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Case reports in heart valve disease 2022

Edited by
Verena Veulemans, Maximillian A. Rogers and Giuseppe Tarantini

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Case reports in heart valve disease: 2022

Topic editors

Verena Veulemans — University Hospital of Düsseldorf, Germany
Maximillian A. Rogers — Intellia Therapeutics, Inc., United States
Giuseppe Tarantini — University of Padua, Italy

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Elena Aikawa,
Harvard Medical School, United States

*CORRESPONDENCE
Maximillian A. Rogers
maxarogers@gmail.com

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Editorial: Case reports in heart valve disease: 2022

Maximillian A. Rogers[1]*, Giuseppe Tarantini[2] and Verena Veulemans[3]

[1]Department of Medicine, Harvard Medical School, Boston, MA, United States, [2]Department of Cardiac, Thoracic and Vascular Sciences and Public Health, University of Padova, Padova, Italy, [3]Department of Cardiology, Pulmonology, and Vascular Diseases, University Hospital Düsseldorf, Düsseldorf, Germany

KEYWORDS

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Editorial on the Research Topic
Case reports in heart valve disease: 2022

Heart valve disease affects tens of millions of people worldwide (1), greatly impacting loss of function, quality of life, and mortality. Each year we learn more about conditions impacting patients with the aim of better identifying, treating, and reducing this significant global health burden. 2022 continued this aim, with 10 interesting case reports being published that enhanced our knowledge of these areas, summarized in **Table 1**. Heart valve disease can originate from bacterial infections as well as valve functional and degenerative causes. In low- and middle-income countries, rheumatic heart disease that results from damage to heart valves caused by rheumatic fever incidents is the most common form of heart valve disease. Whereas functional and degenerative valvular diseases predominate in high-income countries (1). The case reports in this collection span these conditions, giving a large array of heart valve disease causes, identification, and treatment recommendations relevant to heart valve clinicians and scientists around the world. A high impact was reached by this collection with thousands of article views and downloads in the past year.

Understanding emerging causes, effective treatments as well as gaps enables the clinical and research communities to best address heart valve disease originating from bacterial infections. Rheumatic heart disease, an autoimmune inflammatory reaction with streptococci has been almost eradicated in several parts of the world. However, it remains the most common cardiovascular disease in children and young people worldwide, impacting vulnerable communities in sub-Saharan Africa, the Middle East, South-East Asia, and Western Pacific. Despite declining rheumatic heart disease burden, the 2015 Global Burden of Disease study estimated 29.7–43.1 million cases and about 300,000 associated deaths (2). Early diagnosis through means like echocardiography when prophylaxis is most likely to be effective in treating patients is a major strategy in managing this disease (3). Beyond early prevention, knowing treatment options likely to benefit patients, particular with less commonly observed complications is of importance. In this collection, Zhou et al. report a successfully managed case of rheumatic right-sided valve disease, a rarely affected tissue that may result in severe rheumatic pulmonary regurgitation, by surgical valvular reconstruction.

Infective endocarditis occurs by infection of the endocardial surfaces of the heart and can be fatal if not treated. The annual incidence is estimated at 3–10/100,000 and has a mortality of up to 30%, with *Staphylococcus aureus* being the most prevalent cause followed by

TABLE 1 Summary of 2022 case reports in heart valve disease.

Heart valve disease	Article title and reference	Key points and implications
Rheumatic heart disease	Surgical valvular pulmonary reconstruction for a previous unreported rheumatic right-sided valve disease with severe pulmonary regurgitation Zhou et al.	A very rare case of rheumatic right-sided valve disease with severe pulmonary valve contracture and regurgitation was successfully managed with surgical valvular reconstruction
Infective endocarditis	Infective endocarditis cause by Streptococcus sinensis: the first case in mainland China and literature review Zhang et al.	*Streptococcus sinensis* isolated from a young patient with infective endocartisis in mainland China, supporting that may be an emerging pathogen of interest
Native valve endocarditis and valve prostheses endocarditis	Treatment of left-sided valve endocarditis using the transapical AngioVac System and cerebral embolism protection device: a case series Fiocco et al.	Combined use of AngioVac System and cerebral embolism protection system Triguard may be useful for treating left native valve and valve prostheses endocarditis in prohibitive-surgical-risk patients
Aortic stenosis with coronary artery disease	Transcatheter aortic valve replacement in patients undergoing robotic totally endoscopic coronary artery bypass: a case series Srivastava et al.	Demonstration of a hybrid approach treating aortic stenosis with TAVR under conscious sedation prior to robotic off-pump totally endoscopic coronary artery bypass graft surgery as an effective treatment
Aortic valve replacement complication	Paravalvular regurgitation post transcatheter aortic valve replacement: when in doubt choose cardiac magnetic resonance Hadley et al.	Cardiac magnetic resonance provides a more accurate assessment of paravalvular leak severity following TAVR
Aortic valve replacement complication	Severe structural valve deterioration after TAVR with ACURATE Neo: report of two cases Schaeffer et al.	Structural valve deterioration of TAVR prostheses is an uncommon complication that can occur
Aortic valve replacement complication	Emergently alteration of procedural strategy during transcatheter aortic valve replacement to prevent coronary occlusion: a case report Dai et al.	Comprehensive assessment of coronary risk should be made prior to TAVR. A short-stent prosthesis is feasible for patients with high coronary occlusion risk; however, TAVR should be called off when extremely high risk coronary obstruction is identified and no solution can be found
Quadricuspid aortic valve	Surgical repair of a quadricuspid aortic valve with severe regurgitation utilizing "tricuspidization" and annular banding: a case and technique details report Yu et al.	In a rare case a patient with flexible and reservable cusps allowed for aortic root reconstruction using a tricuspidization and annular banding technique
Surgical tricuspid valve repair complication	Transcatheter edge-to-edge repair after prior surgical tricuspid annuloplasty Afzal et al.	Tricuspid transcatheter edge-to-edge repair is an alternative and less invasive option for patients with a failed previous annuloplasty repair for tricuspid regurgitation
Mitral valve regurgitation	Cardiovalve in mitral position additional solution for valve replacement Sherif et al.	Transfemoral mitral valve replacement treated severe mitral regurgitation due to severe restriction of the posterior mitral leaflet

streptococci infection (4). Zhang et al. report a case of infective endocarditis in mainland China associated with streptococcus sinensis, contributing to an increasing number of cases reported with this emerging pathogen. Surgery is used in acute heart failure following large vegetations, but a substantial number of patients have high surgical risk necessitating alternatives that have low or acceptable risk for patients. One alternative is the AngioVac System for mass removal. Also in this collection of case reports, Fiocco et al. present a case series with AngioVac System utilization and the cerebral embolism protective system Triguard. These authors validate this hybrid approach by treating prohibitive-surgical-risk patients in a way that reduces cerebral embolization risk stemming from this mass removal system.

Transcatheter aortic valve replacement (TAVR) is a minimally invasive procedure used frequently in high-income countries to treat aortic stenosis patients who are at risk for death from surgery. TAVR has also been suggested to be noninferior to surgery in low-surgical-risk patients (5). TAVR may also be combined with other procedures, as exemplified by Srivastava et al., who report a case series in which TAVR was safely completed prior to coronary revascularization for patients with coronary artery disease and aortic stenosis. Although highly effective, TAVR is not entirely without risk. Paravalvular leak is a complication that can follow TAVR, and one with which Hadley et al. provide support of using cardiac magnetic resonance to more accurately assess. While uncommon, structural valve deterioration of TAVR prostheses is another concern, as shown in the cases reported by Schaeffer et al. in this collection. Coronary occlusion is another uncommon but fatal complication of TAVR, which Dai et al. highlight the importance of performing a comprehensive coronary risk assessment to avoid. The management of coronary artery disease with severe aortic stenosis is particularly important with extension of transcatheter aortic valve implantation to younger and lower-risk patients, discussed in detail in a consensus statement on this topic (6). Quadricuspid aortic valve is a rare congenital disease, in which most patients are treated with aortic valve replacement. However, valve reconstruction can be an alternative to replacement. In this collection, Yu et al. report a case in which tricuspidization and annular banding technique was applied in a patient with cusps that allowed for corrective reconstruction. In addition to the aortic valve, both surgical and minimally invasive procedures are used to treat patients with other forms of heart valve disease. Surgical tricuspid valve repair is another lifesaving procedure but is also with risk. Tricuspid regurgitation may occur following surgical tricuspid valve repair, and Afzal et al. report a case where tricuspid transcatheter edge-to-edge repair was successfully used in a patient with massive tricuspid regurgitation after surgery. Mitral regurgitation is similarly a risk factor for mortality, and Sherif et al. support minimally invasive transcatheter mitral valve replacement to correct this condition.

Knowing the major and emerging causes of heart valve disease, and how to effectively treat them with minimal risk to patients is paramount to achieving declines in patient mortality. While the

reports here represent a single or in some instances a small series of cases, they add to that larger goal by providing the heart valve community with greater knowledge on rare conditions as well as best practices to reduce patient treatment risks.

Author contributions

MR: Writing – original draft, Writing – review & editing. **GT:** Writing – review & editing. **VV:** Writing – review & editing.

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CASE REPORT
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Surgical Repair of a Quadricuspid Aortic Valve With Severe Regurgitation Utilizing "Tricuspidization" and Annular Banding: A Case and Technique Details Report

*Yang Yu, Ruixuan Huang, Zheng Ding, Enyi Shi and Tianxiang Gu**

Department of Cardiac Surgery, The First Hospital of China Medical University, Shenyang, China

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Edited by:
Cuntao Yu,
Chinese Academy of Medical Sciences and Peking Union Medical College, China

Reviewed by:
Shintaro Katahira,
School of Medicine, Tohoku University, Japan
Vladimir Uspenskiy,
Almazov National Medical Research Centre, Russia
Payam Akhyari,
Heinrich Heine University of Düsseldorf, Germany

****Correspondence:***
Tianxiang Gu
sey2004@sina.com

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The quadricuspid aortic valve (QAV) is a rare congenital disease with a prevalence of 0. 013–0.043% of cardiac cases. Most patients with QAV are treated with aortic valve replacement. A Type B QAV with dilated ascending aorta of 47.9 mm; combined with severe regurgitation is reported here. In this case, considering the patient's cusps are flexible and reservable, the aortic root was reconstructed utilizing tricuspidization and annular banding technique, and dilated ascending aorta was replaced at the same time.

Keywords: quadricuspid aortic valve (QAV), aortic valve replacement (AVR), aortic valve repair (AV repair), root banding, heart failiure

INTRODUCTION

The quadricuspid aortic valve (QAV) is a rare congenital disease that is prevalent in 0.013–0.043% of cardiac cases (1). Most patients with QAV are treated with aortic valve replacement (3). A patient with Type B QAV, a dilated ascending aorta of 47.9 mm, and severe regurgitation was reported here (2). In this case, considering that the patient's cusps were flexible and reservable, the aortic root was reconstructed utilizing tricuspidization and annular banding techniques as the dilated ascending aorta was replaced (**Figures 1**, **2**).

CASE PRESENTATION

A 45-year-old man suffered from a dysfunctional QAV (Hurwitz classification, type B) with severe aortic insufficiency (AI), decompensation heart failure, and intermittent atrial fibrillation. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) indicated a Type B QAV with a dilated ascending aorta of 47.9 mm (**Figure 2A**). TTE found that the left ventricular end-diastolic diameter was 77 mm and had a reduced ejection fraction of 39%. Modified "tricuspidization" of QAV, an innovative technique, and aortic valve annular banding were utilized to correct aortic valve insufficiency, and the ascending aorta was replaced at the same time.

Surgery was performed under moderate hypothermic cardiopulmonary bypass (CPB) support. After clamping, QAV was further confirmed by direct exploration. After cross-clamping, cardiac arrest was induced by antegrade cardioplegia solution perfusion and protected by continuous retrograde perfusion. Four interrupted U sutures were used to retract each commissure upward

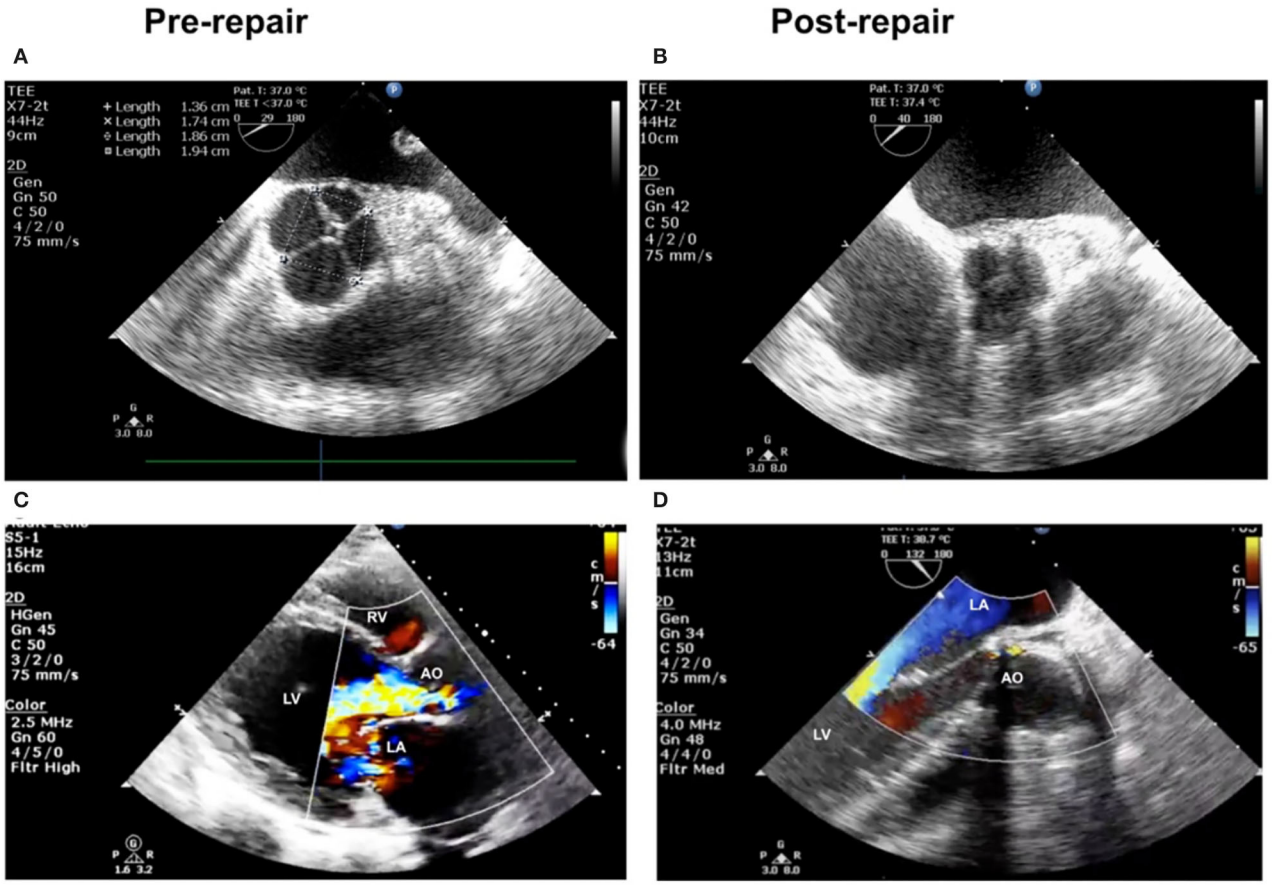

FIGURE 1 | (A) Pre-operation: quadricuspid aortic valve (QAV). **(B)** Post-operation: QAV to tricuspidization aortic valve (TAV). **(C)** Transthoracic echocardiogram (TTE) demonstrated severe regurgitation before operation. **(D)** Post-operation image of transesophageal echocardiography (TEE) showed no regurgitation.

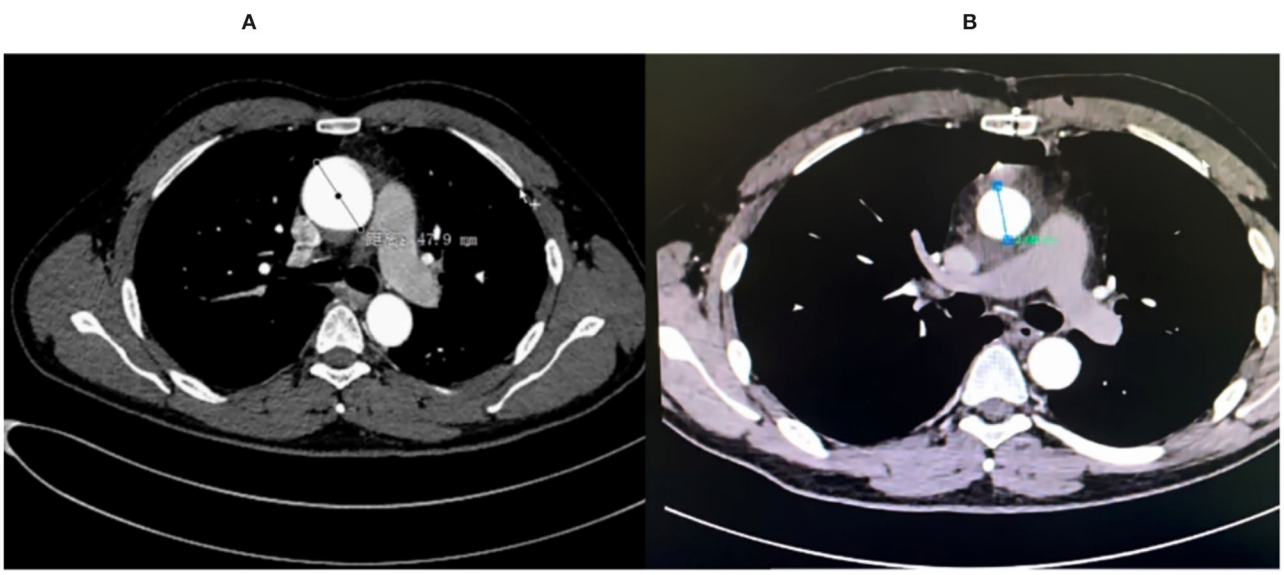

FIGURE 2 | (A) The pre-op CT angiography (CTA) showed ascending aortic aneurysm of 47.9 mm. **(B)** The post-op CTA scan showed normal ascending aortic size.

