Aortic valve disease: multimodality imaging for risk stratification and evaluation of therapy

Vollema, E.M.

6

AORTIC VALVE CALCIUM LOAD: DIAGNOSTIC AND PROGNOSTIC IMPLICATIONS IN AORTIC STENOSIS

E. Mara Vollema, Victoria Delgado, Jeroen J. Bax

Published in Circ Cardiovasc Imaging. 2018; 11(3): e007643.

In aortic stenosis (AS), patient management is highly dependent on the accurate evaluation of AS severity. A mean transvalvular pressure gradient ≥40 mmHg, peak aortic jet velocity ≥4 m/s, and an aortic valve area <1.0 cm^2 measured with echocardiography reflect severe AS [1–3]. In the majority of patients with severe AS, these criteria are always present. However, up to 30% of patients with severe AS may show an aortic valve area <1.0 cm^2 despite a low mean transvalvular pressure gradient (<40 mmHg) [4]. This low-gradient severe AS is often the consequence of a low-flow state that may be a result of impaired left ventricular (LV) systolic function (ejection fraction <50%, so-called classical low-flow low-gradient severe AS) or in the setting of severe LV hypertrophy with normal LV ejection fraction (≥50%) and a small LV cavity (paradoxical low-flow low-gradient severe AS) [4]. In patients with classical low-flow low-gradient severe AS, the question is whether the aortic valve does not open because of degenerative (calcific) changes (true severe AS) or because the dysfunctional LV is unable to generate enough stroke volume to open the valve (pseudosevere AS). By increasing LV contractility with low-dose dobutamine infusion, Doppler echocardiography can demonstrate a >20% increase in stroke volume (so-called flow reserve). If the mean pressure gradient increases >40 mmHg and the aortic valve area remains narrow, the diagnosis of true severe AS can be established [5]. However, if the aortic valve area increases to >1.0 cm^2, the underlying problem is likely the LV dysfunction, and the diagnosis is pseudosevere AS. Nevertheless, normalization of the flow cannot be achieved in a considerable number of patients [6]. In patients with paradoxical low-flow low-gradient severe AS, the use of low dose dobutamine stress echocardiography is suboptimal. Assessment of the morphology and calcification burden of the aortic valve can help to identify the patients with true severe AS who may benefit from intervention. Computed tomography is a high spatial resolution imaging technique that clearly displays the morphology of the valve and permits estimation of the aortic valve calcium score (computed tomography aortic valve calcium scoring [CT-AVC]), which has shown good correlation with hemodynamic AS severity and clinical outcomes [7–9]. It is important to note the sex differences in aortic valve calcification burden shown in previous CT-AVC studies [10, 11]. Women have lower aortic valve calcium load than men despite similar hemodynamic AS severity, and therefore, sex-specific thresholds have been proposed (1275 arbitrary units in women and 2065 arbitrary units in men) [9].

In this issue of Circulation: Cardiovascular Imaging, Pawade et al. [12], using data from an international multicenter registry of 918 patients with at least mild AS, aimed to validate those cutoff values and demonstrate the additive clinical value of CT-AVC, in identifying patients with true severe AS among those with low-gradient AS and also to assess the association with clinical outcomes. Patients were divided into (1) concordant nonsevere or severe AS group (N = 708), (2) discordant low-flow AS group (N = 79), and (3) discordant normal-flow AS group (N = 131). In the concordant AS group, 437 (62%) patients had severe AS. Based on these patients, the sex-specific CT-AVC thresholds that provided optimal discrimination of severe AS were 1377 arbitrary units in women and 2062 arbitrary units in men. Among patients with discordant flow AS, 49% presented with a CT-AVC score equal or higher than these thresholds and could have been diagnosed with true severe AS. Specifically, 56% of patients with paradoxical low-flow low-gradient severe AS and 50% of patients with classical low-flow low-gradient severe AS

had CT-AVC values above the proposed thresholds. Interestingly, among patients with high-flow and an aortic valve area >1.0 cm^2, 74% had CT-AVC values exceeding the proposed thresholds.

These findings question the accuracy of CT-AVC to identify the patients with true severe AS based on hemodynamic criteria. The management of patients with AS is not solely based on an isolated number (CT-AVC, aortic valve area, or peak aortic jet velocity) but on an integrated approach that includes symptoms, hemodynamic consequences on the LV, and various morphological and hemodynamic aortic valve variables, all well-known predictors of outcome [2].

