Aortic stenosis (AS) is a common valvular heart disease in the elderly, which causes varying degrees of cardiac dysfunction and, in severe cases, can be life-threatening. It is mostly asymptomatic at an early stage, and symptoms such as chest pain, syncope, and dyspnea are often accompanied by rapid aggravation. A retrospective study by Varadarajan, et al. showed that the 5-year survival rate of patients with severe AS who accepted standard treatment was only 32%, and drug therapy could not improve the prognosis. Traditional surgical aortic valve replacement (SAVR) is effective with low mortality and has been considered as the main treatment. However, at least 30% of severe AS patients with symptoms cannot receive SAVR due to factors such as age, decreased left ventricular function, and comorbidity. Recent studies have shown that transcatheter aortic valve replacement (TAVR) is relatively safe and effective in severe AS patients at intermediate-to-high surgical risk who are considered contraindicated for surgery. This report illustrates a successful procedure in a patient with severe AS and multiple organ dysfunction.

Case Report

A 77-year-old woman was admitted to our Department of Cardiology because of aggravating chest distress and polyneum accompanied by oliguria in 2 days after invalid drug therapy including diuretics and β-blockers at a local hospital. The patient had a diagnosis of severe AS and moderate aortic regurgitation, moderate bicuspid and tricuspid regurgitation, and a pulmonary artery systolic pressure (PASP) of about 91 mmHg 17 months ago. Aortic valve replacement was recommended but rejected by the patient and her family. Chest distress and polyneum recurrently occur due to the irregular use of antihypertensive and diuretic drugs.

On admission, her vital signs included a blood pressure of 91/38 mmHg, heart rate of 130 beats/minute, and oxygen saturation of 80%. Physical examination included distension of the jugular vein and symmetrical edema of lower limbs. Little moist rale could be heard in the lower lungs. The cardiac border was slightly enlarged to the left. Frequent ventricular premature beat and systolic murmurs of grade 4/6 could be heard in the auscultation area of the aortic valve. Laboratory studies showed elevated alanine aminotransferase (174.2 U/L) and creatinine (154.6 umol/L), extremely high brain natriuretic peptide (> 5000 pg/mL), and the estimated glomerular filtration rate was 20.5 mL/minute. Electrocardiography (ECG) showed sinus tachycardia, frequent atrial premature beats with short-term atrial tachycardia, and frequent multifocal ventricular premature beats. Transthoracic echocardiography (TTE)
showed mild mitral regurgitation, calcified aortic valve with severe stenosis, and moderate regurgitation (Figure 1 A), accompanied by weakened activity of the left ventricular wall, peak flow velocity of 5.40 m/second, maximum valve gradient of about 117 mmHg, and mean pressure gradient of 70 mmHg (Figure 1B). The inner diameter of the left atrium was 47 mm, and the left ventricular end-diastolic diameter was 51 mm. The left ventricular ejection fraction was 42%, and PASP was 47 mmHg (Table). Examinations upon admission showed an emergency situation of this patient diagnosed with severe AS with multiple organ dysfunction, including the heart, liver, and kidney. She immediately received continuous blood purification and mechanical ventilation to relieve symptoms.

The Society of Thoracic Surgeons (STS) risk score was 30.82%, and the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II was 21.95%. In consideration of the advanced age, low BMI (14.6 kg/m², 35 kg in weight and 155 cm in height), patient frailty, comorbid conditions, and patient preferences, TAVR was recommended after evaluation by our Heart Team as the patient’s calculated risk of mortality was over 30%, which was at high risk.

Preoperative evaluation and sizing were performed with further computed tomography angiography of the aorta and coronary artery, which was converted into a three-dimensional reconstruction. It showed a tricuspid aortic valve (TAV) with incrassation and mild calcification. The mean diameter of the aortic annulus was 22.0 mm, and the sinus of Valsalva was 26.5 mm × 24.1 mm × 25.5 mm (Figure 1C). Ostium heights of the left and right coronary artery were 10.7 mm (Figure 1D) and 14.9 mm. The diameter of the right femoral artery at the narrowest was 6.7 mm. A Venus A-Valve 23 mm (Venus Meditech,
Hangzhou, China) was successfully implanted. Moderate paravalvular regurgitation was discovered after the release of the valve through angiography and TTE; the aortic valve gradient was about 28 mmHg as measured by catheters. We performed the aortic balloon dilation, and angiography showed a mild leak accompanied with moderate aortic regurgitation after the operation (Figure 2A-D). The aortic valve gradient decreased from 72 mmHg to 15 mmHg (Figure 3A, B). Short-term pulmonary hypertension (Table) and moderate mitral regurgitation (Figure 4A) occurred after TAVR and gradually returned to normal (Figure 4B-D). A 24-hours ambulatory ECG was performed 5 days after the procedure because of a dizziness complaint, which showed a first-degree atrioventricular block (AVB) and frequent intermittent sinus arrests. RR intervals longer than 3000 ms appeared 23 times, and the longest RR interval was 5736 ms. As a result, a permanent pacemaker was implanted. In a follow-up consultation 5 months after the procedure, the patient reported improved cardiac function and symptoms (Table). Currently, the patient weighs 42.5 kg, has a BMI of 17.7 kg/m², and her nutritional condition improved.