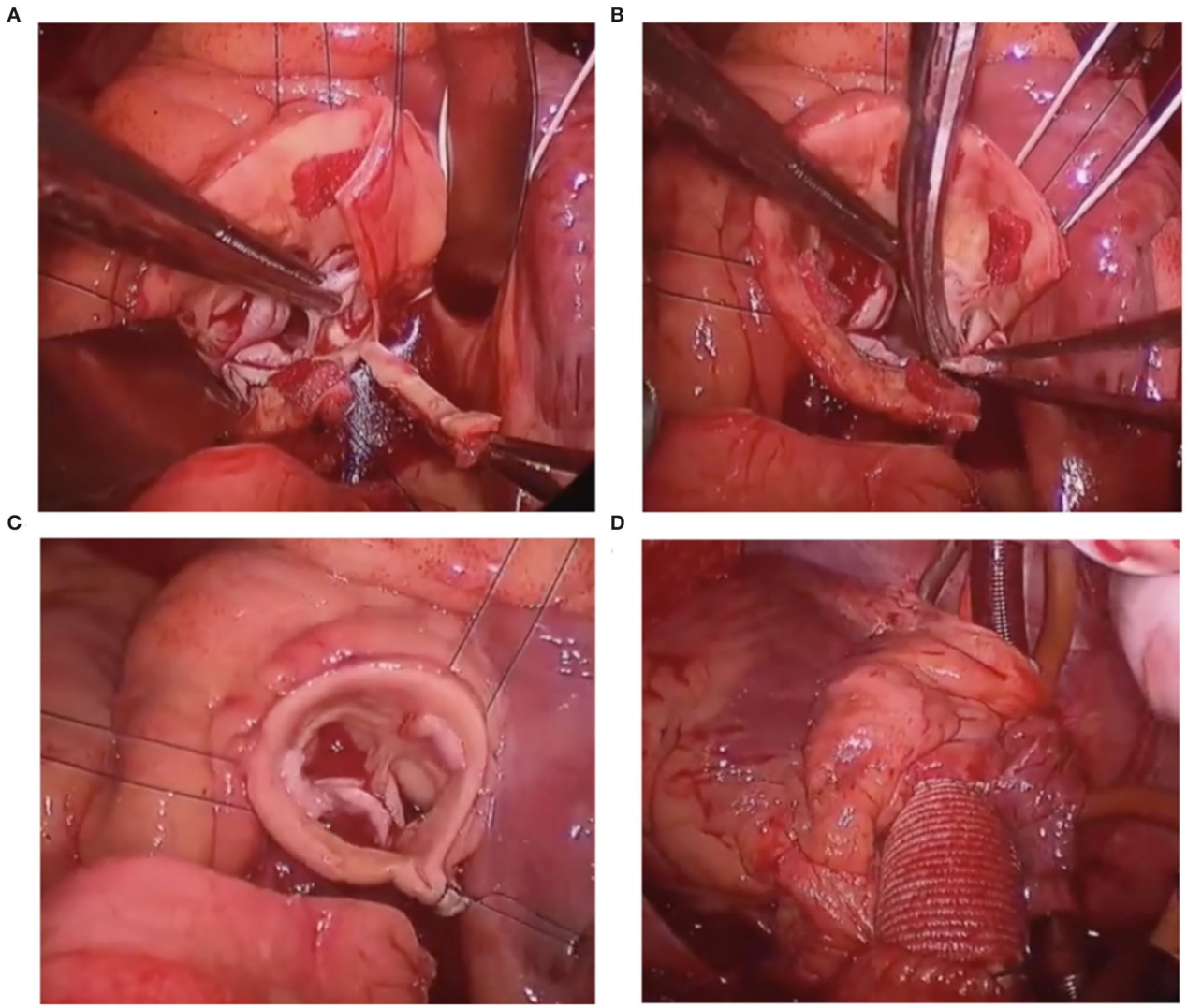

FIGURE 3 | (A) Resect the aortic tissue from sinotubular junction (STJ) downwards to the sinus nadir of the smallest cusps. **(B)** Resect the smallest cusp. **(C)** Reconstruct the root by a horizontal running mattress suture. **(D)** Utilizing a 24-mm Dacron graft to replace the ascending aortic aneurysm.

to assess the cusps after cutting open the ascending aorta transversely. QAV was asymmetrical, and there were three cusps of equal size and one smaller cusp. This smaller cusp was twisted and prolapsed, which contributed to the regurgitation. The aortic root was further dissected to the annular level, and two coronary orifices were identified. A continuous suture, using CV-0 sutures, was performed around the annulus. Thereafter, vertical resection of the smaller sinus and the cusp was performed. The aortic root was reconstructed by horizontal running mattress sutures, with 5-0 Prolene sutures, for "tricuspidization". The CV-0 sutures were then tied with a 20-mm Hegar dilator into the left ventricular outflow tract (LVOT). Afterward, the aortic valve function, cusps position, and coaptation were carefully examined to ensure that there was no leakage or stenosis. Finally, a 24-mm Dacron graft was used to replace the ascending aorta (all the main surgical steps are shown in **Figure 3**).

Heartbeat was reinitiated, and there was no arrhythmia after unclamping. TEE showed that the residual three cusps functioned well without regurgitation or stenosis (**Figures 1B,D**). The patient recovered uneventfully and was discharged within 2 weeks. A short-term follow-up of 12 months showed no recurrence of AI, and the aortic aneurysm was resolved (**Figure 2B**). The left ventricle diameter decreased to 51 mm as the EF value increased to 64%. The patient did not experience significant complications or discomfort.

DISCUSSION

Dysfunctional QAV with aortic aneurysm is rare, and surgical repair to preserve the valve is challenging. Tricuspidization, a rare but efficient technique, was chosen to simultaneously repair

aortic cusps and replace a dilated ascending aorta. A study of QAV by Dr. Pattersson and Dr. Svensson from Cleveland Clinic (4) indicated that 7 patients with QAV underwent surgical repair, 4 of whom underwent "tricuspidization". According to Dr. Pattersson and Dr. Svensson, accessory cusps were resected but the sinus and related aortic root components were not resected. With their technique, residual cusps may have unequal pressure on blood flow. We modified "tricuspidization" by cutting off all the root tissue, including the cusp, sinus, and related STJ, to obtain better performance for blood flow based on our limited understanding. Annular banding was performed at the same time to avoid the recurrence of AI, which was attributed to dilation of the aortic annulus. Moreover, the **Supplementary Materials** show the surgical steps and techniques in detail (case presentation and video clips).

In some reports, QAVs are seen as abnormal septation of the truncus arteriosus or abnormal septation of one of the endocardial cushions (5). A biomechanical study of QAV has been reported for normal aortic valves (6), which means that QAVs have a high risk of forming aortic aneurysms due to congenital defects. In similar operations to correct QAV, transcatheter aortic valve implantation is used to cure QAV stenosis (7). A patient with a Type F QAV underwent surgery to remove the entire aortic root and repair the remaining cusps with its pericardial patch (8). Similarly, a patient with a Type A QAV underwent surgical repair to convert four aortic valves into two (9). The David procedure was applied to 2 QAV patients with dilated roots and AI in our center.

This technique prevents complications associated with anticoagulant use or reoperation. Therefore, valve function can be restored with better hemodynamic performance compared with that of prosthetic valves and other surgical techniques according to short-term follow-up. However, long-term follow-up is necessary to further evaluate the technique.

CONCLUSION

The tricuspidization technique of asymmetrical QAV concomitant with aortic annulus banding can be implemented safely and effectively in well-selected patients with QAV. Larger cohort studies and long-term follow-up are needed to find a more durable and reliable technique to treat QAV.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding authors.

AUTHOR CONTRIBUTIONS

YY, ZD, and ES wrote the first draft of the manuscript. YY, ZD, ES, and TG wrote sections of the manuscript. All authors performed operation. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2022.871818/full#supplementary-material

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EDITED BY
Maximillian A. Rogers,
Moderna Therapeutics, United States

REVIEWED BY
Symeon Panagiotakis,
University Hospital of Heraklion, Greece
Fabrice Compain,
L'Institut Mutualiste Montsouris Paris, France

*CORRESPONDENCE
Tian Qin
qintian@icdc.cn
Zhongxin Lu
luzhongxin@zxhospital.com

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Case report: Infective endocarditis caused by *Streptococcus sinensis*: The first case in mainland China and literature review

Yingmiao Zhang[1], Jing Wang[1], Yu Zhan[1], Ruizhi Tang[1], Hui Wang[1], Tian Qin[2]* and Zhongxin Lu[1,3]*

[1]Department of Medical Laboratory, The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [2]State Key Laboratory for Infectious Disease Prevention and Control, Chinese Center for Disease Control and Prevention, Beijing, China, [3]Cancer Research Institute of Wuhan, The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Streptococcus sinensis was originally described as a causative agent for infective endocarditis in three Chinese patients from Hong Kong in 2002. Subsequently, several cases were reported outside Hong Kong, indicating that it is an emerging pathogen worldwide. We isolated a closely related strain in a young patient diagnosed with infective endocarditis in mainland China. In this paper, we reviewed the course of infection and provided a comprehensive comparison of its clinical characteristics with the reported cases.

KEYWORDS

***Streptococcus sinensis*, infective endocarditis, emerging pathogen, 16S rRNA sequence, case report**

Introduction

Infective endocarditis (IE) is a potentially fatal disease that occurs on the endocardial surface of the heart, usually involving the heart valves. The viridans group streptococci is second only to *Staphylococcus aureus* as a causative agent of IE, which presents in ~20% of cases worldwide (1). Among these streptococcal species, *Streptococcus sinensis* (*S. sinensis*) was reported as a new pathogen isolated from a 42-year-old Chinese woman in Hong Kong with mitral regurgitation due to chronic rheumatic heart disease and IE in 2002 (2). Subsequent studies by Woo et al. found another two strains screened from 302 patients with bacteremia caused by viridans streptococci over a 6-year period, and demonstrated that *S. sinensis* is the common ancestor of the anginosus and mitis groups of streptococci (3, 4). In 2008, using the 16S rRNA sequencing method, the same group concluded that the oral cavity is the natural reservoir of *S. sinensis* (5). The increasing number of cases reported outside Hong Kong indicates that the organism is an emerging pathogen that is of interest globally (6–9).

Case presentation

A 19-year-old man with no obvious incentive for intermittent joint pain in both knees and the right elbow over the previous 2 months was admitted to our hospital on December 26, 2020. At admission, the patient complained of occasional numbness and pain in both feet, difficulty squatting, and lower extremity edema. Physical examination showed a sick male, with a blood pressure of 135/85 mmHg, a temperature of 38.1°C, a pulse of 110 beats/min, and a respiratory rate of 19 breaths/min. Laboratory tests revealed the following: a white blood cell (WBC) count of 12.9 × 10^9/L (83.9% neutrophils), an erythrocyte sedimentation rate of 114 mm/h (normal, 0–20 mm/h), hypersensitive C-reactive protein (CRP, whole blood) of 16.5 mg/dl (normal, 0–0.8 mg/dl), hemoglobin of 87 g/L (normal, 120–160 g/L), total protein of 81 g/L (normal, 65–85 g/L), albumin of 25.9 g/L (normal, 40–55 g/L), and rheumatoid factor (RF) of 68.3 IU/ml. Urinalysis revealed a red blood cell count of 2,442/μl with heterogeneous morphology, urine protein of 2+, and a WBC count of 188/μl. Two sets of blood cultures were prepared before empirical antibiotic treatment with intravenous (i.v.) teicoplanin 1 g/day (qd) and cefoselis 2 × 1 g/day (q 12 h). Over the cardiac apex, a grade 2/6 proto-mesosystolic murmur was audible. Transthoracic echocardiography (TTE) revealed aortic valve bicuspid malformation (Type 0), flocculent hypoechoic vegetations of the aortic valve and anterior mitral valve leaflets (Figure 1A), and moderate regurgitation bundles on the left ventricular outflow tract side during diastole of the aortic valve (Figure 1B), supporting the diagnosis of IE. In all blood culture bottles, Gram-positive cocci were observed. The strain named BC1012612 was identified as *S. sinensis* by matrix-assisted laser desorption ionization/time of flight mass spectrometry (MALDI-TOF MS, Bruker Daltonik GmbH, Germany) with a high confidence level. A definite diagnosis of IE requires two major, one major with three minor, or five minor criteria (10). Thus, 6 days after admission, IE was diagnosed by the presence of two major and two minor criteria according to the modified Duke criteria (10).

An antibiotic susceptibility test *via* the Kirby–Bauer method showed the strain was susceptible to levofloxacin (32 mm), ceftriaxone (32 mm), linezolid (31 mm), vancomycin (23 mm), cefepime (32 mm), and chloramphenicol (28 mm). In addition, the minimal inhibitory concentrations (MICs) for penicillin G (0.064 mg/L) and meropenem (0.048 mg/L) were tested *via* an E-test. Based on the drug susceptibility result, the antimicrobial drug was changed to ceftriaxone (2 g/day). The patient underwent mechanical aortic valve replacement and mitral valve repair with no postoperative complications on Day 6 after his diagnosis. Histochemical analysis of the valve tissue showed local myxoid and hyaline degeneration, missing endothelial cells, and a large number of necrotic attached substances, and there were many neutrophils in the valve wall at the bottom of the necrotic substances (Figure 1C). The WBC count (Figure 1D) and CRP (Figure 1E) remained at high levels post-operation, and intravenous teicoplanin (1 g/day) and meropenem (1 g/8 h) were used for treatment. Due to the occurrence of delirium and muscle spasms during anti-infective therapy, meropenem was changed to ceftriaxone. After 2 weeks of symptomatic and supportive treatment, the patient's physiological conditions and inflammatory indicators were normalized, and he was discharged with a monthly follow-up 26 days after admission. At the time of writing, the patient has remained clinically stable for more than 18 months. Additionally, we present a timeline for the case presentation (Figure 2).

16S rRNA gene sequence analysis was conducted to classify the isolated strain BC1012612 with universal 16S rRNA primers (forward primer: 5′-AGTTTGATCMTGGCTCAG-3′, reverse primer: 5′-GGTTACCTTGTTACGACTT-3′). A total of 1,439 contiguous nucleotides were determined. The complete 16S rRNA sequence was analyzed with the Basic Local Alignment Search Tool (BLAST) at the GenBank Database (https://blast.ncbi.nlm.nih.gov). The strain BC1012612 exhibited the highest (99.93%) 16S rRNA gene sequence similarity with the type strain of *S. sinensis* HKU4^T (GenBank accession No. AF432856). Among the 1,439 bases, there was only one base difference from strain HKU4^T. Multiple alignments with sequences of the most closely related streptococci and the calculations of the levels of sequence similarity were carried out using CLUSTALW (11). A phylogenetic tree was constructed using the neighbor-joining method by using MEGA software version 11 (12). The topology of the phylogenetic tree was evaluated by using the bootstrap resampling method of Felsenstein (13) with 1,000 replicates. The phylogenetic tree showed that strain BC1012612 was clustered with strains HKU4^T, HDP 2005-0155, and 11026353, and this cluster was strongly supported with a bootstrap value of 100% (Figure 3). The results of the comparative 16S rRNA gene sequence analysis demonstrated that the isolated strain BC1012612 belongs to the *S. sinensis* species. We have submitted the 16S rRNA sequencing results to GenBank (accession No. OM780285).

