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Symptomatic aortic regurgitation treated by transcatheter aortic valve implantation in young patients with congenital aortic stenosis

Short title: Transcatheter aortic valve implantation in two very young males

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INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is a treatment method especially used for older patients with severe aortic stenosis (AS). Although it is also used in patients younger than 75 years old, and the long-term performance of TAVI bioprosthetic valves appears to be good [1], this method is still rarely used in patients under 30 years of age. Since its introduction by Cribier et al. [2], the TAVI method has gained recognition in guidelines following numerous studies confirming its effectiveness in AS [3]. In cases of severe aortic regurgitation (AR), surgical aortic valve replacement (SAVR) is the preferred treatment. However, in some patients where

SAVR is not feasible, TAVI may be used [4]. Short-term outcomes in patients with AR after TAVI are acceptable [5], but data from randomized clinical trials are still lacking [6].

METHODS

We retrospectively screened the tertiary heart center database for patients treated with TAVI between 2018 and 2022. The inclusion criteria specified that patients needed to have very high risk of SAVR, and that AR had to be the indication for TAVI. Additionally, the patients had to be under 30 years of age and give written informed consent for the procedure. Patients eligible for SAVR were excluded. Data regarding medical history, comorbidities, diagnostic and hemodynamic procedures, and TAVI outcomes were extracted.

Statistical analysis

We calculated the ratios of pre-TAVI to post-TAVI hemodynamic and echocardiographic measurements as percentages for all patients included in the study and compared them using the plain observation.

RESULTS AND DISCUSSION

Two young patients who had undergone TAVI due to AR were identified.

The first patient was a 24-year-old male with severe symptomatic AR. His medical history included congenital AS, which was repaired by surgical aortic valvulotomy in the first year of life, and balloon aortic valvuloplasty at the age of 11. He developed persistent atrial fibrillation (AF), requiring multiple electrical cardioversions, and pulmonary hypertension (PH) with increased pulmonary capillary wedge pressure (PCWP) as an etiology. The patient complained of decreased exercise tolerance — New York Heart Association (NYHA) class III — stinging chest pain, heart palpitations, and fainting episodes. Transthoracic echocardiography (TTE) showed severe AR with mild AS, severe tricuspid regurgitation, moderate mitral regurgitation, and mild pulmonary regurgitation. Cardiac magnetic resonance imaging revealed enlargement of both atria and the right ventricle. In a 6-minute walking test, he achieved a distance of 405 m. The patient declined consent for SAVR due to the associated surgical risk and was therefore qualified for TAVI. The implantation was performed at the age of 24 without complications, resulting in optimal hemodynamic outcomes: mean pulmonary arterial pressure (mPAP) decreased from 45 to 22 mm Hg — a reduction of 51.11% - and PCWP decreased from 21 to 14 mm Hg — a reduction of 33.33% (Figure 1A–C). After the procedure, significant clinical improvement was observed in all symptoms, with exercise tolerance

increasing to NYHA class I. Two ablations were performed to treat AF episodes. At the 1-year follow-up, reductions in the degree of regurgitation of other valves and the sizes of heart chambers were observed in TTE. For example, the right ventricle inflow diameter 1 decreased from 58 to 40 mm — a reduction of 31.03% - and the right atrial area decreased from 22 to 16 cm^2 — a reduction of 27.27%.

