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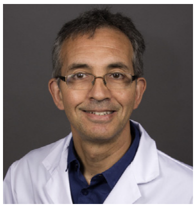

Imaging Is the Cornerstone of the Management of Aortic Valve Stenosis

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Aortic stenosis (AS) is the most prevalent valvular heart disease in developed countries (1.7% in the population older than 65 years) and is directly responsible for approximately 20,000 deaths and 100,000 valve procedures per year in North America. Intervention (either surgical or catheter-based) is the sole effective treatment for symptomatic patients with severe AS, and when to intervene is a critical decision that essentially depends on the assessment of severity, symptoms, and the extent of cardiac damage. Imaging can best assess at least 2 of these 3 triggers, and thus, is key for rational decision making and the performance of the intervention (especially when catheter-based), as well as follow-up post-procedure. Over the years, *iJACC* has published many important papers clarifying the role of imaging in AS (1–8). However, this is an effervescent field with a lot of new and exciting discoveries happening all the time. This month, *iJACC* focuses on "Imaging Aortic Stenosis" as it tries to collate leading research ideas and summarize the current state of the art regarding the role of imaging in the management of AS, both before and after aortic valve replacement (AVR).

IMAGING BEFORE AVR

Doris et al. (9) presents a state-of-the-art review of the role of imaging in measuring disease progression and assessing novel pharmacotherapies in AS. Doppler echocardiography remains the central modality, but aortic valve calcium scoring with non-contrast multidetector computed tomography (MDCT) is a powerful tool to measure the culprit lesion of AS (i.e., valve leaflet calcification) and follow its progression over time. Furthermore, the aortic valve uptake of sodium fluoride measured by positron-emission tomography/computed tomography is a new emerging tool that is able to detect micro-calcification within the valve; therefore, it can detect the disease in its early stage. This imaging technique could provide a robust endpoint for future pharmacotherapy trials in AS.

Low-gradient AS is characterized by the combination of a small aortic valve area (AVA) consistent with severe AS and with a low gradient consistent with nonsevere AS. This entity raises important diagnostic and therapeutic challenges (1). Expanding on their previous work (3,10), Vamvakidou et al. (11) show that mean transvalvular flow rate (stroke volume and/or left ventricular [LV] ejection time) may provide incremental value in terms of post-operative outcomes beyond the stroke volume index in both high- and low-gradient AS. Hybrid (or fusion) imaging that

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combines LV outflow tract area measured by MDCT and flow velocities by Doppler to re-calculate AVA has been proposed to reconcile cases with discordant grading (i.e., small effective orifice area [EOA] with low gradient) on transthoracic echocardiography (TTE). However, in this issue of *iJACC*, Arangalage et al. (12) report that hybrid imaging is probably not the ultimate solution to corroborate AS severity in low-gradient AS because it may increase the proportion of patients with discordant grading. Chetcuti et al. (13) also report that the clinical and hemodynamic outcomes in patients who received transcatheter aortic valve replacement (TAVR) for low-gradient AS in the EUS (CoreValve Expanded Use Study) trial are similar to those with high-gradient AS from the CoreValve US Pivotal Extreme Risk Trial. In contrast to the results of some previous but smaller studies, the current study reports that patients with paradoxical (i.e., preserved LV ejection fraction [EF]) low-flow, low-gradient AS have excellent outcomes following TAVR. The patients with classical (low LVEF) low-flow, low-gradient AS who had no significant flow reserve on dobutamine stress echocardiography also appeared to benefit from TAVR to a similar extent as patients with high-gradient AS. Hence, the message of this study is that TAVR is a valuable option to treat patients with low-gradient severe AS.

The scores that are generally used to assess the risk of mortality following cardiac surgery are not necessarily applicable and suitable for risk stratification in the context of TAVR. Several factors besides the classical risk factors may also influence the outcomes following TAVR. In this issue, 3 articles emphasize the incremental prognostic value of the extent of LV outflow and thoracic aorta calcification measured by MDCT in patients who have undergone TAVR (14–16). In the context of a large multicenter study, Lantelme et al. (16) developed and validated a new score that combines the thoracic aorta calcification assessed by contrast MDCT with classical prognostic factors to predict 1-year mortality following TAVR. This new score may be helpful to assess the balance between treatment usefulness and futility when assessing a patient with severe AS who is being considered for potential TAVR.

IMAGING AFTER AVR

As reviewed by Pibarot et al. (17), prosthesis–patient mismatch (PPM) is characterized by a prosthesis that functions normally but is too small in relation to patient's body size, and thus, cardiac output requirements. PPM is the most frequent cause of high residual transprosthetic gradients following AVR. The differential diagnosis with prosthetic valve stenosis is challenging and requires a thorough imaging assessment that includes primarily TTE and other modalities, such as transesophageal echocardiography (TEE), MDCT, and cinefluoroscopy. One of the key pieces of information needed to be able to predict the risk of PPM before AVR and to make a differential diagnosis between PPM and valve stenosis after AVR is the normal reference values of EOAs for each model and the size of the prosthetic valve. This information was previously available for surgical valves but not for transcatheter valves. In this issue, Hahn et al. (18) report the normal values obtained by the echo core laboratories in several major trials for the most frequently used transcatheter valves according to model and size of prosthesis, as well as the aortic annulus size of the patients. As opposed to the EOAs of surgical valves, the EOA of a given model and the size of transcatheter valve may also vary depending on the aortic annulus size. This article provides a reliable source of reference EOAs that is helpful to assess transcatheter valve function and to identify the cause of high gradient AS, if any. As further emphasized by Coisne et al. (19), the best cutpoint of indexed EOAs to identify PPM and predict outcomes following AVR is <0.85 cm^2/m^2. However, this association between PPM and outcomes was found in lean and overweight patients but not in obese ones, potentially because the indexed EOA might have overestimated the degree of PPM in the latter patients.