Literature review and discussion

S. sinensis, a newly described species of viridans streptococci, was originally isolated in 2002 from blood cultures of a female patient with chronic rheumatic heart disease in Hong Kong (2). It has subsequently been reported in a few case reports outside Hong Kong, such as in Switzerland, France, Great Britain, and the Netherlands (6, 8, 9, 14–16), highlighting its importance as an emerging pathogen in the healthcare field. Continuous studies by Woo et al. revealed that the oral cavity is the natural reservoir of *S. sinensis* in healthy individuals, and that *S. sinensis* may be the common ancestor of the anginosus and mitis groups of streptococci according

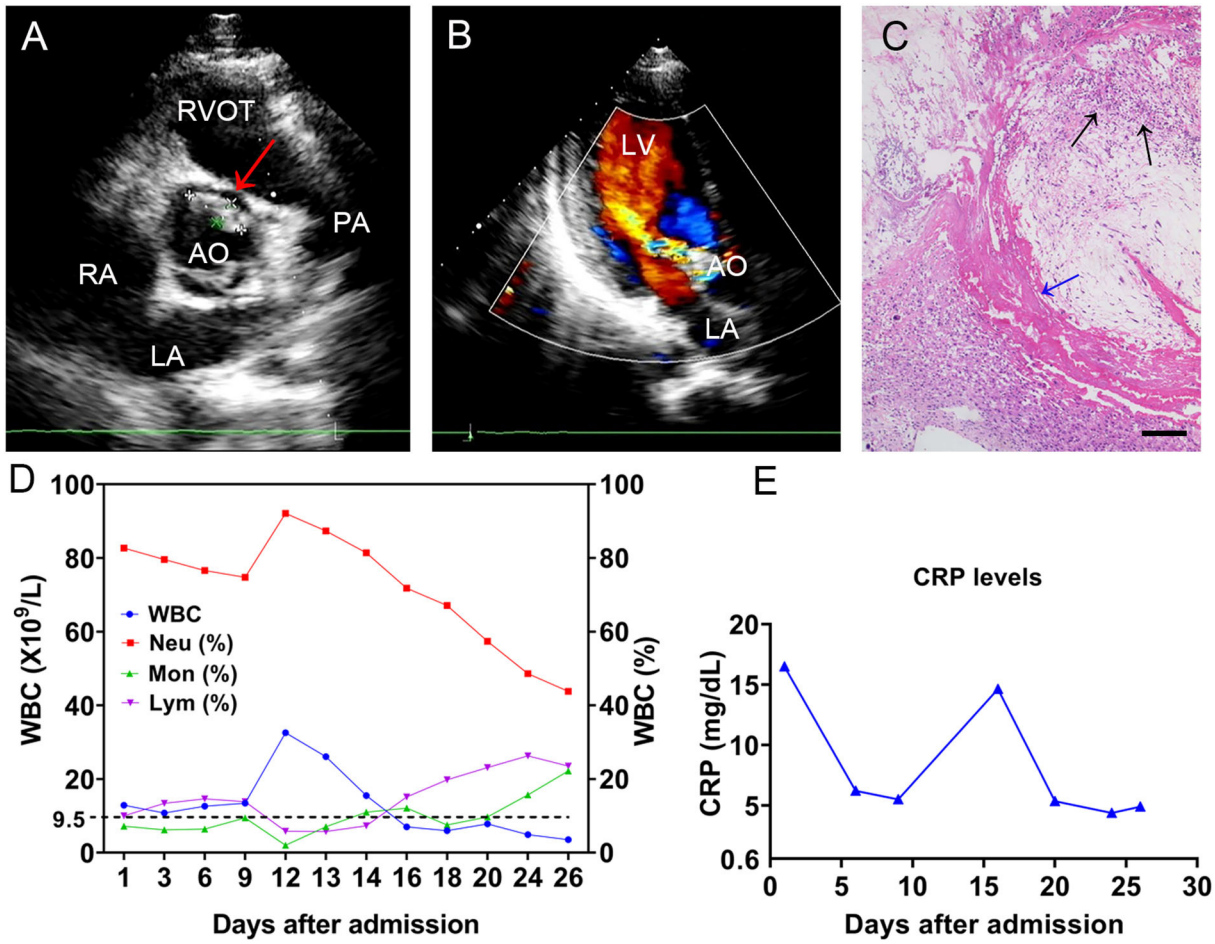

FIGURE 1
The TEE results of the mitral valve and WBC levels. TTE revealed **(A)** flocculent hypoechoic vegetations of the aortic valve (the red arrow) and **(B)** a moderate regurgitation bundle on the left ventricular outflow tract side during diastole of the aortic valve. **(C)** The histochemical analysis of the valve tissue revealed local myxoid and hyaline degeneration, missing endothelial cells, necrotic attached substances (the blue arrow), and neutrophil aggregation (the black arrows). Scale bars approximate 50 μm in length. The **(D)** WBC count and cell proportions and **(E)** CRP throughout the course. TTE, transthoracic echocardiography; LA, left atrium; LV, left ventricle; RA, right atrium; RVOT, right ventricular outflow tract; AO, aorta; PA, pulmonary artery; WBC, white blood cell; CRP, C-reactive protein.

to clinical, phenotypic, and genotypic comparisons of these strains (4, 5). Based on phylogenomic and MALDI-TOF MS analysis, they proposed a new group called the "*sinensis* group," which includes *S. sinensis*, *Streptococcus oligofermentans* (*S. oligofermentans*), and *Streptococcus cristatus* (*S. cristatus*), in 2014 (7). Jensen et al. reported *S. oligofermentans* as a later synonym of *S. cristatus* (17). With the development of genome sequencing technology, increasingly more details of *S. sinensis* have been explored.

IE caused by *S. sinensis* was diagnosed by blood cultures collected before antibiotic therapy. We isolated a strain of *S. sinensis* BC1012612 from the blood of a young patient with IE. The strain was identified by MALDI-TOF MS, and 16S rRNA sequencing was performed for further analysis. Among a total of 1,439 bases, the 16S rRNA sequence of this strain was found to have only one base difference from the type strain HKU4. A phylogenetic tree also showed a cluster within the previously reported *S. sinensis* strains and our strain BC1012612, suggesting that our strain is most closely related to the type strain. According to the emended taxonomy of the Mitis group of the genus *Streptococcus* carried out by Jensen et al., *S. sinensis*, together with *S. cristatus*, belongs to the *S. cristatus* clade but is distantly related to other strains and may represent a distinct taxon at the species level (17). The 16S rRNA sequencing method alone is inadequate for bacterial classification, and multidimensional analysis will be helpful for the accurate classification of the large numbers of species within genus *Streptococcus*.

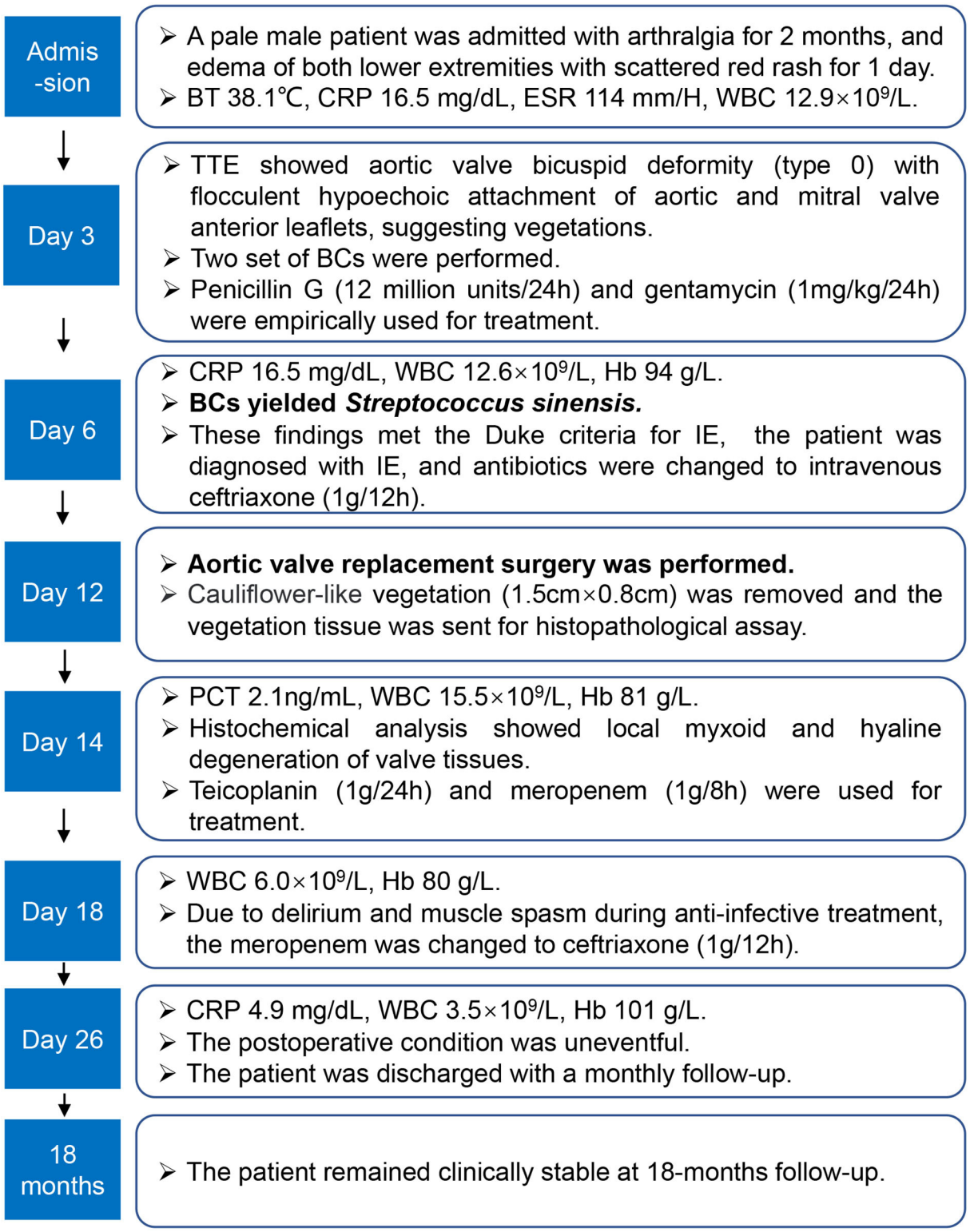

FIGURE 2
The timeline of the case presentation. The patient was discharged with a monthly follow-up 26 days after his admission. BT, body temperature; ESR, erythrocyte sedimentation rate; BCs, blood cultures; IE, infective endocarditis; PCT, procalcitonin.

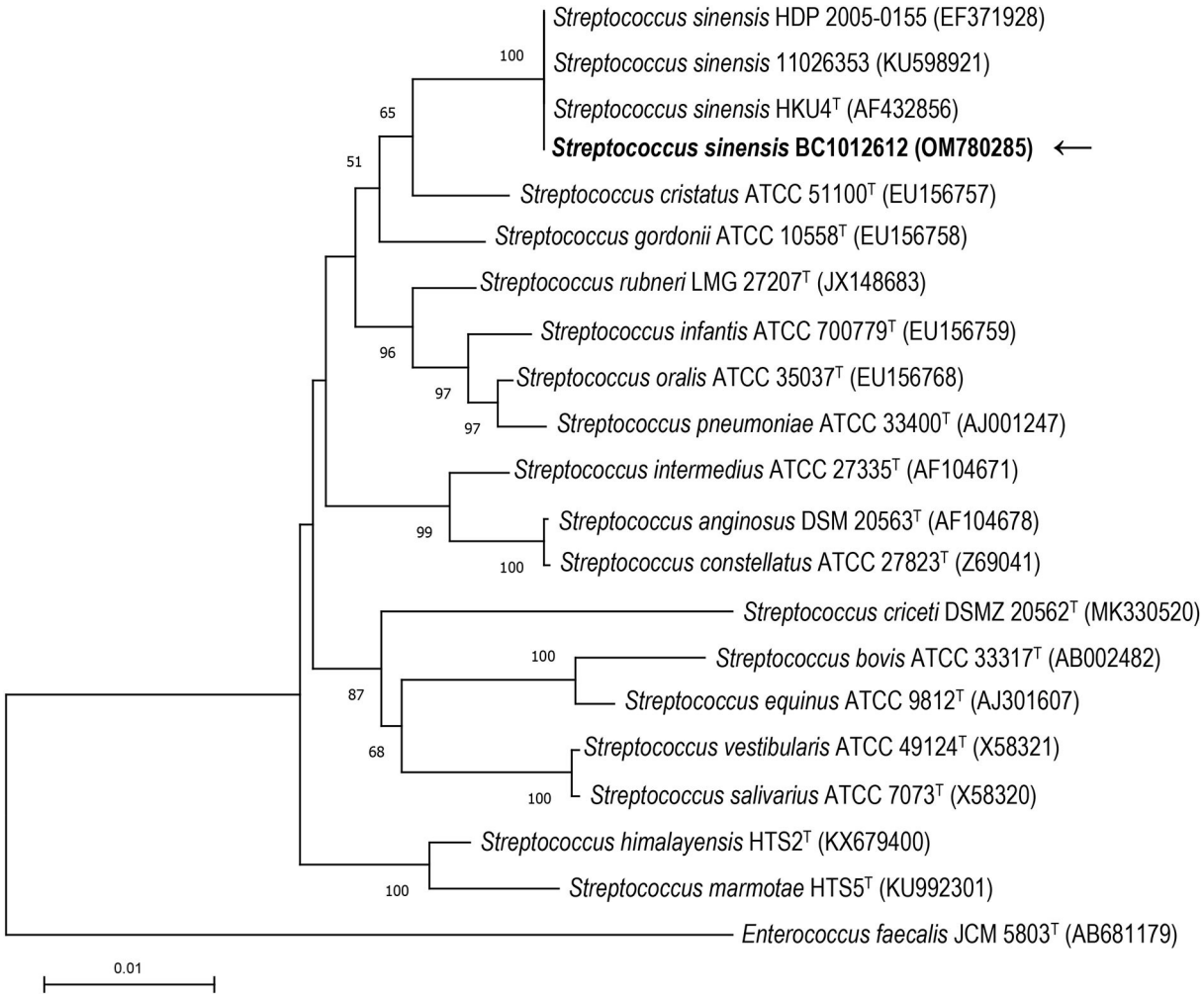

FIGURE 3
The phylogenetic tree based on the 16S rRNA gene sequences showing the relationship of isolated strain BC1012612 (the black arrow) and members within the genus *Streptococcus*. The tree was reconstructed by the neighbor-joining method, and *Enterococcus faecalis* JCM5803T was used as an outgroup. Bootstrap values (>50%) based on 1,000 replicates are shown at branch nodes. T, type strain.

The extant literature on *S. sinensis*-related IE is presented in Table 1. Unfortunately, a small number of cases have been reported without any clinical descriptions, making it impossible for a comprehensive summary and analysis of these cases (6, 18). Among the eight listed observations, including ours, there were only two female patients, and the age of the patients ranged from 19 to 63; the patient in our case is the youngest reported yet. All the patients had acquired congenital heart disease, and six out of eight patients were found to have vegetations and varying degrees of mitral regurgitation *via* echocardiography. It is intriguing that at least three patients with IE caused by *S. sinensis* had tooth problems, which may corroborate the oral origin of this organism. *S. sinensis* was also identified by a multiple PCR method in the subgingival plaque of two subjects with localized severe chronic periodontitis (19). However, more evidence is needed to ascertain whether *S. sinensis* is present in the oral cavity of individuals living in other regions outside Hong Kong. Two patients were reported to have travailed to Hong Kong or had undergone dental procedures there, thus hinting at the geographical reservoirs for *S. sinensis*. In addition, studies of the stomach and gut microbiota also revealed the presence of *S. sinensis* from gastric mucosa and stool samples at the genetic level *via* 16S rRNA sequencing (20, 21), but without any isolated strains. To date, no infections other than IE caused by *S. sinensis* have been reported in humans, suggesting that this organism may possess specific virulence factors to invade heart valves and cause damage. The sequence analysis of the manganese-dependent superoxide dismutase gene (sodA) *via* a PCR assay based on degenerate primers was initially carried out by Poyart et al. to identify the genus *Streptococcus* to a

TABLE 1 Cases reported in *Streptococcus sinensis*-related IE.

Strains	Gender	Age	Place	Asia origin	Vegetation	Antibiotics	Antibiotic duration[a]	Mitral involvement	Surgery	Follow-up	Years	References
HKU4^T	F	42	Hong Kong	Yes	No	AMP, CN	6 weeks	No	NA	NA	2000	(2)
Geneva	M	57	Switzerland	No	Yes	P, CN	6 weeks	Yes	Yes	Survival	1998	(6)
HDP2005-0155	M	55	France	No	No	AML, CN	8 weeks	Yes	Yes	Survival	2005	(14)
NA	F	20	France	No	Yes	AML, CN	4 weeks	No	Yes	Survival	2015	(15)
NA	M	63	Britain	Travel	Yes	AML,CN CRO	6 weeks	No	Yes	Survival	2019	(8)
11026353	M	37	France	No	Yes	AMC, CN	4 weeks	Yes	Yes	NA	2019	(16)
NA	M	58	Netherlands	Yes	Yes	P, CN	1 week	Yes	No	Death	2020	(9)
BC1012612	M	19	Mainland China	Yes	Yes	P, CN,CRO, MEM	6 weeks	Yes	Yes	Survival	2020	This study

[a]Antibiotic duration includes the duration of treatment before and after surgery. NA, not available; F, female; M, male; AMP, ampicillin; CN, gentamycin; P, penicillin G; AML, amoxicillin; CRO, ceftriaxone; AMC, amoxicillin-clavulanic acid; MEM, meropenem.

species level (22). A high congruence of strain grouping by MALDI-TOF MS in comparison with sodA sequence analysis regarding *streptococcus bovis/equinus*-complex was observed by Hinse et al., demonstrating the accuracy and reliability of MALDI-TOF MS in comparison to the DNA sequence-based method (23). It is difficult to identify viridans streptococci by traditional biomedical methods, even MALDI-TOF MS; genetic characterization should be performed to distinguish strains isolated in infectious diseases and the epidemiology of each species.

