Evaluation and Prognosis of Paradoxical Severe Aortic Stenosis after Transcatheter Aortic Valve Replacement

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Abstract

Paradoxical low-flow, low-gradient aortic stenosis (PLFLG-AS) is clinically difficult to diagnose because some moderate grade PLFLG-AS cases can have an aortic valve area under 1 cm^2. Dobutamine stress echocardiogram is one diagnosis method to determine true aortic stenosis, however, not all patients can be identified because the stroke volume might not be increased after dobutamine infusion. Computed tomography is another complementary diagnostic method for determination of severity of aortic stenosis.

The prognosis of PLFLG-AS is worse than the classic high-flow, high-gradient type of aortic stenosis because these patients usually have high comorbidities such as hypertension and atrial fibrillation. LV fibrosis in CMR and hypertrophy on echocardiography reveal impaired LV concentric remodeling. These factors mean poor prognosis at baseline.

TAVR can improve the quality of life and NYHA functional class in PLFLG-AS patients. However, to date, no survival benefit has been shown for this procedure.

Better selection of suitable candidates for TAVR may result in better clinical outcomes.

Keywords: PLFLG-AS, TAVR, severe aortic stenosis

Introduction

According to the ESC guidelines for valvular heart disease, severe symptomatic aortic stenosis without prohibitively high risk for intervention, such as high PARTNER TAVI score or FRANCE 2 TAVI score, should be treated by valve replacement after heart team evaluation.[1] Paradoxical, severe, aortic stenosis diagnosed in patients with normal left ventricular ejection fraction but low transaortic flow (stroke volume index < 35 mL/m^2), is known as paradoxical low-flow, low-gradient (PLFLG) AS.[2]

Medical therapy, transvalvular- and surgical valve replacement are three main treatment choices. Compared with medical therapy, transvalvular aortic valve replacement (TAVR) has obvious mortality benefits and is similar to surgical valve replacement (SAVR).[3]

However, the prognosis, such as survival, for paradoxical severe aortic stenosis is even worse than for normal flow-, pressure gradient-

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and ejection fraction severe aortic stenosis types.[4] Therefore, the proper selection of candidates who are suitable for this intervention is imperative with these patients.

Definition

The 2021 ESC guidelines for valvular disease define severe PLFLG-AS as having an aortic valve area (AVA) less than 1 cm^2, or AVA index less than 0.6 cm^2/m^2, but mean transvalvular pressure gradient less than 40 mmHg, with maximum transvalvular velocity less than 4 m/s, left ventricular ejection fraction (LVEF) more than 50% and stroke volume less than 35 ml.

Outcome after TAVR in paradoxical low-flow, low-gradient aortic stenosis

Most study opinions support that there are survival benefits after the procedure.[5] However, Tribouilloy et al., published in 2015, takes an opposing stance. The study shows similar outcomes in moderate- to severe aortic stenosis for both high-gradient and low-gradient types, but, more importantly, transcatheter aortic valve replacement in PLFLG-AS does not provide an improvement. The rate of heart failure induced hospitalization is also higher after TAVR than after other types of intervention.[6]

Although the one-year functional state after TAVR with PLFLG-AS is worse than with classic severe AS, survival is similar, as found in a prospective TAVR registry.[7]

There are several types of severe aortic stenosis, including normal-flow, high-gradient stenosis (Classic); preserved LVEF (Paradoxical) low-flow, low-gradient stenosis; and reduced LVEF, low-flow, low-gradient aortic stenosis. Compared with the classic type, the paradoxical type has higher CT valve calcium score, usually over 1650 AU. Higher plasma NT-proBNP levels exceeding 1500 pg/ml are also commonly seen in the paradoxical type.[8] The CMR image reveals diffuse fibrosis in the myocardium. Furthermore, paradoxical severe aortic stenosis is accompanied by underlying atrial fibrillation and atrial flutter, with a higher prevalence among females, the elderly and those with impaired LV concentric remodeling. Those who accept the TAVR procedure appear to have worse prognosis, such as higher all-cause mortality, hospitalization related to the valve problem, worsening pulmonary congestion and advanced New York Heart Association functional class, compared to normal-flow, normal-gradient severe aortic stenosis.[9] Chronic pulmonary obstructive disease and initially lower stroke volume index can further increase the risk of treatment futility.[10] Overall, these characteristics contribute to the poor prognosis for PLFLG-AS patients.

