Prognostic influence of paravalvular leak following TAVI: is aortic regurgitation an active incremental risk factor or just a mere indicator?

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This editorial refers to ‘Paravalvular regurgitation after transcatheter aortic valve replacement with the Edwards sapien valve in the PARTNER trial: characterizing patients and impact on outcomes’, by S. Kodali et al., on page 449.

Transcatheter aortic valve implantation (TAVI) has become the treatment of choice for inoperable patients with severe aortic stenosis and is a valuable therapeutic option for patients at high risk. Recent data suggest that TAVI can also be adopted in intermediate risk patients with competitive results when compared with surgery.

For further expansion of indications, TAVI should, however, be demonstrated to be safe and effective in the longer term, and reduce the rate of complications. Paravalvular leak (PVL) after TAVI is a frequent problem and is considered the Achille’s heel of TAVI. A recent meta-analysis including 12,926 TAVI patients reported a pooled estimate incidence of moderate or severe PVL of 11.7%. A recent meta-analysis including 12,926 TAVI patients reported a pooled estimate incidence of moderate or severe PVL of 11.7%. Residual moderate/severe PVL has a relevant negative prognostic impact and has been associated with an increased risk of all-cause mortality.

More recently, it has been suggested that mild PVR may also be a relevant predictor of mortality, but this association remains controversial.

This report from Kodali et al. represents the largest published single study to evaluate the impact of PVL following TAVI with the Edwards Sapien valve (and one of the largest overall ever reported) on clinical and echocardiographic outcome.

In this analysis, the impact of varying degrees of PVL on mortality as well as changes in ventricular function was evaluated in 2434 patients from the randomized cohorts and continued access registries of the PARTNER Trial. PVL was graded as none/trace in 52.9%, mild in 38.0%, and moderate/severe in 9.1%. Significant differences in baseline clinical and echocardiographic characteristics were observed among the groups, suggesting that patients with moderate/severe PVL were in slightly worse clinical condition. Overall, all patients demonstrated an improvement, with an increase in systolic function and a reduction in left ventricular (LV) mass index. For the first time, it has been reported that the magnitude of mass regression was significantly reduced in patients with residual moderate/severe PVL. The 30-day mortality was not different according to the severity of the PVL, but at 1 year all-cause mortality, cardiac-related mortality, and re-hospitalization rate were significantly increased with worsening PVL. The presence both of moderate/severe PVL [hazard ratio (HR) 2.18] and of mild PVL (HR 1.27) was independently associated with higher late mortality at multivariable analysis.

As the authors stated, the main finding of this study is that, although the differences in the baseline clinical and echocardiographic profile in either mild or moderate/severe PVL independently resulted in impaired clinical outcome and significantly higher 1-year mortality, patients with moderate/severe PVL demonstrated increases in LV end-diameter (LVED) and less reduction in LV mass index when compared with patients with less PVL.

The finding that even mild degrees of regurgitation have a prognostic impact in aortic stenosis patients is in contrast to the traditional belief that aortic regurgitation is a well tolerated condition. Turina et al. reported in a cohort of 80 patients with isolated aortic regurgitation undergoing right and left heart catheterization that all patients suffering from moderate aortic regurgitation were still alive after 4 years. In this cohort, 10-year survival was as high as 79%, irrespective of symptom status. In the same line were the results from the extreme risk CoreValve trial, showing only severe but not mild or moderate PVL being associated with increased 1-year mortality.

What is behind this dissimilarity? Is it patient characteristics? Measurement bias? Haemodynamics of TAVI? Valve properties? The issue remains open. Figures 1 and 2 show an example of PVL management (CoreValve snaring) and an algorithm of the different PVL treatment option, respectively.

Patients’ characteristics may play a role. The French registry has demonstrated that patients with baseline mixed aortic stenosis and...
regurgitation tolerate post-procedural regurgitation better than patients with pure aortic stenosis. The prognostic impact of an acute aortic regurgitation in a patient with diminished LV compliance needs to be further elucidated. In addition, organ function in patients with significant aortic regurgitation can be reduced by acute haemodynamic impairment.
Another confounding factor for the correct interpretation of data is quantification of aortic regurgitation: the majority of the studies reporting PVL incidence and related outcome after TAVI rely on operator-dependent PVL assessment. The study by Kodali et al. tries to overcome this limitation by assessing PVL entity and LV parameters by an independent core lab, even if this is done with semi-quantitative methods. Three-dimensional imaging would permit more accurate quantification of PVL, allowing direct visualization and planimetry of the vena contracta and calculation of the regurgitant fraction. Beside 3D echocardiography, velocity-encoded magnetic resonance imaging (MRI) may be helpful to assess PVL more accurately; it has been demonstrated that 2D transthoracic echocardiography underestimates aortic regurgitation by at least one grade compared with MRI in a substantial proportion of patients. The lack of a standardized methodology to evaluate PVL after TAVI is the main bias determining the discrepancy in the prognostic implications and late evolution observed in the different studies.

As expected, in this study less oversizing (lower cover index) was associated with higher PVL severity. Aortic annulus sizing is crucial to minimize the incidence and severity of PVL. In routine clinical practice, the choice of technique for annulus sizing is multidetector row computed tomography (MDCT), which has been used only in a minority of the patients included in the study by Kodali et al. (the percentage has not been specified). Three-dimensional imaging modalities are superior to 2D techniques to assess the elliptical geometry of the aortic annulus and to minimize the risk of oversizing or undersizing. Implantation of a prosthesis with a nominal area <10% greater than the MDCT annulus area is associated with an increased risk of significant PVL. MDCT is a helpful tool in the assessment of the patients undergoing TAVI, giving a precise one-shot assessment of all the information needed to plan the procedure (visualization of the vascular axis, choice of the access, choice of the prosthesis type and size, evaluation of the coronary artery, and assessment of the calcification). MDCT should be avoided only in selected patients with advanced renal impairment, but use of pre-procedural MDCT may be mandatory to expand TAVI towards lower risk populations.

Multidetector row computed tomography can characterize valve anatomy and, more specifically, calcium distribution and quantification within the annulus and the leaflets. Calcium score and distribution may be associated with PVL due to device malposition and more challenging delivery of the prosthesis. Patients with a higher calcium score carry a higher risk of residual aortic regurgitation, but also higher cardiovascular risk due to the atherosclerotic burden; therefore, residual aortic regurgitation could just be an indicator of higher atherosclerotic burden.

There is light at the end of the tunnel, since the new TAVI prostheses are superior to 2D techniques to assess the elliptical geometry of the aortic annulus. Calcium score and distribution within the annulus and the leaflets. Calcium score and distribution may be associated with PVL due to device malposition and more challenging delivery of the prosthesis. Patients with a higher calcium score carry a higher risk of residual aortic regurgitation, but also higher cardiovascular risk due to the atherosclerotic burden; therefore, residual aortic regurgitation could just be an indicator of higher atherosclerotic burden.

Conflict of interest: F.M. is a consultant for Abbott Vascular, Medtronic, St Jude, and Valtechcardio, receives royalties from Edwards Lifesciences, and is co-founder of 4Tech. F.N. is a consultant for Edwards and Biotronix. M.T. has no disclosures to declare.

References