All previously reported patients were treated with ampicillin or amoxicillin, or with combined therapy with gentamicin. It seems that the strain is susceptible to the majority of antibiotics tested, especially β-lactam antibiotics, so the routinely used antibiotics could achieve an antibacterial effect. However, more antibiotics were applied in this case, such as ceftriaxone and teicoplanin, mainly due to the persistently high level of inflammatory markers during anti-infective therapy. Almost all the patients received mitral valve replacement because of the severity of the preexisting mitral regurgitation, and had a good outcome. The patient in this case underwent mechanical aortic valve replacement and mitral valve repair. Surgical exploration showed scattered and small vegetations on the left ventricular surface of the anterior mitral valve without obvious valve leaf thickening, ulceration, or involvement of chordae tendineae, so mitral valve repair was performed. Several studies have shown that mitral valve repair has low mortality, fewer complications, and a better long-term prognosis than mitral valve replacement (24–26). Of these cases, only one death occurred in a 58-year-old man who refused surgery and died of multiple cerebral infarctions several days after admission, suggesting that timely treatment is of great importance in the acute phase of infection.

Conclusion

Herein, we report the first case of IE caused by *S. sinensis* in mainland China. The patient in our case is the youngest ever reported, and his initial symptoms were mainly joint pain. The patient was diagnosed with IE after the isolation of *S. sinensis* from blood cultures and treated with drug-sensitive antibiotics as well as surgery. The early identification of *S. sinensis* is critical to the diagnosis and treatment of IE, but routine biochemical methods and MALDI-TOF MS are not sufficient because of the variety of species within genus *Streptococcus*. Certain genetic methods, such as 16S rRNA sequencing, are required for the accurate classification of those obtained strains. In addition, the patients' travel history should be taken into consideration when determining the possible geographical reservoirs for this agent, as it has been proposed to be an oral flora present in Hong Kong. Our case highlights the importance of *S. sinensis* as an emerging pathogen and provides a comprehensive understanding of *S. sinensis*-related IE.

Data availability statement

The datasets for this article are not publicly available due to concerns regarding participant/patient anonymity. Requests to access the datasets should be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Medical Ethics Committee of The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Sciences and Technology. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Designed and conceived the experiments: ZL, HW, and YZhang. Performed the experiments: YZhang, JW, and YZhan. Analyzed the data: YZhang and RT. Wrote and reviewed the manuscript: YZhang, TQ, and ZL. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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CASE REPORT
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Emergently Alteration of Procedural Strategy During Transcatheter Aortic Valve Replacement to Prevent Coronary Occlusion: A Case Report

Hanyi Dai[1,2†], Dao Zhou[1,2†], Jiaqi Fan[2], Lihan Wang[2], Abuduwufuer Yidilisi[1,2], Gangjie Zhu[1,2], Jubo Jiang[2], Huajun Li[2], Xianbao Liu[1,2] and Jian'an Wang[1,2*]*

[1] Internal Medicine, Zhejiang University School of Medicine, Hangzhou, China, [2] Department of Cardiology, The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China

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Edited by:
Giuseppe Tarantini,
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Reviewed by:
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Kefang Guo,
Fudan University, China
Mauro Massussi,
University of Brescia, Italy

***Correspondence:**
Xianbao Liu
liuxb@zju.edu.cn
Jian'an Wang
wangjianan111@zju.edu.cn

† These authors have contributed equally to this work and share first authorship

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Background: Coronary occlusion is an uncommon but fatal complication of transcatheter aortic valve replacement (TAVR) with a poor prognosis.

Case Presentation: A patient with symptomatic severe bicuspid aortic valve stenosis was admitted to a high-volume center specializing in transfemoral TAVR with self-expanding valves. No anatomical risk factors of coronary occlusion were identified on pre-procedural computed tomography analysis. The patient was scheduled for a transfemoral TAVR with a self-expanding valve. Balloon pre-dilatation prior to prosthesis implantation was routinely used for assessing the supra-annular structure and assessing the risk of coronary occlusion. Immediately after the tubular balloon inflation, fluoroscopy revealed that the right coronary artery was not visible, and the flow in the left coronary artery was reduced. The patient would be at high-risk of coronary occlusion if a long stent self-expanding valve was implanted. Therefore, our heart team decided to suspend the ongoing procedure. A transapical TAVR with a 23 mm J-valve was performed 3 days later. The prosthesis was deployed at a proper position without blocking the coronary ostia and the final fluoroscopy showed normal flow in bilateral coronary arteries with the same filling as preoperatively.

Discussion: Our successful case highlights the importance of a comprehensive assessment of coronary risk and a thorough understanding of the TAVR procedure for the heart team. A short-stent prosthesis is feasible for patients at high risk of coronary occlusion. Most importantly TAVR should be called off even if the catheter has been introduced when an extremely high risk of coronary obstruction is identified during the procedure and no solution can be found.

Keywords: aortic valve stenosis, transcatheter aortic valve replacement, emergent, pre-dilatation, procedural strategy

Abbreviations: TAVR, transcatheter aortic valve replacement; NYHA, New York Heart Association; LVEF, Left ventricular ejection fraction; MDCT, multi-detected computed tomography; LMA, left main coronary artery; RCA, right coronary artery; SAVR, surgical aortic valve replacement.

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has currently revolutionized as the guideline-recommended therapy for the elderly with severe aortic valve stenosis (1). Coronary occlusion is an uncommon but potentially fatal complication with an incidence of less than 1% (2). Coronary occlusion would result in unplanned surgical or interventional treatment, myocardial infarction, and even death (2, 3). As TAVR has advanced notably in recent years, the evaluation and prevention of coronary occlusion are still the main concerns.

CASE PRESENTATION

A 75-year-old woman diagnosed with severe aortic valve stenosis was admitted to our hospital for progressive exertional dyspnea in the last 3 years ago with New York Heart Association (NYHA) Class III functional status. She had clinical comorbidities of Parkinson's disease and pulmonary space-occupying lesions. Cardiac auscultation detected a 3/6 mid-systolic murmur with maximum intensity in the area of the right upper sternal border. Echocardiography demonstrated severe calcified aortic valve stenosis with mild-to-moderate regurgitation (valve area = 0.85 cm^2; peak velocity = 4.23 m/s; and mean transvalvular gradient = 42 mmHg). Left ventricular ejection fraction (LVEF) estimated by the two-dimensional methods was 61.4%. Multi-detected CT (MDCT) identified that the aortic valve was bicuspid aortic valve type 1 and a raphe with a bulky calcification between the left and non-coronary sinuses (4, 5). Further anatomical measurements on MDCT included an annular perimeter of 73.1 mm, an annular area of 414.1 mm^2, and the left main coronary artery (LMA) ostium height of 11 mm and right coronary artery (RCA) of 14.1 mm (**Figures 1A,B,D,E**). The dimensions of left-, right-, and non-coronary sinuses were 31.6, 30.7, and 30.7 mm, respectively (**Figure 1B**). The average dimension and the height of the sinotubular junction were 27.6 and 16 mm (**Figure 1C**). Measured on the plane of the right coronary ostium, the distance of the edge of the calcified nodule to right coronary ostium was 23 mm (**Figure 1F**). The average internal diameters of the right femoral-, external iliac-, and common iliac arteries were 6.7, 6.5, and 7.3 mm, respectively. The patient was deemed at intermediate surgical risk with the Society of Thoracic Surgeons score of 5.13% and was recommended for surgical aortic valve replacement (SAVR). However, the patients refused SAVR and were determined to undergo minimally invasive TAVR.

The procedure was performed in our hybrid operating room for TAVR as previously described (4). At the beginning of the TAVR procedure, bilateral coronary arteries were patent under intraoperative fluoroscopy (**Figure 2A**). Balloon pre-dilatation was routinely performed to assess the supra-annular structure and evaluate the risk of coronary occlusion using a 23 mm × 40 mm Z-Med^{TM} balloon based on the annulus perimeter derived diameter (6). Unexpectedly, the right coronary artery was invisible and the blood flow reduced in the LMA, immediately after balloon dilatation (**Figure 2B**), indicating RCA completely occluded and LMA partially occluded by the native left coronary leaflet. The patient's blood-oxygen saturation dropped sharply from 100 to 72%. Intraoperative transthoracic echocardiography revealed a transvalvular gradient of 20 mmHg following balloon deflation. Therefore, the multidisciplinary team decided to suspend the procedure. A careful and comprehensive reassessment of the patient's anatomy was performed and the transapical TAVR with J-valve (JieCheng Medical Technology Co., Ltd., Suzhou, China) was planned for safety consideration.

Subsequently, transapical TAVR with J-valve was performed under general anesthesia 3 days later. A 23-mm J-Valve system was introduced and repeatedly adjusted to ensure the three graspers were properly placed in the left-, right-, and non-coronary sinuses and accurately surround the native leaflets. The prosthetic valve was gradually released after positioning at 1 cm below the aortic annulus under rapid ventricular pacing. The procedure was uneventful and the final fluoroscopy showed the proper position of the prosthetic valve and the patency of bilateral coronary arteries (**Figure 2C**). The final echocardiography showed mild perivalvular leakage and the residual transvalvular gradient was 3 mmHg. The patient was discharged without obvious symptoms of heart failure and could carry out daily activities with ease after discharge. At 30 days follow-up, she had an NYHA class II functional status and echocardiography showed normal aortic valve function with a transvalvular mean gradient of 5 mmHg.

DISCUSSION

To the best of our knowledge, this is the first case of suspending an ongoing procedure for an elective procedure with another type of valve when faced with an extremely high risk of coronary occlusion during the procedure.

Coronary occlusion is defined as complete or partial obstruction of coronary ostia during or after the procedure by native aortic leaflets, the prosthesis valve, calcified nodules, etc. It is a devastating complication that compromises survival and affects prognosis (2, 3). Preprocedural MDCT assessment is an optimal assessment technique to identify anatomical risk factors of coronary occlusion (7). Redundant leaflet, heavy calcification, coronary ostia height $<$ 10 mm, sinus of Valsalva dimensions $<$ 30 mm, and leaflet length to coronary sinus height ratio greater than 1 are anatomic predictors of coronary occlusion (2, 8). A comprehensive review of our case especially pre-procedural MDCT analysis could not identify any of the typical anatomical risk factors for coronary occlusion. However, the length of the left coronary cusp was greater than the height of the left coronary ostium, and the bulky calcium nodule located on the L-N raphe may force the valve displacement to hinder the contralateral right coronary ostium (**Figure 1**). Thus, the heart team considered the patient's coronary occlusion risk cannot be ignored but not at high risk. Balloon pre-dilatation was considered for evaluating the possibility of coronary compromise during the procedure (3). Luckily, the extremely high risk of coronary occlusion was detected by balloon pre-dilatation.

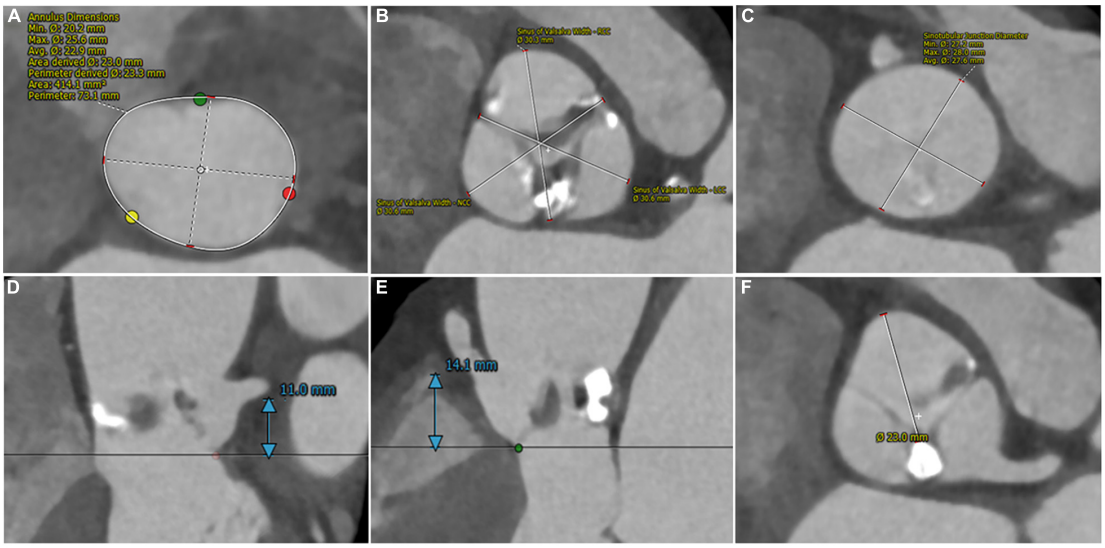

FIGURE 1 | Pre-procedural computed tomography assessment of aortic root. **(A)** Annular perimeter: 73.1 mm and annular area: 414.1 mm^2. **(B)** Left-, right- and non-sinuses of Valsalva dimensions: 31.6 mm * 30.7 mm * 30.7 mm. **(C)** Average sinotubular junction diameter: 27.6 mm. **(D,E)** The height of coronary arteries: 11 mm (left) and 14.1 mm (right). **(F)** The distance from the edge of the calcified nodule to right coronary ostium: 23 mm.

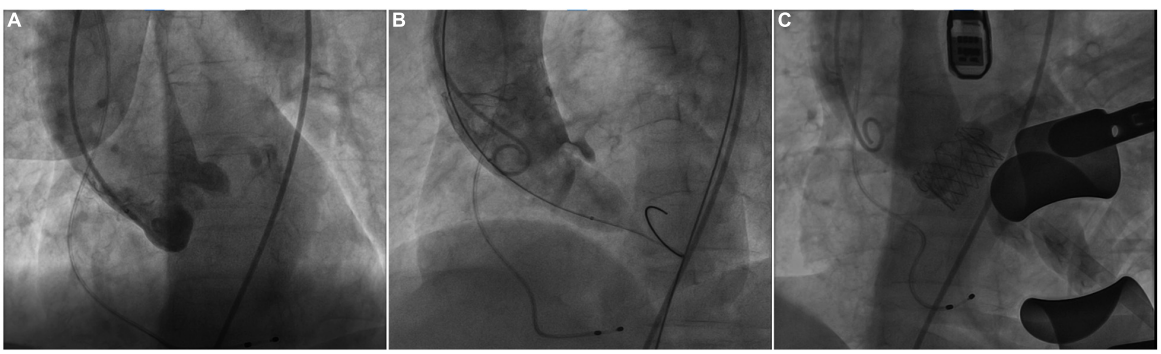

FIGURE 2 | Intraoperative fluoroscopy. **(A)** Fluoroscopy showed bilateral patent coronary arteries before balloon pre-dilatation. **(B)** The right coronary artery was invisible and reduced blood flow in the left coronary artery during the balloon dilatation. **(C)** Fluoroscopy showed the patency of bilateral coronary arteries after J-valve deployment.

However, we thought there existed no great backup methods for this patient during that procedure. BASILICA technique allows flowing into the coronary ostia by intentionally splitting native or bioprosthetic leaflets (9). However, this technique is targeted at coronary occlusion caused by valve displacement and it may not be suitable for our case. The chimney stenting implantation technique is a bailout technique used to treat coronary occlusion during TAVR. The interaction between the prosthetic valve edge and the chimney stent may lead to deformation of the coronary stent and prosthesis. Long-term effects on stent thrombosis and valve durability remain unknown. Besides, this technique is mainly targeted at LMA. Only 6 patients in the International Chimney Registry received bilateral chimney stents contemporarily and the prognosis is unclear (10). The several techniques mentioned above might not be our best option to avoid coronary occlusion. Severe aortic stenosis was temporarily relieved through balloon pre-dilatation. Thus, we called off the procedure to avoid harm to the patient, comprehensively re-assessed the procedural

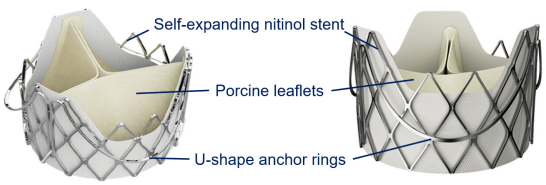

FIGURE 3 | The J-Valve system design. The J-Valve aortic system consists of a self-expanding nitinol stent surrounded by three U-shaped anchor rings, with porcine aortic valve leaflets sutured inside. This draft was provided by the company JieCheng Medical Technology Co., Ltd., Suzhou, China.

strategy, and decided to replace it with another short-stent valve.

The J-Valve system is a self-expanding prosthesis with a transapical delivery sheath for both aortic stenosis and aortic regurgitation (**Figure 3**). The unique structure with three anatomical orientated U-shaped anchors, short stent frame and even lower profile in the regions of the coronary ostia is effective for positioning stabilizing, and avoiding coronary occlusion (11). Patients with bicuspid aortic valve without raphe (Type 0) are considered to be the contraindication for the J-valve system and are always excluded from well-designed studies (12, 13). Type 1 represents three coronary cusps with one fusion raphe between two adjacent cusps. Tung et al. reported that the 1- year major adverse cardiovascular events-free survival was similar between tricuspid vs. bicuspid aortic valve (log-rank $p = 0.25$), which indicated the safety and efficacy of the J-Valve implantation in patients with bicuspid morphology (12). Thus, our heart valve team decided to discontinue the current procedure and reschedule another procedure with J-Valve to avoid fatal coronary occlusion. As the result, we avoided coronary occlusion which may occur after long-stent valve implantation and obtained satisfactory results. Our successful case suggests that the patients' safety is paramount. It is feasible to suspend the procedure when extremely high operative risk is detected during the procedure, even if the catheter has been introduced. In this situation, reassessing the patient's anatomic structure comprehensively, modifying the procedural strategy, and even recommending patients to undergo the procedure again should be considered.

CONCLUSION

Coronary artery occlusion is a fatal complication with high mortality. Our case emphasizes the importance of a comprehensive assessment of the interaction between the coronary ostia and surrounding structures for TAVR candidates and the feasibility of emergently restructuring strategy intraoperatively. A short stent prosthesis is feasible for patients with high coronary occlusion risk. More importantly, ceasing the procedure which would do harm to patients was necessary, even if the catheter has been deployed into the patient's body.

