a recently reported United Kingdom population-based cohort study in 144 403 subjects aged >80 years demonstrated a significant association between lower SBP and all-cause mortality, independent of frailty status.[12] The association appeared to be explained, in part, by a terminal decline in SBP in the final 2 years of life. The investigators concluded that reverse causation might have pertained if lower SBP resulted from temporal proximity to death and that the observed (nonrandomized) association between higher SBP

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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(*Circ Cardiovasc Imaging*. 2017;10:e006683. DOI: 10.1161/CIRCIMAGING.117.006683.)

***Circ Cardiovasc Imaging* is available at http://circimaging.ahajournals.org**

DOI: 10.1161/CIRCIMAGING.117.006683

and greater longevity could have been confounded.[12] A single blood pressure determination in elderly patients 30 days after TAVR may not provide enough information from which to draw firm conclusions on causality.

The current study's observations on the differential effects of total, pulsatile, and resistive arterial loads, and their interactions with SBP, are important reminders of the complex ventricular–valvular–arterial interactions that ensue in an elderly, predominantly hypertensive patient cohort after relief of aortic valve obstruction.[13–15] The deleterious effects of increased arterial stiffness and pulsatile load in this population are vastly underappreciated although likely not remediable with medical therapy in advanced age.

Blood pressure management in patients with AS can be challenging for clinicians and patients. A reluctance to reduce preload or arterial resistance for fear of precipitating hypotension in the setting of a fixed cardiac output usually dominates the clinical picture despite the known long-term deleterious consequences of elevated impedances in series. Low diastolic blood pressure levels (<70 mm Hg) may be particularly hazardous in the context of reduced coronary flow reserve, especially under conditions of increased myocardial oxygen demand. High diastolic blood pressure levels (>90 mm Hg), on the contrary, are consistently associated with adverse outcomes across a range of cardiovascular conditions, including AS.[16] International practice guidelines recommend treatment for hypertension in patients with AS.[17,18] Data from the SEAS trial (Simvastatin and Ezetimibe in Aortic Stenosis) describe a J-shaped relationship between blood pressure and outcomes and suggest that a target blood pressure of 130 to 139/70 to 90 be considered for patients with asymptomatic mild-to-moderate AS.[16] The optimal range for systemic blood pressure in patients with severe AS, however, has not been established. The picture is further clouded by individual variation in dose–response relationships, polypharmacy, drug side effects, drug–drug interactions, and patient comorbidities.

Lindman et al[8] have redrawn the clinician's attention to the evaluation and management of blood pressure in elderly, prohibitive-, or high-surgical risk patients after TAVR. Their findings suggest that lower SBP may be a marker for reduced survival in this cohort and may best be avoided if possible and as circumstances and drug choices allow. Other studies have shown that SBP increases in ≈50% of patients after TAVR possibly in relation to higher postprocedural stroke volume and cardiac output,[13] but more likely as a consequence of stiffer (less compliant) vascular behavior that is unmasked by the relief of the upstream valvular obstruction.[14] Higher SBP may be a good thing, but apparently not when it is accompanied by signs of reduced vascular compliance.[8,14] Understanding the factors that summate into a single measurement of blood pressure may be more important than routinely recognized. Manipulating these factors, and finding the sweet spot for arterial load after aortic valve intervention, would seem to depend critically on the optimization of vascular health in the decades leading up to the procedure.[19]

Disclosures

None.

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KEY WORDS: Editorials ■ aortic valve stenosis ■ blood pressure ■ hypertension ■ survival ■ transcatheter aortic valve replacement

Circulation
Cardiovascular Imaging

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Circ Cardiovasc Imaging. 2017;10:
doi: 10.1161/CIRCIMAGING.117.006683
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-9651. Online ISSN: 1942-0080