The present study also provides prognostic information. The association between these sex-specific CT-AVC thresholds and clinical outcomes was evaluated in only 215 (23%) patients of the concordant nonsevere or severe AS group. During a median follow-up of ≈3 years, 79 patients underwent aortic valve replacement (AVR; N = 59) or died (N = 20). CT-AVC was independently associated with outcomes (hazard ratio [HR]: 1.04; P<0.001).

In the groups of discordant low or normal flow, 17 of 41 patients with follow-up underwent AVR or died. CT-AVC was independently associated with outcomes in these groups (HR: 3.31; P=0.03). Although the number of patients with follow-up was relatively limited, these findings contribute to the existing evidence showing the association between aortic valve calcification load and adverse events. In patients with concordant severe AS and symptoms or impaired LV ejection fraction, assessment of CT-AVC will not be of help because current guidelines recommend AVR (class I)[2, 3]. However, in patients with concordant severe AS who are asymptomatic and have an LV ejection fraction >50% and in patients with paradoxical low-flow low-gradient severe AS, the assessment of CT-AVC may help in the decision making because current recommendations for AVR in these groups of patients are not strong (class IIa) [2, 3]. Whether such an approach will impact on the outcomes of these patients will require randomized clinical trials. The ongoing EARLY-TAVR trial (Evaluation of Transcatheter Aortic Valve Replacement Compared to SurveilLance for Patients With AsYmptomatic Severe Aortic Stenosis, URL: https://clinicaltrials.gov. Unique identifier: NCT03042104), for example, randomizing asymptomatic patients with severe AS to transcatheter AVR versus medical therapy may help to better understand the impact of CT-AVC quantification on outcome.

REFERENCES

[1] Baumgartner H, Hung J, Bermejo J, Chambers JB, Edvardsen T, Goldstein S, et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. Eur Heart J Cardiovasc Imaging. 2017;18(3):254-75.

[2] Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017;38(36):2739-86.

[3] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63(22):e57-185.

[4] Clavel MA, Magne J, Pibarot P. Low-gradient aortic stenosis. Eur Heart J. 2016;37(34):2645-57.

[5] Monin JL, Quéré JP, Monchi M, Petit H, Baleynaud S, Chauvel C, et al. Low-gradient aortic stenosis: operative risk stratification and predictors for long-term outcome: a multicenter study using dobutamine stress hemodynamics. Circulation. 2003;108(3):319-24.

[6] Annabi MS, Touboul E, Dahou A, Burwash IG, Bergler-Klein J, Enriquez-Sarano M, et al. Dobutamine Stress Echocardiography for Management of Low-Flow, Low-Gradient Aortic Stenosis. J Am Coll Cardiol. 2018;71(5):475-85.

[7] Cueff C, Serfaty JM, Cimadevilla C, Laissy JP, Himbert D, Tubach F, et al. Measurement of aortic valve calcification using multislice computed tomography: correlation with haemodynamic severity of aortic stenosis and clinical implication for patients with low ejection fraction. Heart. 2011;97(9):721-6.

[8] Messika-Zeitoun D, Aubry MC, Detaint D, Bielak LF, Peyser PA, Sheedy PF, et al. Evaluation and clinical implications of aortic valve calcification measured by electron-beam computed tomography. Circulation. 2004;110(3):356-62.

[9] Clavel MA, Messika-Zeitoun D, Pibarot P, Aggarwal SR, Malouf J, Araoz PA, et al. The complex nature of discordant severe calcified aortic valve disease grading: new insights from combined Doppler echocardiographic and computed tomographic study. J Am Coll Cardiol. 2013;62(24):2329-38.

[10] Aggarwal SR, Clavel MA, Messika-Zeitoun D, Cueff C, Malouf J, Araoz PA, et al. Sex differences in aortic valve calcification measured by multidetector computed tomography in aortic stenosis. Circ Cardiovasc Imaging. 2013;6(1):40-7.

[11] Simard L, Côté N, Dagenais F, Mathieu P, Couture C, Trahan S, et al. Sex-related discordance between aortic valve calcification and hemodynamic severity of aortic stenosis: is valvular fibrosis the explanation? Circ Res. 2017;120(4):681-91.

[12] Pawade T, Clavel MA, Tribouilloy C, Dreyfus J, Mathieu T, Tastet L, et al. Computed Tomography Aortic Valve Calcium Scoring in Patients with Aortic Stenosis. Circ Cardiovasc Imaging. 2018;11(3):1-11.