DATA AVAILABILITY STATEMENT

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Board of The Second Affiliated Hospital Zhejiang University School of Medicine. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

HD and DZ contributed to composing the manuscript. JF collected the patient's data and draw figures. LW, AY, GZ, JJ, and HL revised the manuscript. XL and JW analyzed and explained the steps of procedures, as well as conceived and revised the manuscript. All authors contributed to the article and approved the submitted version.

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EDITED BY
Ernesto Greco,
Sapienza University of Rome, Italy

REVIEWED BY
Alberto Repossini,
Cardiochirurgia Spedali Civili, Italy
Concetta Zito,
University of Messina, Italy

*CORRESPONDENCE
Stamatios Lerakis
stamatios.lerakis@mountsinai.org

†These authors have contributed equally to this work and share first authorship

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Case report: Paravalvular regurgitation post transcatheter aortic valve replacement: When in doubt choose cardiac magnetic resonance

Michael B. Hadley[1†], Francesca Romana Prandi[1,2†], Francesco Barillà[2], Samin Sharma[1], Annapoorna Kini[1] and Stamatios Lerakis[1*]

[1]Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, NY, United States, [2]Division of Cardiology, Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy

Paravalvular leak (PVL) is a common complication following transcatheter aortic valve replacement (TAVR). Significant PVL is associated with adverse prognosis, but may be challenging to assess accurately. We report the case of an 81-year-old man with shortness of breath 5 months post TAVR. Echocardiography classified PVL as either moderate or severe depending on the parameter utilized, while angiography found only mild PVL. Cardiac magnetic resonance allowed an exact quantification of regurgitant flow volume, classified as clinically and hemodynamically significant. This case highlights the role of multimodality imaging assessment including cardiac magnetic resonance for a more accurate assessment of PVL severity, especially when other imaging modalities show discordant results.

KEYWORDS

transcatheter aortic valve replacement (TAVR), paravalvular leak (PVL), cardiac magnetic resonance (CMR), multimodality imaging, case report, structural heart disease

Introduction

Paravalvular leak (PVL) is a potential complication following transcatheter aortic valve replacement (TAVR), due to incomplete sealing of the aortic annulus by the bioprosthesis. Significant PVL is associated with adverse prognosis (1), may be challenging to assess accurately, and should be treated appropriately when diagnosed (2, 3).

Case report

We present a case of an 81-year-old man that presented with progressively worsening shortness of breath 5 months post transfemoral TAVR with a 29 mm Medtronic

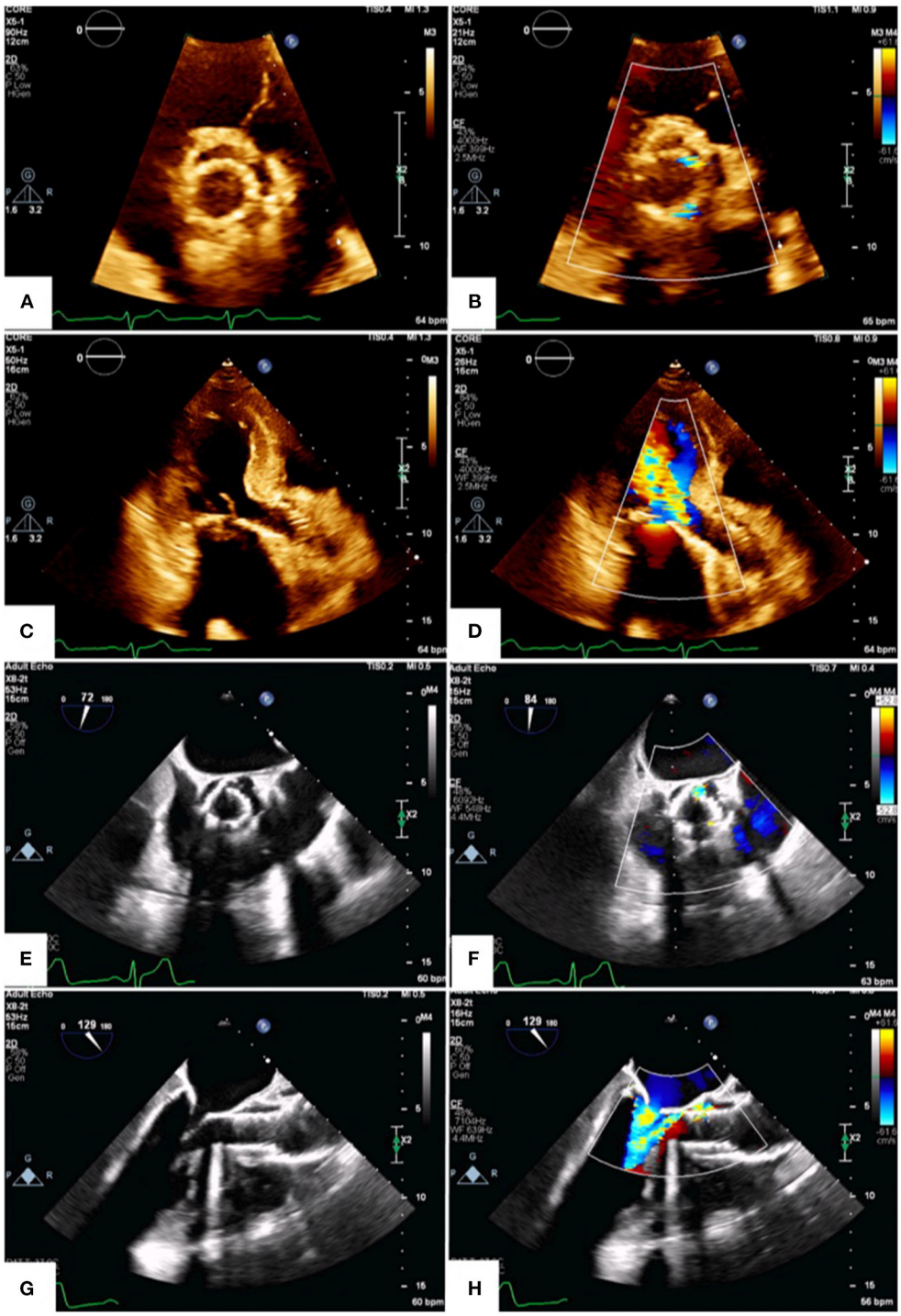

FIGURE 1
Transthoracic and transesophageal echocardiography. Transthoracic **(A–D)** and transesophageal **(E–H)** echocardiograms demonstrate multiple PVL jets on short-axis view **(B,F)**; Supplementary Videos 1, 2). The largest jet is in the 1 o'clock position and is well-visualized on long-axis views **(D,H)**; (Supplementary Videos 3, 4).

Evolut PRO + valve. His medical history included hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, iron deficiency anemia, paroxysmal atrial fibrillation on anticoagulation, coronary artery disease treated with percutaneous coronary angioplasty and benign prostatic hyperplasia. His family history did not include any significant

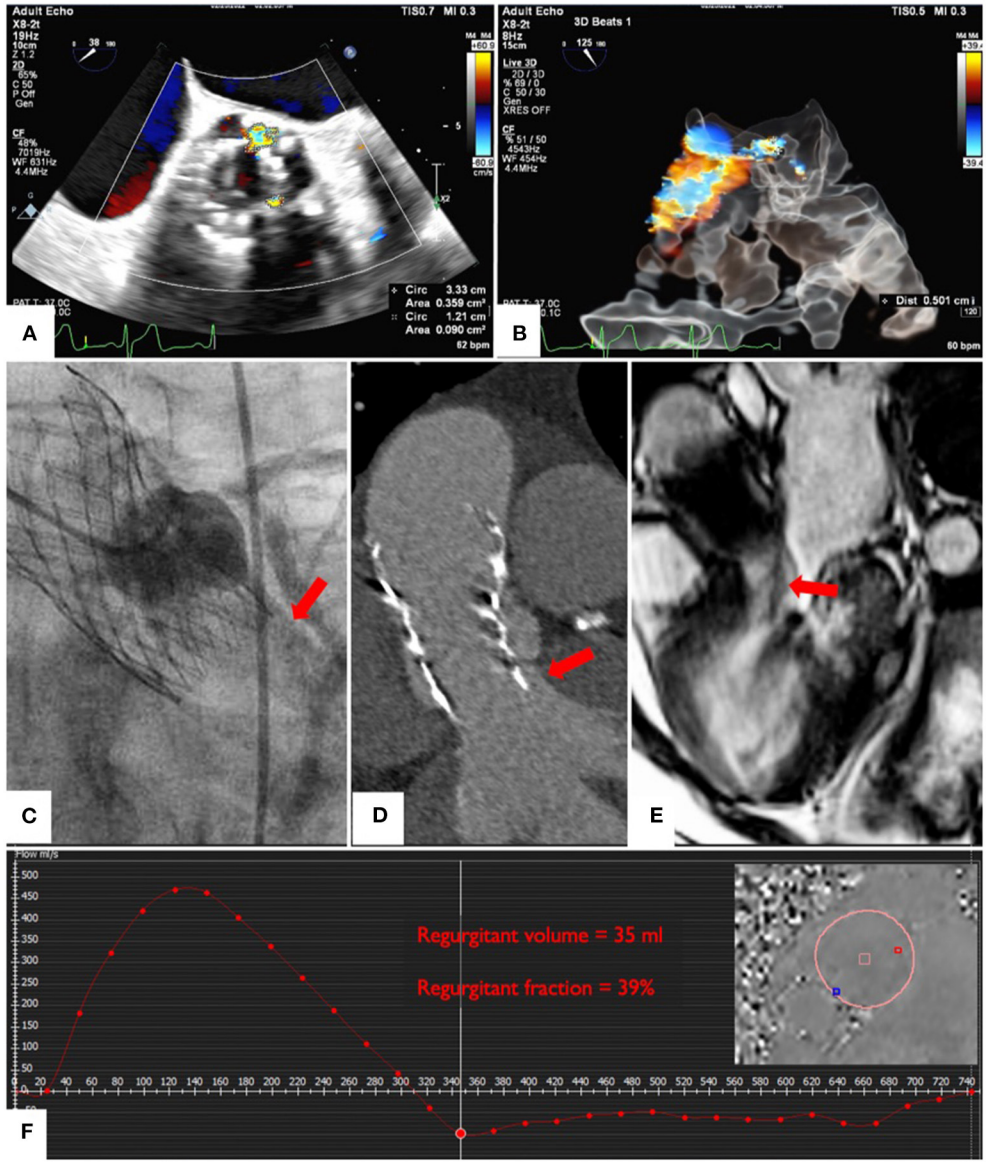

FIGURE 2
Multiparametric assessment of PVL severity. Echocardiographic quantification of jet size by planimetry **(A)** and by VC using glass image processing **(B)**; (Supplementary Video 5). Angiographic assessment of PVL **(C)**. Computed tomography showing prosthesis under-expansion **(D)**. CMR of the largest PVL jet **(E)** and quantification of the total regurgitant volume and fraction **(F)**; (Supplementary Video 6).

disease. Physical examination documented regular cardiac rhythm with 3/6 end-diastolic murmur and 3/6 mid-systolic murmur, with lungs clear to auscultation bilaterally.

Multiparametric diagnostic assessment

Echocardiography demonstrated normal biventricular function (left ventricular ejection fraction 68%), severe mitral stenosis, multiple jets of prosthetic aortic PVL classified as either moderate or severe depending on the parameter[2] (Figure 1; Supplementary Videos 1–4) and otherwise normal prosthetic valve function (peak velocity 2.16 m/sec, mean transvalvular gradient 9 mmHg, Effective Orifice Area 1.8 cm2, Effective Orifice Area Indexed 0.98 cm2/m2). The largest PVL jet vena contracta (VC) area measured 0.36 cm^2 (Figure 2A) with a large flow convergence, suggestive of severe PVL. However, the VC width measured 0.5 cm on glass image processing (Figure 2B; Supplementary Video 5) and the circumferential extent of

the PVL was <30%, suggesting moderate PVL. Conversely, angiography found only 1+ PVL (Figure 2C). Computed tomography (CT) demonstrated that the cause of the PVL was the under-expansion of the prosthesis (Figure 2D).

Cardiac magnetic resonance (CMR) phase contrast imaging allowed exact quantification of flow through the proximal aorta (Figures 2E,F; Supplementary Video 6) bypassing the need to assess multiple jets separately (2–4). On CMR, the regurgitant fraction (RF) was 39% with regurgitant volume of 35 ml, most consistent with clinically and hemodynamically significant PVL.

Based on CMR evaluation and following Heart Team discussion, the patient underwent surgical explant of TAVR, re-do aortic valve replacement (AVR) with a 23 mm St. Jude Medical Epic Supra porcine tissue heart valve, mitral valve replacement (MVR) with a 25 mm St. Jude Medical Epic tissue heart valve and left atrial appendage ligation, followed by clinical improvement and no residual aortic regurgitation on follow-up echocardiograms.

Discussion

Echocardiography is the first-line modality to assess PVL, but may be limited by a subjective assessment of multiple, eccentric jets with irregular orifices (4). Both transthoracic and transesophageal echocardiography may also present attenuation due to native calcification and implanted prosthetic material (5).

CMR is highly reproducible and offers an accurate, quantitative approach that bypasses the need to identify and characterize individual jets (2–6); it is particularly useful in patients with difficult acoustic windows. In symptomatic post-TAVR patients, CMR commonly reclassifies PVL grade at least one grade lower compared to semi-quantitative echocardiography, and at least one grade higher compared to qualitative echocardiography (5). CMR is technically feasible for PVL assessment in the currently approved balloon-expandable and self-expandable valves.

This approach has applications beyond TAVR. Compared with transesophageal echocardiography (TEE), CMR appears to have higher sensitivity to detect significant periprosthetic regurgitation after both surgical AVR or MVR (7, 8). Semiquantitative TEE underestimates a considerable number of AVR or MVR PVL (7). 4D flow CMR has also been used in a patient to detect a PVL after pulmonary valve replacement, and it was helpful to accurately quantify an effective regurgitant volume for decision making (9).

Accurate assessment of PVL severity is important, given implications for prognosis and management. CMR derived PVL quantification was shown to provide prognostic value superior to both qualitative and semi-quantitative echocardiography (5).

A higher RF as determined by CMR post-TAVR has been independently associated with late cumulative all-cause mortality [hazard ratio (HR) 1.18 for each 5% increase in RF; 95% confidence interval (CI): 1.08–1.30; $p < 0.001$], the combined endpoint of late cumulative all-cause mortality and heart failure (HF) rehospitalization (HR 1.19 for each increase of 5%; 95% CI: 1.15–1.23; $p < 0.001$) and the combined endpoint of late cardiovascular mortality, HF rehospitalization or reintervention in the transcatheter valve (HR 1.25 for each increase of 5%; 95% CI: 1.17–1.34; $p < 0.001$) (6). Furthermore, CMR-quantified AR performed at a median of 40 days post-TAVR had a greater association with post-TAVR clinical events compared with early (median of 6 days post-TAVR) echocardiography ($p < 0.01$). This demonstrates the important additional value of CMR-quantified AR in predicting clinical events beyond that of echocardiography-quantified AR (6). A RF ≥30% was associated with increased all-cause mortality ($p < 0.001$) and mortality and heart failure rehospitalization ($p < 0.001$) at 2-year follow-up (6).

Therefore, CMR may help to identify patients with severe PVL that should be considered for corrective intervention; it is particularly useful in patients with mild-to-moderate PVL on transthoracic echocardiography but who have signs/symptoms of heart failure, and those with moderate-to-severe PVL on echocardiography (10).

Overall, multimodality imaging assessment including CMR can provide a more accurate assessment of PVL severity, especially when a therapeutic intervention is under consideration and other imaging modalities show discordant results.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary materials, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the relevant individual for the publication of any potentially identifiable images or data included in this article.

Author contributions

Conception and design: SL. Drafting of the manuscript: MH, FP, and SL. Manuscript revision: MH, FP, FB, SL, SS, and AK. Final approval of the manuscript submitted: SL, SS, and AK. All authors have read and approved the manuscript.

Conflict of interest

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2022.925120/full#supplementary-material

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EDITED BY
Giuseppe Tarantini,
University of Padua, Italy

REVIEWED BY
Alessandro Iadanza,
Siena University Hospital, Italy

*CORRESPONDENCE
Mohammad Sherif
mohammad.sherif@charite.de

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Cardiovalve in mitral valve position—Additional solution for valve replacement

Mohammad Sherif[1,2]*, Simon H. Sündermann[2,3,4], Francesco Maisano[5], Elisabeth Pieske-Kraigher[1,2], Juliane Riess[2,6], Markus Reinthaler[2,6], Gunther Mai[7] and Tobias Daniel Trippel[1,2]

[1]Department of Cardiology, Charité – Universitätsmedizin Berlin, Campus Virchow Klinikum, Berlin, Germany, [2]German Centre for Cardiovascular Research (DZHK), Partner Site Berlin, Berlin, Germany, [3]Department of Cardiovascular Surgery, Charité – Universitätsmedizin Berlin, Berlin, Germany, [4]Department of Cardiothoracic- and Vascular Surgery, German Heart Center Berlin, Berlin, Germany, [5]Department of Cardiac Surgery, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) San Raffaele University Hospital, Milan, Italy, [6]Department of Cardiology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [7]Department of Cardiac Anesthesia, Charité – Universitätsmedizin Berlin, Berlin, Germany

We report on a 72 years old male patient with recurrent heart failure hospitalizations caused by severe mitral regurgitation due to severe restriction of the posterior mitral leaflet treated with the transfemoral mitral valve replacement (TMVR) system Cardiovalve. Immediate interventional success was obtained resulting in a quick mobilization and discharge.