The big unknown aspect about TAVR is the long-term durability of transcatheter valves and whether the durability will be equated with that of surgical aortic valve replacement. This question becomes even more critical because the indications of TAVR may expand to lower risk populations in the near future. Prosthetic valve stenosis may occur as a result of nonstructural dysfunction (e.g., thrombosis or endocarditis) or structural dysfunction (e.g., calcific leaflet degeneration). In this issue, Seller et al. (20) report a histopathological analysis of explanted transcatheter valves that suggests that there might be a link between valve thrombosis and structural valve degeneration in transcatheter valves. Based on their observations, they propose that structural valve degeneration might be a sequence of several pathobiological events over time, initiated first by valve leaflet thrombosis, followed by fibrosis, and, then finally, resulting in calcification. Salaun et al. (21)

present a series of cases that illustrate: 1) the role of multimodality imaging in identifying structural valve degeneration in transcatheter valves; and 2) the usefulness of the TAVR procedure to treat failed transcatheter valves.

IMAGING OF LV DAMAGE ASSOCIATED WITH AS

Ultimately, it is more the extent of cardiac damage related to (or associated with) AS, rather than the stenosis severity, per se, that determines the occurrence of symptoms and adverse events. A paper in *iJACC* last year proposed a schema for predicting decompensation based on the degree of damage assessed via cardiac magnetic resonance (CMR) (6). This is the reason why, besides grading AS severity, it is also crucial to assess the degree of cardiac damage at the level of the LV, left atrium, right ventricle, and right atrium chambers (22–26). In this context, approximately one-third of asymptomatic patients with severe AS and preserved LVEF present with some degree of subclinical dysfunction, and these patients have worse outcomes. Early and accurate recognition of subclinical myocardial dysfunction offers the opportunity to optimize the timing of intervention in severe AS. In this issue, Dahl and Carter-Storch (22) present a comprehensive review on this topic and discuss the different imaging modalities and parameters that may be used to identify subclinical dysfunction.

A LVEF of <50% is currently the sole criterion that is included in the American and European guidelines to identify LV systolic dysfunction and trigger intervention in patients with severe AS. However, this criterion lacks sufficient sensitivity to identify subclinical LV dysfunction. In this regard, Bohbot et al. (23) provide further evidence that the current cutoff value of LVEF (<50%) is too low and that a value of <55% would be more appropriate to identify LV dysfunction and to consider AVR in severe AS. Other recent studies even suggested using a LVEF value of <60% for this purpose (22). Gu et al. (22) also proposed a new imaging parameter (i.e., the first-phase LVEF), and they found that this parameter might be superior to the standard LVEF to detect early stages of LV systolic dysfunction in AS. LV global longitudinal strain is another parameter that has been shown to be more sensitive than LVEF to identify LV subclinical dysfunction and to predict outcomes in asymptomatic severe AS. In a meta-analysis of individual participant data, Magne et al. (24) report, that in asymptomatic patients with significant AS and preserved LVEF, impaired LV global longitudinal strain is associated with reduced survival. The studies published in this issue obviously underline the need to refine the parameters and criteria proposed in the guidelines to identify LV systolic dysfunction and consider AVR in severe AS. These refinements include changing the cutoff value for LVEF to 55% or 60% and/or the inclusion of new imaging parameters, such as LV global longitudinal strain.

The extent of myocardial fibrosis as estimated by CMR has emerged as a new valuable tool to assess the extent of LV cardiac damage and enhance risk stratification in AS. In this issue, Park et al. (25) showed that the percentage of extracellular volume measured by CMR using T1 mapping pre- and post-gadolinium injection has the best accuracy to quantitate the extent of diffuse myocardial fibrosis. Several previous studies revealed that there are important differences between women and men with respect to the pathophysiology, diagnosis, outcomes, and response to treatment of AS (27). In this issue, Singh et al. (28) report that, compared with men, women tolerate the AS-related LV pressure overload with less concentric remodeling and myocardial fibrosis but are more likely to develop symptoms. Bartko et al. (29) also report that, among patients with classical low-flow, low-gradient AS who have undergone AVR, women display a higher risk of mortality compared with men. Further studies are needed to understand the sex-related differences in the extent of cardiac damage associated with AS and in the response to treatment. The metabolic milieu may also influence the progression of the disease at both the valvular and ventricular levels. In this regard, Davin et al. (30) found that excessive epicardial adipose tissue was associated with worse outcomes in asymptomatic AS.

Finally, Pibarot et al. (31) presents a review article that makes the argument that even moderate AS may be detrimental in the context of a patient with a depressed LVEF. The outcomes in AS are primarily determined by the imbalance between the magnitude of the LV hemodynamic burden and the capacity of the LV to handle this burden. This article also discusses the provocative hypothesis that TAVR may improve outcomes in patients with moderate AS and systolic heart failure. This hypothesis is currently being tested by the EARLY-TAVR trial.

In summary, this issue of *iJACC* clearly shows the power of multimodality imaging in AS management, both pre- and post-intervention, and sheds light on some of the new ways of looking at this old disease for important insights. Although echocardiography is still the primary modality to fulfill these goals, multimodality imaging provides important complementary information for the optimal management of AS.

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