**Discussion**

We, herein, have reported a patient with severe AS, multiple organ failure, and recurrent occurrence of shock. Preoperative examinations proved that this patient has severe AS at a high surgical risk. TAVR, which has not been carried out in our center, is a new vascular interventional technique developed rapidly in recent years and is only available in large clinical centers. In China, a considerable population of AS patients, who are often at intermediate-to-high surgical risk, is accompanied with hypertension, diabetes mellitus, and other comorbidities and admitted at a terminal stage. The AHA/ACC Guidelines, which are based on large clinical trials published recently, has provided evidence for such kind of population.

The 2017 AHA/ACC Guidelines recommended TAVR for patients with severe AS and a prohibitive risk for SAVR. TAVR is non-inferior to SAVR in patients at a high or intermediate surgical risk with AS. The newly published PARTNER3 trial included 1000 patients with severe AS at low surgical risk from 71 centers globally. The average STS score was 1.9%. They were randomly assigned to TAVR or SAVR.
allocated into the TAVR group and SAVR group. The TAVR group was performed transfemorally with SAPIEN 3. The SAVR group used biological prosthetic valves. The rates of the primary composite end-point (including all-

Figure 3. Transaortic valve pressure curve. A: Pre-procedure maximum aortic valve gradient (72 mmHg). B: Post-procedure maximum aortic valve gradient (15 mmHg).

Figure 4. Echocardiography image of mitral regurgitation. A: Moderate mitral regurgitation at 3 days after TAVR. B: Mild to moderate mitral regurgitation at 1 week after TAVR. C: Mild regurgitation at 1 month since operation. D: Trivial mitral regurgitation half a year later.
cause mortality, stroke, and readmission) at 30 days and 1 year were significantly lower in the TAVR group than in the SAVR group (4.2% versus 9.3%, \( P < 0.01 \), 8.5% versus 15.1%, \( P < 0.01 \)). There was no significant difference between the 2 groups with regard to the incidence of vascular complications, permanent pacemaker implantation, or intermediate-to-severe paravalvular regurgitation. At the same time, Popma, et al. carried out an Evolut research and found that TAVR with self-expanding valve in low-risk AS patients is not inferior to SAVR.

This patient suffered from chronic AS and lack of standard treatment, which resulted in increased resistance of the left ventricular ejection and intra-cardiac pressure. The pressure reversely transmitted to the pulmonary artery and finally led to heart failure. Low cardiac output caused hypoperfusion of organs, which brought about liver and kidney failures. Severe AS patients with logistic EuroSCORE score > 20%, STS > 10%, or EuroSCOREII ≥ 7% are at high surgical risk. In this case, TAVR was an optimal choice.

The professional evaluation of the aorta and coronary artery before TAVR is significant. Ribeiro, et al. have reported that the mean left coronary artery ostium height was 10.6 ± 2.1 mm, which could be obstructed after TAVR. The left coronary artery ostium height, in this case, was 10.7 mm, exactly at the critical height of obstruction. A narrow aortic root with shallow sinuses of Valsalva might also be a risk factor associated with coronary obstruction after TAVR. Therefore, this procedure requires experienced TAVR operators and good teamwork. In addition, an oversized valve could easily lead to occlusion of the coronary artery opening and abnormal cardiac conduction after surgery. In severe cases, it may even cause aortic root rupture. Too small a valve may lead to severe paravalvular leakage and even displacement of the valve, increasing the probability of prosthesis-patient mismatch. In addition, our Heart Team inserted the balloon dilation system into the left anterior descending branch beforehand to avoid coronary obstruction.