KEYWORDS

mitral insufficiency, heart valvular disease, heart failure, TMVR, comput(eriz)ed tomography

Introduction

Mitral Regurgitation (MR) is a major risk factor for future morbidity and mortality. Patients with left ventricular (LV) dysfunction who have concurrent MR have a nearly two-fold increased risk of death or hospitalization (1). The current standard is to improve significant MR with surgical mitral valve replacement (MVR) or transcatheter edge-to-edge repair (TEER) (2). Transcatheter mitral valve replacement (TMVR) has emerged as a less invasive approach potentially surmounting some of the current hurdles associated with transcatheter edge-to-edge repair and high-risk mitral valve surgery (3).

Case report

We describe the case of a 72 years old male patient with preserved ejection fraction a recurrent history of decompensated heart failure caused by severe mitral regurgitation due to severe restriction of the posterior mitral leaflet by calcifications (Figure 1,1a) with a consecutive severe excentric posterior jet (Figure 1,1a). The patient has a > 10 years history of coronary heart disease with CABG LIMA/LAD, Vene/RIVP, Vene/D1, and Vene/M1 with preserved left ventricular ejection fraction, a history of stroke, atrial fibrillation, severe chronic obstructive pulmonary disease and

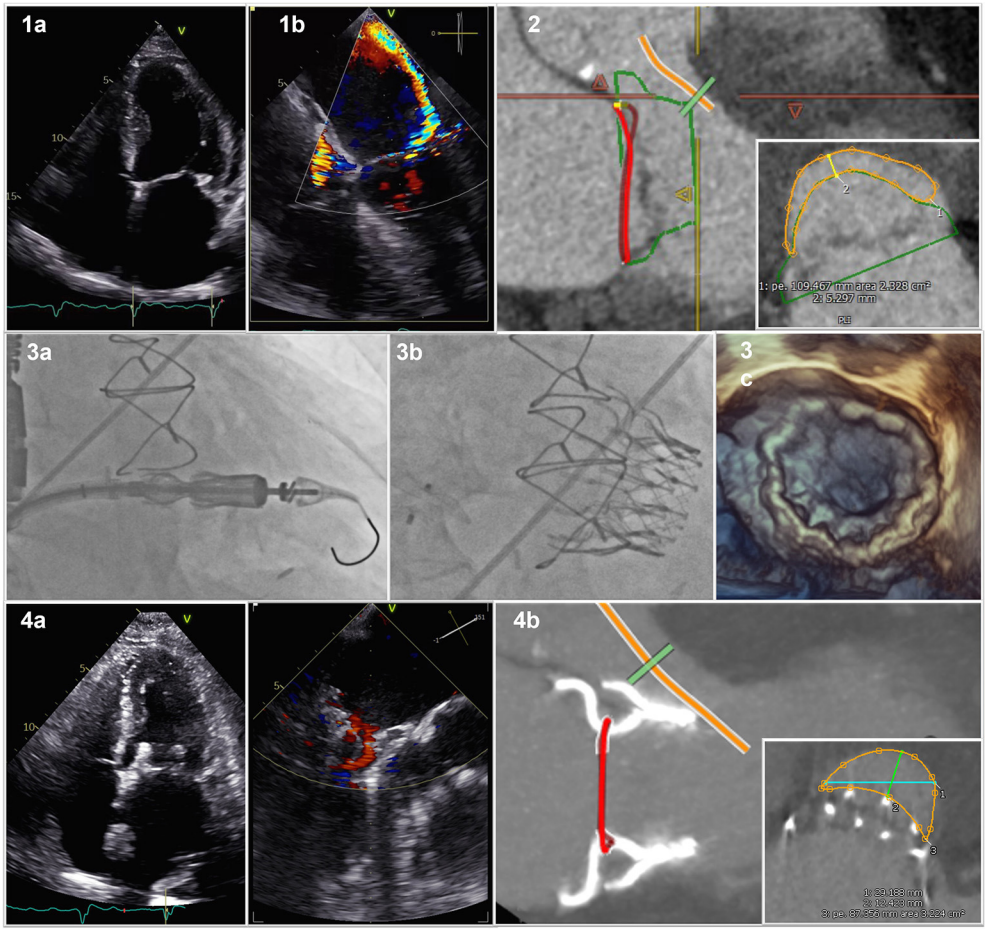

FIGURE 1
Cardiovalve in Mitral Valve Position. (1a) 2D posterior mitral leaflet by calcification; (1b) consecutive severe excentric posterior jet; (2) Pre-procedural computed tomography scan with valve sizing and predicted neo-LVOT; (3a) Fluoroscopy of device delivery; (3b) Fluoroscopy of device with closure of ASD; (3c) 3D transesophageal echocardiography of delivered Device; (4a) post-interventional result; (4b) Post-procedural CT scan with actual neo-LVOT.

pulmonary hypertension as well as chronic kidney disease with a eGFR of 48 ml/min/1.73 m^2 (by CKD-EPI) resulting in a Euro Score II of 19.40% and STS for Morbidity and Mortality of 33.223% (Version 4.2). Given the clinical condition and patient history he was deemed inoperable for conventional MVR, minimal-invasive right thoracotomy surgical treat treatment or TEER by our institutions interdisciplinary heart team in August 2021.

On March 11th, 2022 he was admitted to our institution with New York Heart Association (NYHA) functional class IV, peripheral edema, pleural effusions and jugular vein distension. His NT-proBNP was 2,894 ng/L and recompensation with intravenous diuretic therapy was initiated. Screening computed tomography scan confirmed anatomic suitability for Cardiovalve prosthesis (Figure 1,2) and projected a neo left ventricular outflow tract (LVOT) of ~2.3 cm^2. After approval by AHEAD screening committee patient has been enrolled in the AHEAD-Trial (ClinicalTrials.gov, Identifier: NCT03339115) and scheduled for transcatheter mitral valve replacement (TMVR) with the Cardiovalve (Cardiovalve, Or-Yehuda, Israel).

The Cardiovalve is based on a low-profile design of three scallop-shaped bovine pericardial leaflets designed to be delivered through a transfemoral transseptal approach using a 32-F capsule with a 24-F shaft (4). Three valve sizes are available, covering an intracommissural annular size from 36 to 53 mm (4). The patient underwent the procedure on March 16th, 2022 in our hybrid operation theater under guidance with fluoroscopy and transesephageal echocardiography in full anesthesia. A surgical vascular access of the right femoral vein was established. Transeptal puncture was performed employing the VersaCross® Transseptal (Baylis Medical, München, Germany) System under balloon dilatation of the intraatrial septum with a 10 mm balloon. The delivery system was inserted

into the left atrium and centered with respect to the mitral annulus before final deployment and stabilized with a 300 cm Lunderquist in over the wire technique under fluoroscopic guidance (Figure 1,3a). We implanted a 45 mm Cardiovalve Mitral Valve replacement in a stepwise procedure. Mean transvalvular gradient was < 4 mmHg. The procedure related atrial septum defect was closed using a 12 mm Amplatz Occluder (Abbott, Abbott Park, IL, USA) (Figure 1,3b). Transesophageal echocardiography showed the correct positioning of the valve, with no leak, and no LVOT (Figure 1,3c). The patient was extubated in the hybrid operation theater immediately after the procedure, transferred to our intermediate care ward for 24 h for surveillance and hence transferred to our normal care ward for another 5 days of recompensation and mobilization.

Post-procedural echocardiography showed a satisfactory result (Figure 1,4a), CT scan confirmed prosthesis stability, no evidence of left ventricular outflow tract (LVOT) obstruction (Figure 1,4b) with an actual neo-LVOT of ~3.2 cm^2 before discharge. We did observe a clinical improvement to NYHA functional class II and rapid recompensation. The patient was discharged on 25th of March 2022 and the 30 day post-discharge timeframe was event free. Given the pre-existing indication for oral anticoagulation due to atrial fibrillation, the patient continued to take warfarin after discharge. The present report shows the feasibility of TMVR with a fully percutaneous antegrade system in the setting of a severe restriction of the posterior mitral leaflet.

Discussion

The case we report here focuses on a patient with clinical signs and symptoms of heart failure with recurrent heart failure hospitalizations due to significant mitral valve disease. Despite his young age, he was deemed inoperable. Severe leaflet restriction and calcification hindered the option of TEER. The ongoing interventional revolution in the field of structural heart disease brought a novel treatment option to the hybrid operation table: Cardiovalve.

Thanks to the rapidly evolving field, we were able to treat this patient within the European Feasibility Study of the Cardiovalve Transfemoral Mitral Valve System (AHEAD) and obtained fine short term clinical, structural and imaging results. Of special note, the actually obtained neo-LVOT was greater than the predicted neo-LVOT. The low-profile design of three scallop-shaped bovine pericardial leaflets employed in the Cardiovalve enabled a considerate treatment in a patient deemed clinically unfit for conventional MVR as well as anatomically unfit for minimal-invasive right thoracotomy surgical treat treatment or TEER.

Yet, structured outcome data on short and long-term morbidity and mortality remain lacking. Safety, performance and outcome data of TMVR devices such as Cephea®, Evoque®, Intrepid®, Sapien M3®, and NaviGate® competing with Cardiovalve® in some aspects will have to be taken into account.

TMVR will further advance the field of transcatheter treatments of mitral valve disease and allow promising treatment options for many patients.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by LAGESO, BfArM. The patients/participants provided their written informed consent to participate in this study.

Author contributions

MS and TT conceptionalized, drafted, and wrote the article. SS, FM, GM, MR, JR, and EP-K reviewed the article for important intellectual content. All participated in patient care. All authors contributed to the article and approved the submitted version.

Conflict of interest

Author MS reports to be principal investigator of the AHEAD trial at the respective site and received honoraria from Edwards Lifesciences, Abbott and Cardiovalve. Author FM reports honoraria from Edwards Lifesciences, Abbott and Cardiovalve.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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EDITED BY
Alexander Assmann,
Heinrich Heine University, Germany

REVIEWED BY
Amin Polzin,
University Hospital of Düsseldorf, Germany
Ram Sharony,
Rabin Medical Center, Israel

*CORRESPONDENCE
Ankur Srivastava
ankur.srivastava@uchospitals.edu

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Transcatheter aortic valve replacement in patients undergoing robotic totally endoscopic coronary artery bypass: A case series

Ankur Srivastava[1]*, Jennifer Smazil[1], Lauren Roark[1], Hayla A. Shah[2], Husam H. Balkhy[3] and Atman P. Shah[1]

[1]Section of Cardiology, University of Chicago Medicine, Chicago, IL, United States, [2]University of Chicago Laboratory Schools, Chicago, IL, United States, [3]Section of Cardiac Surgery, University of Chicago Medicine, Chicago, IL, United States

Transcatheter aortic valve replacement (TAVR) has been utilized to treat patients with symptomatic aortic stenosis (AS). Recent trials suggest comparable efficacy compared to surgical aortic valve replacement (SAVR). Robotic off-pump totally endoscopic coronary artery bypass graft surgery (TECAB) had been shown to be a minimally invasive revascularization strategy with clinical results comparable to traditional coronary artery bypass graft surgery (CABG). Traditionally, pre-surgical coronary evaluation is considered necessary to optimize coronary revascularization at the time of AVR. The 2020 ACC/AHA Guideline for the Management of Patients with Valvular Disease gives a moderate recommendation, based on limited data, for CABG at the time of AVR in patients with significant coronary artery disease (CAD). This paper presents two patients with known significant CAD awaiting robotic TECAB who were treated with TAVR, prior to surgical revascularization. Robotic TECAB is unique in that it offers patients the ability to have complete coronary revascularization without a sternotomy and with early ambulation, discharge, and recovery. The case series demonstrates a hybrid approach that offers complete sternotomy sparing cardiovascular care to treat severe symptomatic AS and CAD. Since patients with severe aortic stenosis are at high risk of developing cardiac arrest and cardiogenic shock upon induction of anesthesia, the ability to treat severe symptomatic AS with TAVR under conscious sedation prior to TECAB can be considered as a safe an effective treatment.

KEYWORDS

TAVR, TECAB, CAD, survival, SAVR

Introduction

Patient 1

Patient 1 is a 74-year-old male with severe AS and significant CAD. He was self-referred for a sternal sparing approach to his combined disease after being offered sternotomy at another hospital. Transesophageal echocardiography (TEE) showed an ejection fraction (EF) of 55%, aortic valve area (AVA) of 0.6 cm^2 and a mean gradient of 43 mmHg. Left heart catheterization (LHC) revealed a 70% stenosis in the proximal left anterior descending artery (LAD) with a 90% stenosis of the first OM and a totally occluded second OM with good targets for surgical revascularization. After a multidisciplinary meeting, the decision was made to complete TAVR before TECAB. Pre-TAVR, the patient had dyspnea and fatigue after one flight of stairs (NYHA class II) with an STS Risk Score of 10.708%.

The patient underwent successful TAVR with an Edwards Sapien S3 transcatheter valve via the right common femoral artery (Edwards Life Sciences, Irvine CA). Echocardiogram revealed a transvalvular mean gradient of 1 mmHg and no paravalvular leak. The patient had an uncomplicated hospital course post-TAVR and was discharged home the next day. At 1-month follow-up, he reported improvement of symptoms (NYHA class I). TTE revealed an EF of 64.2% with a mean gradient of 7 mmHg, without AI.

Two months later, the patient underwent a robotic 3-vessel TECAB after his DAPT was discontinued, and he received a RIMA-LAD (due to larger caliber vessel) with a sequential LIMA-OM1-OM2. Robotic TECAB was performed totally endoscopically (Figure 1). The DaVinci Robotic Surgical System (Intuitive Surgical, Sunnyvale CA) is used to endoscopically (no thoracotomy) harvest one or both internal thoracic arteries (ITA) as well as to perform the anastomosis is which is completed in our program off cardiopulmonary bypass on the beating heart.

The patient was discharged on post-op day two and reported resumption of all normal activities at post-op clinic visit with NYHA Class I symptoms.

Patient 2

Patient 2 is a 67-year-old male with CAD who presented as a self-referral for severe AS/CAD. TTE showed an EF> 70%, AVA 1.2 cm^2 with a mean gradient of 47.7 mmHg. Coronary angiography revealed a 70% proximal LAD that involved the ostium of the first diagonal branch and a 75% stenosis in the right coronary artery. Pre-TAVR, the patient reported fatigue with dyspnea on exertion while performing activities of daily living. His exercise tolerance was limited to 3 blocks, putting him in NYHA Class II with an STS risk of 1.9%. Given his obesity (BMI 42), a sternotomy was felt to be too high risk and he was referred for a sternal sparing approach.

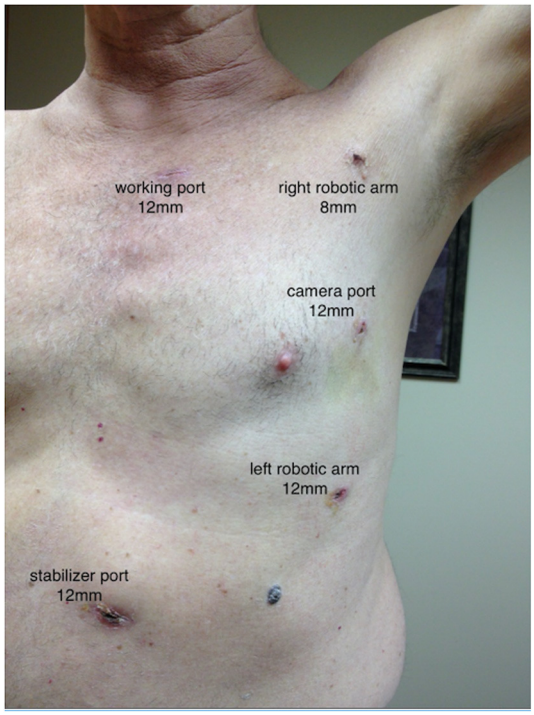

FIGURE 1
Illustration of TECAB approach (courtesy of Dr. H. Balkhy).

The patient was treated with percutaneous coronary intervention of the RCA with a drug eluting stent to treat the 75% RCA lesion and then underwent uncomplicated TAVR with a 26 mm Sapien S3 transcatheter valve via a transfemoral approach. He had an uncomplicated hospital course and was discharged the following day. The patient returned to clinic in 1 month and reported slight improvement in shortness of breath. His follow up TTE revealed an of EF 68.7% with a trans-prosthetic gradient of 16.7 mmHg and mild peri-prosthetic regurgitation.

Robotic 2-vessel TECAB was completed 2 months later with LIMA-D1-LAD. His post-operative course was unremarkable and he reported resumption of pre-procedure activities with minimal complaints.

Discussion

The 2020 ACC/AHA guidelines have deemed it reasonable to consider PCI before TAVR in patients with significant left main disease. However, in patients with multivessel disease, SAVR and CABG are recommended over TAVI and PCI (1). This is grounded in a theoretical concern that coronary ischemia will complicate aortic valve surgery with the thought that

TABLE 1 Clinical characteristics.