Diagnostic coronary angiography

Besides the assessment of aorta and aortic valve, diagnostic coronary angiography should be performed as part of any pre-TAVR workup.[11] Coronary artery disease is very common in elderly patients with multiple CV risk factors. There is no significant difference in the prevalence of coronary artery disease among all types of aortic stenosis, but it does trend higher.[12] Angiography can reveal the severity of coronary artery disease, especially if there are any tight ostium lesions in the left main- and right coronary artery. Obstruction of the coronary arteries during the procedure is a serious complication, contributing to increased morbidity and mortality. For accurate prosthetic valve placement, correct assessments of the location and height of the coronary artery ostium and the capacity of the sinus of Valsalva are very important. Comprehensive evaluation of these measurements can be achieved through coronary angiography, echocardiography and CT scan.

Diagnosis of true, severe PLFLG-AS by transthoracic echocardiography

Classic severe aortic stenosis is usually

marked by a small aortic valve area, defined as less than 1 cm^2, calculated aortic valve index below 0.6 cm^2/m^2 and mean pressure gradient greater than 40 mmHg. However, in paradoxical low-flow severe aortic stenosis, while the valve area is similarly small, the mean pressure gradient lies between 30 and 40 mmHg; the stroke volume is less than 35 mL/m^2 and the ejection fraction is normal. Dobutamine stress echocardiography is one means to confirm whether the case is true severe aortic stenosis. Low dose dobutamine is usually started from 5 μg/kg/min, increasing to a maximum of 20 μg/kg/min. During the infusion of dobutamine, an increase in heart rate and stroke volume may be observed, whereby an increase of 20% in stroke volume is necessary in order to achieve an effective differential result.[13] If the transvalvular pressure gradient increases, but the aortic valve area remains constant, that reveals true aortic stenosis. If the aortic valve area increases, but there is no significant increase in the pressure gradient, severe aortic stenosis is less likely. However, the dobutamine stress exam has some weaknesses, including potential failure to increase the transvalvular pressure gradient due to extremely low LV volume and restrictive filling properties. Moreover, dobutamine infusion may induce LV filling disorder, resulting in cardiac decompensation and arrhythmia.

Another parameter which can be obtained by echo is the measurement of the transvalvular flow rate. It is calculated as the ratio of stroke volume to ejection time. PLFLG-AS patients typically have a lower value than other types of severe AS.[14] Also, the aortic valve area is estimated by the continuity equation and the left ventricular outflow tract (LVOT) size assessment must be as accurate as possible, as a parameter. However, 2D echocardiography assumes that the LVOT is circular, which can obviously lead to measurement error. By contrast, 3D imaging methods such as multi-detector computed tomography (MDCT), cardiac magnetic resonance (CMR) and 3D echocardiography can directly measure the aortic valve area and LVOT area more accurately.

Computed tomography calcium score

According to the ESC guidelines, cardiac CT for the evaluation of aortic valve calcification is suggested in cases of suspected paradoxical severe aortic stenosis. CT imaging can provide anatomic information regarding the sinus of Valsalva, aortic root and ascending aorta. Also, distribution and quality of the aortic valve calcification is a factor of concern for the procedure. The quality of aortic valve calcification can be estimated by computed tomography aortic valve calcium scoring (CT-AVC). The cut-off points for severe aortic stenosis are greater than 2156 Agatston units in males, and greater than 1292 Agatston units for females.[15]

Other authors suggest optimal sex-specific thresholds at 2062 Agatston units in males and 1377 Agatston units in females.[16] Poor prognosis is observed in this group of patients.

Discussion

Severe PLFLG-AS cases are frequently elderly and have comorbidities such as hypertension, atrial fibrillation and coronary artery disease. The imaging characteristics include higher CT calcium score, more hypertrophy as shown by echocardiography and higher fibrosis levels in the myocardium, as shown by CMR. These factors make the outcome of TAVR in PLFLG-AS patients worse than in the typical high-flow, high-gradient type. Also, differentiating true severe PLFLG-AS cases from moderate ones is a very important factor for the prognosis. This is because some of the moderate grade PLFLG-AS cases may have small aortic valve area below 1 cm^2, which should be re-estimated after dobutamine stress echocardiography. However, a routine estimation method is not recommended as it could be graded by high CT calcium score.

No evidence of mortality benefit in severe PLFLG-AS patients has been seen after TAVR. Age, underlying disease, LV remodeling and atrium abnormalities are multiple causes.

Aortic valve replacement can be of benefit

for quality of life, including lowering the NYHA class. This is probably due to improvement of the transvalvular flow rate and pressure gradient. Afterload is decreased once the obstruction by stenosis is relieved.

Conclusion

While there is no survival benefit, we do see a significant improvement in quality of life after the procedure. Pre-procedure evaluation and workup covering comorbidities, valve morphology and aortic calcification can provide predictive post-procedure information.

In addition, accurate diagnosis of true severe aortic stenosis is very important to identify suitable candidates. Given exhaustive pre-procedural evaluation, TAVR is an effective treatment for severe PLFLG-AS patients with high surgical risk.

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