EDITORIAL COMMENT

Paravalvular Regurgitation and Post-Deployment Balloon Dilation After Transcatheter Aortic Valve Replacement
Can We Predict and Prevent?*

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Khalique et al. (1) report in this issue of JACC: Cardiovascular Interventions on the impact that calcification of the aortic valve apparatus may have on the outcome of transcatheter aortic valve replacement (TAVR). In this single-center analysis, the authors showed that calcification at any level, from the outflow track to the aortic valve annulus and leaflets, is a predictor of paravalvular aortic regurgitation (PVR) and the need to perform post-deployment balloon dilations, a surrogate marker of PVR. Because the occurrence of PVR is a predictor of subsequent mortality (2), it seems worth predicting and preventing it. Some conflicting information has been published in prior literature; some authors attributed the risk of PVR to either annular or leaflet calcification; some supported the notion that asymmetry of leaflet calcification is an important predictor, whereas others disputed it; some predicted that annular calcification is more important than commissural or leaflet calcification, and so on. The current report (1) puts to rest the controversy by showing that no matter where the calcification is located, it is a predictor of PVR. So calcium is doing it again! Heavy calcification of the aortic annulus is a warning for the surgeon that the native valve will be much harder to remove without damage to the aortic wall and that a prosthetic valve will not be easily fitted and sutured in place. Calcification of the aorta (porcelain aorta) is a harbinger of complications if clamping or puncturing were to be attempted. Dense calcification of the coronary arteries predisposes to development of dissection during interventional procedures, and is associated with more frequent restenosis. Are all these unfavorable outcomes the result of a mere mechanical problem, one of asymmetry, distortion, and loss of elasticity? Or are there other reasons for such instability? Calcification of the aortic valve and aortic root resembles very closely the process of atherosclerosis, with disruption of the basal membrane, infiltration of inflammatory cells, deposition of lipids, and accompanying calcification (3,4). Calcification is an active process similar to bone formation, with lamellar bone, hematopoietic elements, and active bone remodeling seen in the context of the damaged valvular tissue (5,6). Several epidemiological studies showed that independent risk factors for aortic valve sclerosis are the same as those for atherosclerosis: age, male sex, serum lipoprotein(a), and low-density lipoprotein cholesterol levels, hypertension, and smoking (3,4). Dweck et al. (7) showed that inflammation in a calcified aortic valve can be demonstrated by positron emission tomography-computed tomography imaging. So we are dealing, not with an amorphous, inert, and dystrophic tissue, but with a tissue subject to continuous dynamic changes? The immediate unfavorable outcome of a valve deployment may be dictated by mechanical issues, but the long-term outcome is likely to be dictated in part by the underlying active biological processes. One also wonders whether the balloon valvuloplasty...
performed before TAVR perturbs a very delicate biomechanical balance, inducing further instability in an environment already architectonically challenged. Unfortunately, there are no effective mechanical or pharmacological interventions to reduce the bulk of calcification of the aortic valve, and statins were conclusively shown to have no effect on valvular calcification and the progression of stenosis (8,9). In fact, in vitro cellular experiments suggested a potentially procalcifying effect of statins (10). Hence, as of today, we may be able to predict the development of PVR, but we might not be able to prevent it. The very recent guidelines on treatment of valvular heart disease (11) indicate that TAVR is an acceptable alternative to surgical intervention in patients with a prohibitive risk of surgery (>50% mortality) and a predicted survival >12 months after TAVR (Class I, Level of Evidence: B) and in high surgical risk patients (>10% mortality risk; Class IIa, Level of Evidence: B). However, if a patient has a very high surgical risk, but presents with severe calcification of the aortic valve apparatus, which in turn puts that patient at risk of developing moderate-to-severe PVR, and PVR increases the 30-day and 1-year mortality 2- to 3-fold (2), are we still justified to consider TAVR? Once again, the ever-correct conclusion is that a careful selection of the most suitable patient for the most appropriate procedure is the desirable way to proceed. How does the paper by Khalique et al. (1) help us in this regard? For one thing, it refutes the opinion that one location is worse than another as far as valvular calcification is concerned and refocuses the attention on the extent of calcification rather than geographical considerations. Where the article by Khalique et al. falls short, however, is the lack of an indication of “how much is too much,” that is, a threshold beyond which the risk of moderate-to-severe PVR is too high to attempt the procedure. A few other considerations are also important. The study was performed at a single center by expert operators, and only 1 type of valve was implanted (either of 2 balloon-expandable Sapien valves [Edwards Lifesciences, Irvine, California]). In a recent meta-analysis, Athappan et al. (2) demonstrated that the expected rate of moderate-to-severe PVR is about 12% overall, but the rate is higher for the self-expandable CoreValves (Medtronic, Minneapolis, Minnesota) than the Sapien valves (16.0% vs. 9.1%, p = 0.005). Additionally, the investigators of the current report (1) did not observe any severe PVR (expected in 1.5% to 2% of procedures) and reported moderate PVR in only 9 patients (6%); they further included mild PVR in their analyses of post-procedural complications. According to the large meta-analysis by Athappan et al. (2), mild PVR showed only a trend as a predictor of mortality once sensitivity analyses were conducted by excluding outlier studies and switching meta-analytical methods from random to fixed effect. So are we to be alarmed and forewarned of the dangers of performing TAVR in patients with heavy calcification of the valvular apparatus? More knowledge needs to be accumulated regarding the threshold of calcification that represents a warning sign for development of important post-procedural complications, and whether mild PVR constitutes a true risk. Appropriate pre-procedural planning for TAVR should include careful annulus sizing, quantification of calcium burden, and assessment of left ventricular outflow tract and annulus asymmetry by computed tomography imaging. An accurate assessment of these variables will inform the selection of the most appropriate valve (self-expanding vs. balloon-expanding) to implant, as well as the best patient candidate for TAVR, to improve operative results as well as patient outcomes.

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REFERENCES

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