	Age	Comorbidities	Laboratory data	Smoker	Prior revascularization
Patient 1 (BB)	74	Diabetes Hypertension	Creatinine 0.9 mg/DL Hb (g/dL)/HCT (%): 11.2/39	Yes	None
Patient 2 (WF)	67	Diabetes Hypertension Dyslipidemia	Creatinine 1.3 mg/DL Hb (g/dL)/HCT (%): 10.6/35	Yes	None

Summary of cases by angiography results (*LAD* left anterior descending; *OM* obtuse marginal; *D1* 1st diagonal; *RCA* right coronary), valve hemodynamics, left ventricular ejection fraction, valve type, TECAB results and 90-day survival.

TABLE 2 Summary of cases.

	Age	Angiography	Aortic valve	LVEF (%)	Valve type	TECAB	90 Day survival
Patient 1 (BB)	74	LAD 70% OM1 90% OM2 100%	Mean gradient: 41.9 mmHg Velocity: 3.6 M/sec AVA: 0.76 cm^2	73	Edwards Sapien S3 Ultra 26 mm	RIMA—LAD Sequential LIMA-OM1/OM2	Yes
Patient 2 (WF)	67	LAD 70% D1 80% RCA 75%	Mean Gradient: 47.4 mmHg Velocity: 4.6 M/sec AVA: 1.2 cm^2	>70	Edwards Sapien S3 Ultra 26 mm	LIMA—LAD/D1	Yes

severe AS along with severe CAD would lead to hemodynamic compromise during induction of anesthesia and would result in a more complicated peri-operative course. Similarly, the European Society of Cardiology and European Association for Cardio-Thoracic Surgery recommend coronary angiography before valve surgery in patients with severe aortic stenosis and a history or concern for myocardial ischemia (2). However, the definition of significant CAD is dependent on angiographic assessment rather than functional assessment.

There is a need for more studies to support TAVR being completed before revascularization. In a meta-analysis of 15 studies, CAD was associated with higher all-cause mortality at 1 year in patients undergoing TAVR (3). Studies have found that patients who underwent incomplete revascularization as part of the TAVR workup had a higher incidence of cardiovascular events at 2 years, suggesting the importance of a revascularization strategy around the time of aortic valve surgery (4). In patients undergoing SAVR, with co-existing CAD, Thalji demonstrated a decreased mortality after undergoing concomitant CABG at 5 and 8 years compared to those whose CAD was managed medically (5). After a multidisciplinary discussion, we decided to proceed with the TAVR prior to the TECAB because of the risk of hemodynamic collapse in patients with severe AS at the time of anesthesia induction.

While no randomized trial currently exists studying the role of surgical revascularization prior to SAVR, the ACTIVATION trial reported no benefit to PCI prior to TAVR when looking at 1 year mortality or rehospitalization (6). It also found increased bleeding in patients who underwent PCI (6). Given the purported benefit of fractional flow reserve (FFR) calculations prior to CABG, the ongoing NOTION-3 trial, which is investigating the role of FFR guided revascularization pre-TAVR, may provide additional insights on the timing of revascularization in the setting of AVR (7–9).

Currently, no large randomized trials comparing TECAB to traditional CABG currently exists, but there are a number of non-randomized trials and observational studies that suggest that TECAB is as safe and effective as traditional CABG (10, 11). And further studies are needed to assess the cost-effectiveness of this strategy. The up-front costs of the TAVR and TECAB may be higher than traditional surgery, however, the shortened hospital stay and potentially fewer complications may offset that initial cost.

One additional concern is the duration of antiplatelet therapy after TAVR. Currently, guidelines suggest 6 months of dual antiplatelet therapy (at least aspirin 81 milligrams daily and clopidogrel 75 milligrams daily) after TAVR. However, a number of studies have suggested a shorter duration is safe and effective (8). Therefore, we elected to treat patients with 1 month of dual antiplatelet therapy in advance of their surgical revascularization.

Our hospital is a referral center for robotic heart surgery and routinely offers single and multivessel totally endoscopic

all arterial revascularization for appropriate candidates. As seen in Figure 1, our approach for patients with CAD combined with AS demonstrates that TAVR can be safely completed prior to coronary revascularization (12, 13). They returned to their pre-procedural activities within a few weeks of each procedure respectively and felt improvement of their previous symptoms. These patients will have continuous clinical follow-up to fully assess the clinical efficacy and safety of this combined strategy.

Conclusion

This case series reports that TAVR prior to robotic TECAB offers a safe sternal-sparing approach to patients with combined aortic valve and coronary artery disease who are unwilling or unable to undergo a standard sternotomy (Data in Tables 1, 2). This hybrid technique offers a truly minimally invasive approach to patients with AS and CAD that is not amenable to percutaneous revascularization. Early discharge and recovery are hallmarks of this approach and further studies are needed to not only elucidate the role of coronary revascularization prior to TAVR/SAVR, but also to investigate the hybrid role of TAVR and TECAB.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

ASh, ASr, and HB were responsible for the design of this study, data collection, manuscript creation, and manuscript review. JS, LR, and HS were responsible for manuscript creation and review. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY
Stephanie Sellers,
University of British Columbia, Canada

REVIEWED BY
David Meier,
Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland
Georgios Tzimas,
St. Pauls Hospital, Canada

*CORRESPONDENCE
Patrick Horn
patrick.horn@med.uni-duesseldorf.de

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Case report: Transcatheter edge-to-edge repair after prior surgical tricuspid annuloplasty

Shazia Afzal, Jafer Haschemi, Florian Bönner, Malte Kelm and Patrick Horn*

Division of Cardiology, Pulmonology and Vascular Medicine, Medical Faculty, University Düsseldorf, Düsseldorf, Germany

Residual and recurrent tricuspid regurgitation may occur frequently after surgical tricuspid valve repair. However, reoperation for tricuspid regurgitation is rare, although many patients are again highly symptomatic. Tricuspid transcatheter edge-to-edge repair (TEER) is a promising therapy for severe tricuspid regurgitation. Herein, we report a 77-year-old woman with recurrent symptomatic massive tricuspid regurgitation 2 years after sutured annuloplasty of the tricuspid valve. TEER was successfully performed using the TriClip® device and tricuspid regurgitation was reduced to a mild degree. In conclusion, tricuspid TEER is feasible following surgical suture annuloplasty. TEER is an alternative option for patients with a failed previous annuloplasty repair for tricuspid regurgitation to undergo a less invasive treatment rather than a potentially higher-risk reoperation.

KEYWORDS

TriClip, tricuspid regurgitation, annuloplasty, surgery, percutaneous

Introduction

Residual and recurrent tricuspid regurgitation may occur in 14–30% of patients early after undergoing surgery for all types of tricuspid annuloplasty (1, 2). However, reoperation for tricuspid regurgitation is rare, although many patients are symptomatic (1). The low rate of reoperation may be partly due to the fact that reoperation to repair or replace the regurgitant tricuspid valve is a high-risk procedure in high-risk patients. Transcatheter edge-to edge repair (TEER) is a promising therapy for severe tricuspid regurgitation (3, 4). Up to now, two TEER devices have CE mark for the treatment of tricuspid regurgitation, the TriClip® (Abbott, Santa Clara, CA, USA) and the PASCAL® Implant System (Edwards Lifesciences, Irvine, CA, USA). We here describe a case of a patient who was treated with the TriClip® device for recurrent tricuspid regurgitation after previous tricuspid annuloplasty.

Case presentation

The patient was 77-year-old woman with a history of ischemic cardiomyopathy and severe functional mitral and tricuspid regurgitation. Two years prior, she had undergone

coronary bypass surgery, mitral valve ring annuloplasty, and suture annuloplasty of the tricuspid valve (DeVega).

The patient complained of worsening heart failure symptoms, particularly peripheral edema, decreased physical capacity, and shortness of breath (New York Heart Association (NYHA) Functional Class III). Upon admission, physical examination revealed marked peripheral edema, jugular venous distension, and irregular heartbeat. The electrocardiogram showed atrial fibrillation. NT-proB-type natriuretic peptide level was 2,270 pg/mL.

Echocardiography demonstrated normal left ventricular function and mild mitral regurgitation after mitral ring annuloplasty but massive tricuspid regurgitation (vena contractae width of 15 mm) due to gradual dilation of the tricuspid annulus (diameter of 40 mm) (Supplementary Video S1). The patient was evaluated as to be at high risk for re-surgery of the tricuspid valve (EuroScore II 4.8%) and was considered for TTVr by the heart team.

TEER was performed by using the TriClip® device (Abbott, Vascular GmbH). During the TEER procedure, it was difficult to visualize the septal leaflet of the tricuspid valve in transesophageal echocardiography (TEE) due to shadowing from the annuloplasty ring on the mitral site. This was resolved by utilizing an atypically higher degree of probe rotation (Supplementary Video S2). Previous sutured annuloplasty of the tricuspid valve did not affect imaging of the valve or the procedure itself. The first device was used to grasp the anterior and septal leaflets. The second device was deployed to grasp the posterior and septal leaflets. Tricuspid regurgitation was reduced to a mild degree in postprocedural TEE (Figure 1), and in transthoracic echocardiography that was performed at the time of discharge (Supplementary Video S3). Hemodynamic improvement with slightly reduced left atrial pressure (from 12 mmHg before the procedure to 9 mmHg after the procedure) and markedly increased cardiac index (from 1.8 to 2.5 $L \cdot min^{-1} \cdot m^{-2}$). After 1 month of follow-up, repeat echocardiography demonstrated tricuspid regurgitation grade 1 without stenosis (transvalvular gradient of 1 mmHg). The patient reported that physical capacity and dypnea had improved (to NYHA functional class I).

Discussion

Residual and recurrent tricuspid regurgitation occurs in 14% of patients early during the first month after operation for all types of tricuspid annuloplasty (1). In non-ring annuloplasty as the DeVega technique, substantial worsening of late tricuspid regurgitation has been reported in up to 30% of all patients, presumably due to gradual redilatation of the annulus (1, 2). However, reoperation for tricuspid regurgitation is rare although many patients belong to NYHA class III or IV (1). The low rate of reoperation may be partly due to the fact that reoperation to repair or replace the regurgitant tricuspid valve is a high-risk procedure in high-risk patients (5).

TEER is an alternative option for patients with a failed previous annuloplasty repair for functional tricuspid regurgitation to undergo less invasive treatment, as demonstrated in our case. TEER following surgical tricuspid valve repair has previously been reported in two cases describing the off-label use of the MitraClip® device (6, 7). In another case report, recurrent TR after ring annuloplasty of the tricuspid valve was successfully treated by using the PASCAL® device (8). To our knowledge, this is the first case to demonstrate that TEER using the TriClip® device is feasible following surgical suture annuloplasty.

However, three issues should be considered before considering TEER in patients after previous tricuspid annuloplasty.

First, we must understand the reason for resistant or recurrent tricuspid regurgitation, and have to assess the chance of successfully treating tricuspid regurgitation. In patients with previous sutured annuloplasty, redilatation of the annulus, tethering of leaflets, or tearing of sutures can be easily addressed with TEER. In patients with previous ring annuloplasty, percutaneous valve-in-ring transcatheter heart valve implantation might be an alternative option to TEER. Cardiac CT measurements are required for pre-procedural planning when other devices are considered beyond TEER (valve-in-ring heart valve implantations or transcatheter tricuspid annuloplasty). Treating a tissue tear close to the annuloplasty ring or ring dehiscence may be challenging or even impossible with TEER.

Second, TEER is inherently dependent on echocardiographic image quality during the procedure, as the TEER device must be guided to the tricuspid valve through the right atrium, appropriately oriented on the tricuspid valve leaflets to optimally reduce tricuspid regurgitation, and adequate leaflet insertion of the leaflets must be determined. A previously placed surgical annuloplasty ring may limit the guidance of device placement and the assessment of leaflet insertion by creating an echocardiographic shadow. In the TRILUMINATE study, 25% of the patients who underwent successful TEER had previous mitral intervention (mainly surgery) (9). Thus, imaging may be challenging but there is no limitation for TEER in patients with prior mitral valve procedure. In the present case, even previous surgery at the tricuspid site was no obstacle for TEER. In patients with prior ring annuloplasty on the tricuspid valve, imaging of the leaflets may be challenging because of shadowing of the ring. To overcome these imaging difficulties, intracardiac echocardiography can be used as an alternative imaging approach (10).

Third, in patients with a previously placed surgical annuloplasty ring, there is a potential for tricuspid stenosis, which may be worsened by the reduction in valve area following TEER device placement. Therefore, assessment of the

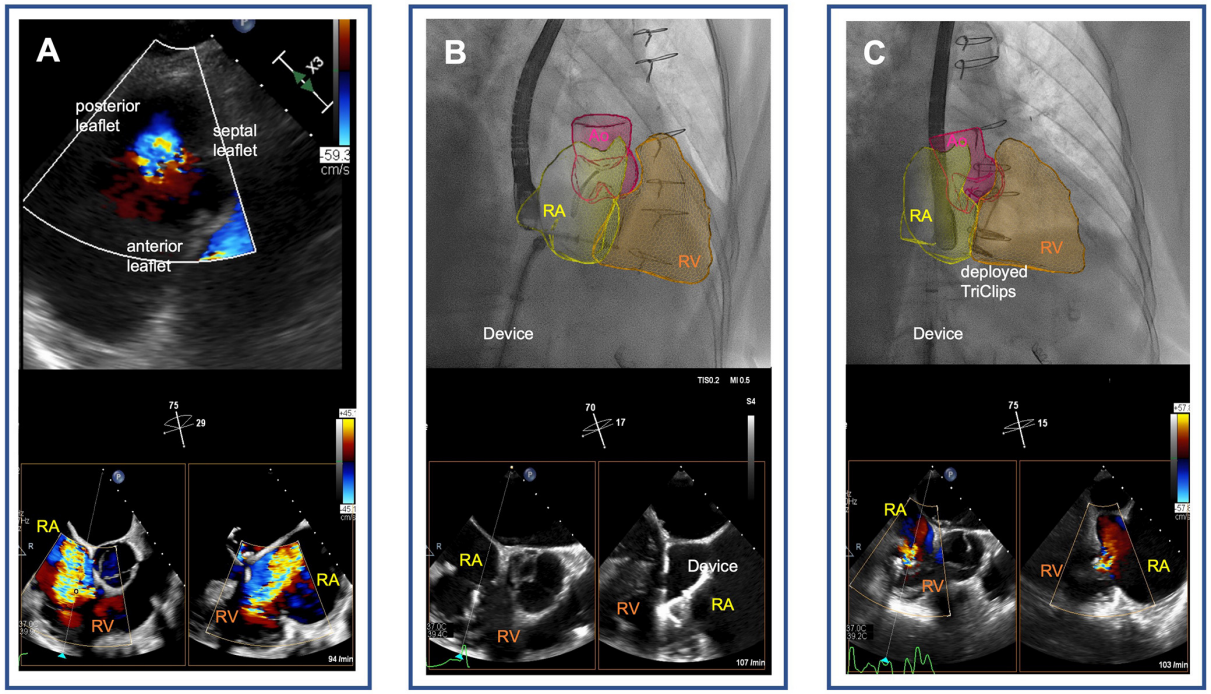

FIGURE 1
Tricuspid transcatheter edge-to-edge repair following surgical tricuspid annuloplasty. **(A)** Severe functional tricuspid regurgitation following sutured annuloplasty [transgastric view on the tricuspid valve **(upper panel)** and biplane transesophageal echocardiographic images of the right ventricular outflow tract **(lower panel)**]. **(B)** Real-time fusion imaging-assisted navigation of the transcatheter tricuspid valve repair device through the right atrium pointing to the tricuspid annulus **(upper panel)**. Biplane transesophageal echocardiographic images of the right ventricular outflow tract showing grasping of the septal and anterior leaflets of the tricuspid valve with the TriClip device **(lower panel)**. **(C)** Mild tricuspid regurgitation after deployment of two TriClips [real-time fusion of echocardiography-derived right heart cavities on fluoroscopy visualizes the TriClips **(upper panel)**, and biplane esophageal echocardiographic image demonstrates reduction of tricuspid regurgitation to mild degree **(lower panel)**]. RA, right atrium; RV, right ventricle; Ao, aortae.

transvalvular tricuspid valve gradient prior to and during the procedure is mandatory.

In our case, tricuspid regurgitation recurrence after annuloplasty was due to redilatation of the annulus, and imaging quality was adequate despite the annuloplasty ring on the mitral site, the transvalvular gradient across the tricuspid valve, and the risk of stenosis induced by an edge-to-edge repair technique was considered low. Thus, in our patient, recurrent tricuspid regurgitation after a previous surgery could be treated safely and efficiently.

Conclusion

TEER is feasible following surgical suture annuloplasty of the tricuspid valve. This is an alternative option for patients with a failed previous annuloplasty repair for functional tricuspid regurgitation to undergo a less invasive treatment rather than a potentially higher-risk reoperation to repair or replace the regurgitant tricuspid valve. More data with longer follow-up are needed to confirm these early findings.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

SA, JH, and PH wrote the original manuscript, performed formal analysis, and revised the manuscript and treated the patient involved in this case report. FB and MK were involved in supervision and manuscript review and editing.

PH conceptualized the study and responsible for the overall content. All authors contributed to the article and approved the submitted version.

Conflict of interest

Author PH has received travel support from Abbott, outside the submitted work.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2022.1044410/full#supplementary-material

SUPPLEMENTARY VIDEO S1
Transgastric echocardiographic **(first loop)** and transesophageal echocardiographic image **(second loop)** of the tricuspid valve demonstrating severe functional tricuspid regurgitation due to redilatation of the annulus following sutured annuloplasty.