The second patient was a 22-year-old male with symptomatic AR. His medical history included congenital critical AS, which was repaired by surgical aortic valvuloplasty on the third day of life, and a persistent arterial duct with a bidirectional shunt that was disqualified from closure. He developed PH and chronic heart failure with preserved ejection fraction. The patient also developed persistent supraventricular arrythmias, including atrial flutter and AF, which were treated with multiple electrical cardioversions, ablations, and amiodaron, leading to liver dysfunction. Four years before the decision on intervention, during a spiroergometric test, he reached a peak oxygen uptake of 20.9 ml/min/kg, which was 42% of the value predicted for his sex and age, and presented with desaturation. The patient also experienced a hypotensive reaction at the peak of exercise during an exercise test. In the 6-min walk test, he covered a distance of 225 m. TTE revealed moderate AR with mild AS, moderate mitral regurgitation, a left ventricle of borderline size with good contractility, enlarged right ventricle, both atria, and other signs of PH. Due to difficulties in TTE evaluation, diagnostic heart catheterization was performed, revealing that AR was hemodynamically significant with increased PCWP. The patient had PH of complex etiology (left heart disease and a bidirectional shunt) and was classified as NYHA class III/IV. Therefore, he was qualified for an intervention on the aortic valve to reduce left ventricular overload. Due to the high surgical risk, he was disqualified from SAVR and qualified for TAVI. The implantation was performed at the age of 22, with an optimal result, showing no residual AR after the procedure: PCWP decreased from 32 to 20 mm Hg — a reduction of 37.50% (Figure 1D–F). After the procedure, clinical improvement to NYHA class I was reported. At the 1-year follow-up, a reduction in the sizes of heart chambers was observed in TTE. For example, the right ventricle inflow diameter 1 decreased from 40 to 32 mm — a reduction of 20.00% — and the right atrial area decreased from 18 to 12,3 cm^2 — a reduction of 31.67%. However, episodes of supraventricular arrythmias, the bidirectional shunt, and severe PH persisted: mPAP was 85 mm Hg before TAVI and 96 mm Hg after TAVI — an increase of 12.94%.

To our knowledge, there are no trials on TAVI in patients younger than 30 years of age. We described two cases of patients in this age group who, in addition, had AR as the indication for the procedure. There are several similarities when comparing these cases. Both patients had

congenital AS repaired at a young age, which later complicated their lives with symptomatic AR, AF, and PH. Among newborns with congenital AS, approximately 10% require aortic valvuloplasty. Within 5 to 14 years, significant AR develops in approximately 30% of these patients, often leading to PH [7]. Development of PH of complex etiology in the second patient was the reason, why bidirectional shunt was not closed in childhood, nor inhaled nitric oxide test was performed. Nonetheless he was under careful cardiological surveillance. Both patients showed acceptable improvements after TAVI, with almost all hemodynamic and echocardiographic measurement ratios being comparable. Achieving this in AR is challenging due to the lack of calcifications for valve deployment, high stroke and regurgitant volumes, and the large size of the aortic annulus [6]. In the second patient, TAVI - being the only treatment option - successfully reduced PCWP, which resulted in higher mean aortic pressure and clinical improvement to NYHA class I with dramatic change in exercise tolerance and quality of life. The higher mPAP observed after TAVI in this patient can be explained by a higher mean aortic pressure after the procedure (96 mm Hg) compared to before the procedure (75 mm Hg), along with the persistent arterial duct with a shunt. In the described cases, challenging lifelong vitamin K antagonist therapy was not needed after TAVI, but it would be required following the implantation of mechanical prostheses during SAVR [8], which is an important consideration for young patients. Additional reasons TAVI can be preferred by patients in this age group are low invasiveness and avoidance of open-heart surgery, but the uncertainty about the long-term survival and valves durability should always be considered [9].

In conclusion, TAVI can be a viable therapeutic option for very young patients with AR. Further studies are needed to assess the efficacy of TAVI in unconventional patient groups and its long-term outcomes.