The patient who had no history of chronic lung diseases showed short-term postoperative PAH, which was confusing. AS elevates the left ventricle filling pressure, which results in a passive backward transmission to the pulmonary circuit. This may even contribute to pathogenic alteration, eventually leading to pulmonary hypertension associated with left heart diseases. When AS is treated, pulmonary pressure could decrease with that of left ventricle if pulmonary arteries remained their compliance. The mechanisms of short-term PAH may be due to multiple factors. We paced the right ventricle with 180 beats/minute to reduce aortic pressure, transient but remarkably reduced cardiac output may lead to hypoxic environment and injured pulmonary vascular endothelial cells and myocardial tissue reversibly as a result. The injuries promoted vasoconstriction and tachyarrhythmias may participate PAH. Impaired vascular endothelial cells, leukocytes, and C-reactive protein (CRP) play significant roles in microvascular thrombosis. Studies have found that impaired vascular endothelial cells can induce a pro-inflammatory phenotype and trigger the recruitment of neutrophils. Platelets support the accumulation of leukocytes and promote the formation of neutrophil extracellular traps, resulting in an immune-inflammatory response leading to the transmission of FXII-dependent thrombi and the reduction of platelets. Inflammation and stress responses are accompanied by an increase in CRP and albumin consumption. Data from Duman, et al. found that thrombus load is associated with the increase of CRP and the CRP-albumin ratio (CAR). The changes in white blood cells, neutrophils, CRP, and CAR in this patient were consistent with the trend of PASP in the perioperative period, while the reverse was observed in platelets (Figure 5). Therefore, it is speculated that microvascular thrombosis may be one of the causes of short-term PAH. Furthermore, pain and psychentonia might increase pulmonary circuit resistance with excitation of the sympathetic nervous system. Therefore, pulmonary artery pressure in some patients with severe PAH will not be significantly improved and will be abnormally elevated in the short-term after TAVR. Perioperative cardiopulmonary protection is helpful to improve hemodynamic status. With the improvement of heart function, BNP gradually decreased until it returned to a normal level 1 month after operation (Figure 5).

Postoperative complications after TAVR include vascular complication, conduction system injury, paravalvular leakage, stroke, myocardial infarction, and aortic valve regurgitation. The rate of conduction system injury, mostly AVB or bundle branch block, ranges from 4% to 30% because the cardiac conduction system is adjacent to the aortic annulus. Approximately 7%~39.3% of the cases require permanent pacemaker implantation after TAVR. To some extent, this kind of injury could be avoided with a sizable valve and attention to the anatomic relationship between the cardiac conduction system and aortic annulus. Sinus arrests and first-degree AVB were found in our patient after the operation. Since there were no symptoms related to sinus node dysfunction, no evidence has been seized in preoperative tests. Sinus node dysfunction could be hardly caused by TAVR because of a certain theoretical distance between the valve implantation site and the sinus node, and the operation did not affect the sinus blood supply. Therefore, we speculate that the patient had a potential sinus node dysfunction before TAVR. Despite this, we cannot utterly rule out the possibilities associated with the operation. The new onset of AVB may be due to TAVR or related to binodal disease. After implantation of the pacemaker, the patient’s heart rhythm became stable with sporadic atrial or ventricular premature beats. Nearly 11 months after surgery, the result of the follow-up showed that the atrioventricular node function almost recovered, but sinus node dysfunction may still exist.

In addition to common TAV lesions, patients with bicuspid aortic valve (BAV) lesions make up a large proportion in China and share common characteristics such as large aortic annulus and sinus of Valsalva, wide ascending aortic dimensions, and severe calcification. Studies have found that there is no significant difference in the incidence of adverse events after TAVR between patients with BAV and those with TAVR. A research that included 2691 propensity-score matched pairs of bicuspid AS and tricuspid AS showed no significant difference between the
BAV and TAV groups, with regard to the incidence of successful valve implantation, valve hemodynamics and functional status, mean aortic valve gradient, procedure complications, and 30-day or 1-year mortality. With a higher stroke rate in patients with bicuspid AS at 30 days but no significantly differ at 1 year between 2 groups. This may be due to the greater calcium burden and more frequent balloon dilation, which could lead to cerebral microthrombus. We are expecting more clinical trials to validate the efficacy and safety of TAVR in patients with bicuspid AS.

The successful treatment of this case of severe AS, multiple organ failure, and recurrent occurrence of shock has provided our center with rich experience. With an increasingly enlarged adaptive population, upgrade of aortic valve bioprostheses, and accumulated experience of operative skills and perioperative management, TAVR will become a preferred interventional treatment of heart valve disease.

Disclosure

Conflicts of interest: None.

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