Article information

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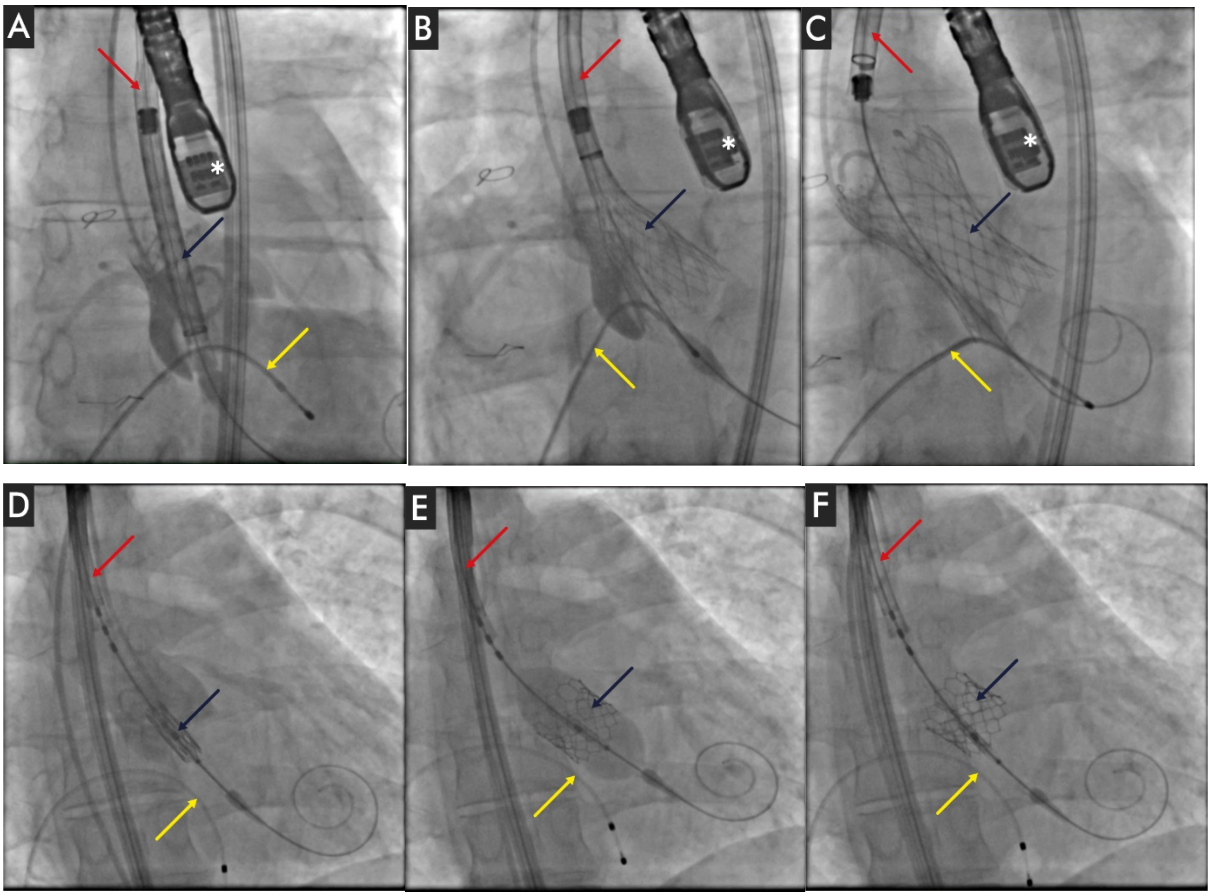

Figure 1. A–C. Course of the transcatheter aortic valve implantation procedure in the first patient: valve positioning (**A**), gradual valve self-expansion by pulling the delivery catheter upwards (**B**), and control fluoroscopy (**C**). The Evolut R34 valve (dark blue arrow), delivery catheter (red arrow), temporary pacemaker lead in the right ventricle (yellow arrow), and transesophageal echocardiography probe (white asterisk) are visible. **D–F.** Course of the transcatheter aortic valve implantation procedure in the second patient: valve positioning (**D**), balloon expansion of the valve (**E**), and control fluoroscopy (**F**). The Sapien 3 valve (dark blue arrow), delivery catheter (red arrow), and temporary pacemaker lead in the right ventricle (yellow arrow) are visible