SUPPLEMENTARY VIDEO S2
Transesophageal echocardiographic image demonstrating difficult visualization of the septal leaflet of the tricuspid valve in transesophageal echocardiography (TEE) due to shadowing from the annuloplasty ring on the mitral site.

SUPPLEMENTARY VIDEO S3
Transesophageal echocardiographic image demonstrating grasping of the septal and anterior leaflets of the tricuspid valve using a high degree of probe rotation to overcome shadowing.

SUPPLEMENTARY VIDEO S4
Biplane transesophageal echocardiographic image demonstrating reduction of tricuspid regurgitation to mild degree after deployment of two TriClips.

SUPPLEMENTARY VIDEO S5
Transthoracic echocardiographic image demonstrating mild tricuspid regurgitation assessed at the time of discharge after a successful transcatheter tricuspid valve repair.

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EDITED BY
Maximillian A. Rogers,
Moderna Therapeutics, United States

REVIEWED BY
Eric Gnall,
Lankenau Medical Center, United States
Federico Migliore,
University of Padua, Italy

*CORRESPONDENCE
Andrea Colli
✉ colli.andrea.bcn@gmail.com

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Case report: Treatment of left-sided valve endocarditis using the Transapical AngioVac System and cerebral embolism protection device: A case series

Alessandro Fiocco, Andrea Colli* and Laura Besola

Department of Surgical, Cardiac Surgery Unit, Medical and Molecular Pathology and Critical Care, University of Pisa, Pisa, Italy

The AngioVac System (AngioDynamics, Latham, NY) was developed for the treatment of right-sided heart and intravenous masses. Lately, it has been employed to deal with left-sided heart masses, in particular, native valve endocarditis (NVE) and valve prostheses endocarditis (VPE) in high-risk patients. Left-sided heart endocarditis has a high morbidity, and it also has a high mortality when open heart surgery is performed. Recently, patients presenting with left NVE and VPE have been treated with the off-label use of the AngioVac System even if the solution presents a considerable cerebral embolization risk issue due to the risk of fragmentation rather than a complete en-bloc aspiration of the masses. A percutaneous cerebral embolism protection system is currently used in TAVI procedures, especially when the native valve presents extensive calcifications and consequent significant embolic risks. We hereby present a clinical case series of a combined utilization of the AngioVac System and cerebral embolism protection system Triguard (Keystone Heart Ltd., Herzliya, Israel) to treat left NVE and VPE in prohibitive-surgical-risk patients.

KEYWORDS

valve endocarditis, AngioVac System, TriGuard embolic protection device, minimally invasive, transapical access, prosthesis endocarditis

Introduction

The incidence of mitral or aortic endocarditis either on the native valve or prosthesis has increased over the last decade (1). Surgery is used in the presence of acute heart failure following valve dysfunction, local tissue destruction, large vegetations, and persistent bacteremia despite optimal prolonged antibiotic therapy (2). When not treated, infective endocarditis has high morbidity and mortality particularly when it involves valve prosthesis (1). However, approximately 20% of patients are not referred for surgery mainly because of their high surgical risk (3). The AngioVac System has FDA approval and a CE mark for the sole treatment of soft masses and embolic material in the right heart. It consists of a suction cannula, an extra-corporeal circuit including a filter, and a reinfusion cannula. Recently, off-label use of this technology has been prescribed for left-sided masses removal (4–6) even with concerns about cerebral embolization. Cerebral embolization prevention systems (TriGuard, Keystone Heart Ltd., Herzliya, Israel; Sentinel, Boston Scientific) are occasionally used in heavy calcified native aortic valves during TAVI procedures. In this study, we describe two cases of left-sided endocarditis

treated with transapical AngioVac vegetation aspiration coupled with the positioning of a cerebral embolic prevention device.

Patient #1 native mitral valve endocarditis

A 57-year-old woman was brought to the emergency room after an incidental fall due to loss of balance. She had a history of insulin-dependent type 2 diabetes complicated with inferior limbs trophic ulcers. She was also on hemodialysis for chronic kidney disease and was being treated for peripheral vasculopathy with right leg arteries and renal arteries stenting. She had severe obesity and was newly diagnosed with a left kidney mass with surgical indications. Her symptoms included bilateral hip pain, exertional dyspnea, fatigue, and drowsiness. Blood tests did not show significant alterations except for anemia, a critical increase in the white cell count ($21.80\times^{*}10^{3}/\mu l$), and inflammatory markers (CRP 19.63 mg/dl and 2.96 ng/ml procalcitonine). Creatinine was 7.47 mg/dl and urea was122 mg/dl. A transthoracic echocardiography (TTE) showed a large floating mass attached to the atrial surface of the posterior leaflet of the mitral valve close to the annular leaflet insertion. The mass freely prolapsed into the ventricular chamber during diastole, showing a mobile behavior and a small implant basis. Mild-to-moderate mitral regurgitation was associated with mass prolapse. These findings were later confirmed by transesophageal echocardiography (TEE), measuring a 20×8 mm neoformation (**Figures 1A,B**).

Considering her high surgical risk, the patient was accepted for mass aspiration using the AngioVac system. A cerebral embolic protection device TriGuard (Keystone Heart Ltd., Herzliya, Israel) was used before the procedure. The left subclavian artery was exposed and cannulated with a 16 Fr cannula (Biomedicus, Medtronic, Minneapolis, MN, USA) for blood reinfusion. Transapical access was obtained through a left anterolateral mini-thoracotomy at the 5th intercostal space. Two perpendicular pledgeted U-shaped purse strings were placed at the entry site. After full heparinization, to reach an ACT above 450 s, the ventricle was punctured, and an extra-stiff guidewire was inserted in the left ventricle (LV), carefully crossing the MV under real-time bi-plane TEE guidance. A 26 French GORE DrySeal (W.L. Gore & Associates, Newark, DE) was inserted on the guidewire into the left ventricle and was used to advance a 22 French 180

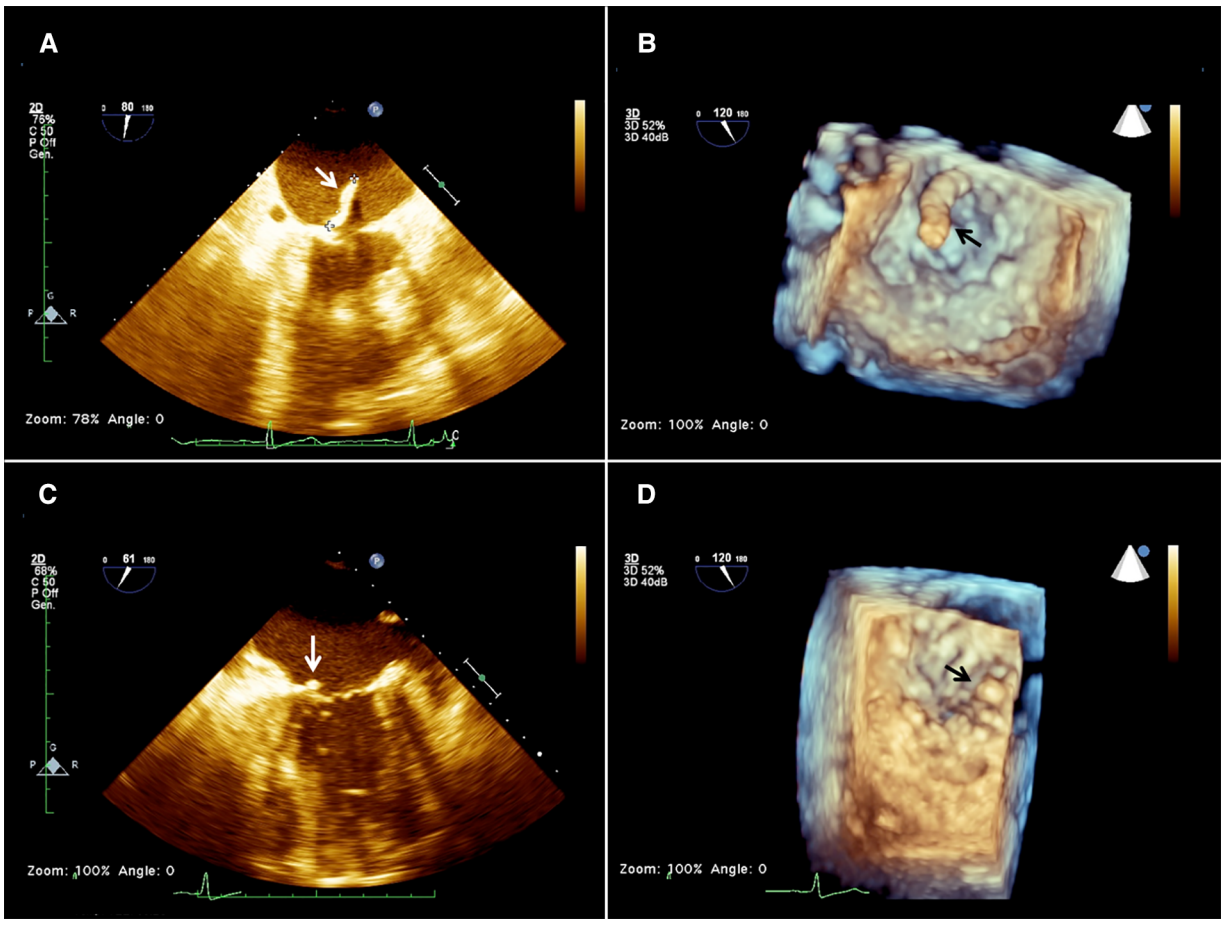

FIGURE 1
2d (A) and 3D (B) preoperative transesophageal echocardiography (TEE) showing the presence of a mass (arrow) attached to the base of the anterior mitral leaflet on the atrial aspect of the mitral valve, and 2D (C) and 3D (D) postoperative TEE showing a residual minimal stump (arrow).

degrees AngioVac aspiration cannula. The circuit was then established by connecting the outflow to the apical suction cannula and the inflow to the subclavian arterial cannula. An oxygenator (Horizon, Eurosets, Medolla, Italy) was interposed in the circuit, distally to the filter and to the centrifugal pump. The AngioVac cannula was maintained below the MV plane, and the suction was initiated till the mass disappeared on the TEE image and only the stump was left (**Figures 1C,D**). The suction cannula and the sheath were withdrawn from the heart, reinfusion of the blood was completed, the subclavian arterial cannula was removed, protamine was administered, and purse strings were tied. The TriGuard device was finally retrieved from the right femoral artery which was closed using a percutaneous suture-mediated closure system (PercloseProGlide SMC System, Abbot Vascular, CA, USA). The patient remained hemodynamically stable during the whole procedure with minimal blood loss. At extubation time in the operating room (OR) her neurological status was intact and no bowel/limb ischemia was observed. No specimens were available for histologic examination. Since we could not ascertain the true nature of the mass, intravenous antibiotic therapy was carried on for 6 weeks as part of the endocarditis protocol. TTE was performed 1 week after the procedure, and mild mitral regurgitation (MR) and no regrowth of the mass were reported.

Patient #2 mitral and aortic bioprosthesis endocarditis

A 54-year-old man with a history of previous aortic valve replacement with a mechanical prosthesis in 2018 and aortic and mitral valve replacement with bioprosthesis, both following valve endocarditis and permanent pace-maker implantation and intravenous (IV) drug abuse was brought to the emergency department for severe asthenia. On physical examination, he was sarcopenic and his vitals were normal. His blood test revealed anemia and kidney dysfunction. Considering his cardiac medical history, he underwent a TTE and a TEE that showed moderate biventricular dysfunction and the presence of vegetation on the mitral and aortic prosthesis with no regurgitation or signs of valve dysfunction (**Figures 2A,B**). Blood cultures tested positive for Enterococcus Faecalis, and IV antibiotic therapy was started. A total body CT scan showed spleen embolization. Because of the prohibitive risk related to the patient's poor general

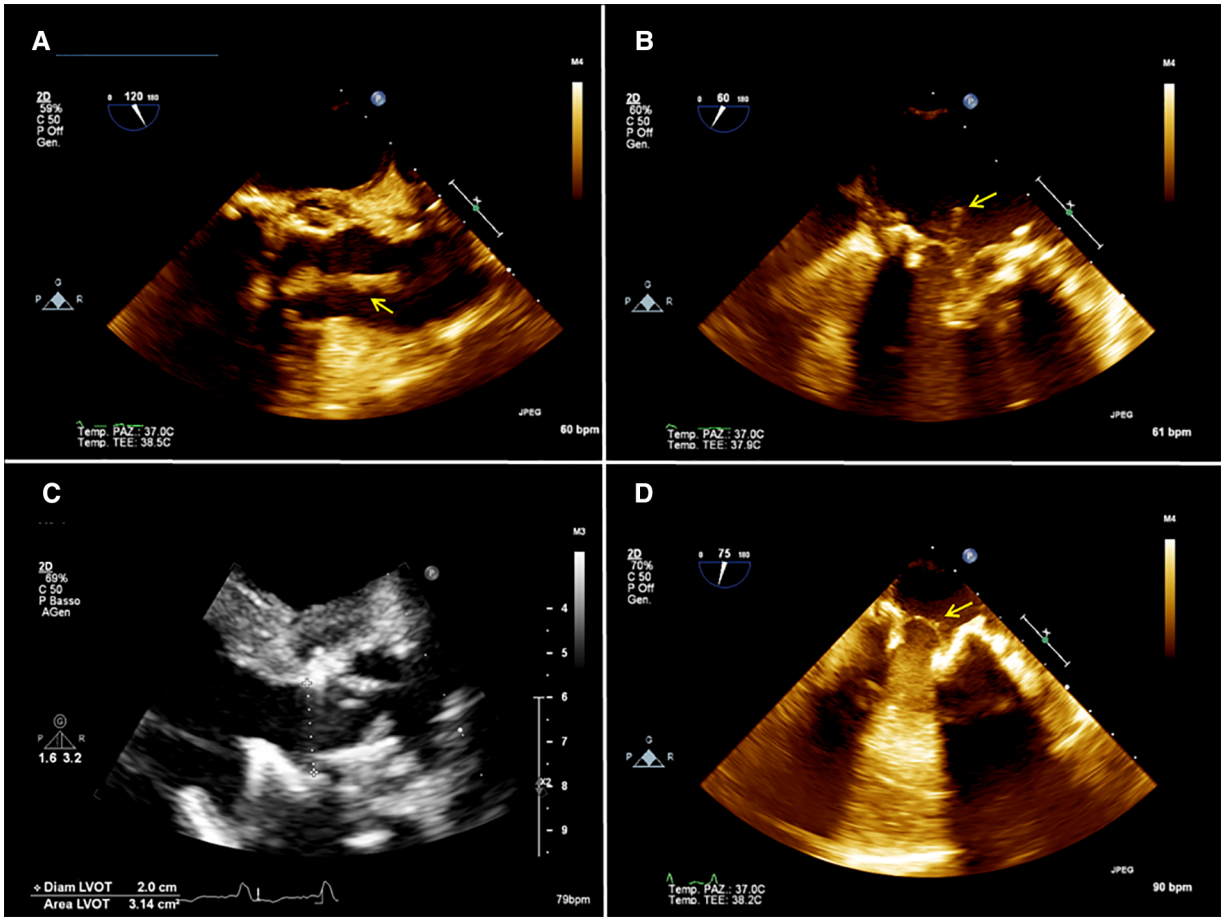

FIGURE 2
(A) 2D preoperative transesophageal echocardiography (TEE) showing the presence of a mass (arrow) attached to the aortic prosthesis and floating in the aortic root. (B) 2D preoperative TEE showing a mass (arrow) attached to the mitral prosthesis on the atrial side. (C) postoperative 2D TEE showing no residual mass on the aortic prosthesis. (D) postoperative 2D TEE showing a residual minimal stump (arrow) on the mitral prosthesis.

conditions, the complexity of the potential surgical correction of the disease, and the ongoing IV drug use, the AngioVac system was used to perform aspiration on the patient. A TriGuard was inserted through the left common femoral artery at the beginning of the procedure, then the left subclavian artery was isolated and cannulated with a 16 Fr Biomedicus cannula. The heart apex was exposed and prepared as previously described; a 26 French GORE DrySeal was inserted over a guidewire, and under real-time 2D bi-plane and 3D TTE, the 22 Fr 180° AngioVac cannula was connected to the circuit (with the same setup used for patient 1) and advanced just below the aortic plane and suction was initiated until most of the vegetations disappeared. With real-time 2D bi-plane and 3D TEE guidance, we crossed the mitral prosthesis with the AngioVac cannula; the cannula was bent to 180° and suction was started until satisfactory aspiration of the mitral vegetations was achieved. The final TEE showed no significant residual mass, trivial intraprosthesis aortic, and mitral regurgitation (**Figures 2C,D**). The procedure was completed as described above. The TriGuard was removed in the standard fashion and small vegetation fragments were found and sent for a culture test. The patient was extubated in the OR, and he did not report any neurological impairment or bowel and limb ischemia. At 1 month, TTE showed partial detachment of the aortic prosthesis with a moderate paravalvular leak (PVL) and absence of new vegetation. Considering the patient's surgical risk and good hemodynamic conditions, we preferred conservative management. Six-month TTE showed no leak progression and no vegetation.

Discussion

The AngioVac System has become a viable alternative to surgery to treat tricuspid valve/prosthesis and intravenous leads for permanent rhythm devices in patients with high surgical risk (7–9). Recent reports (10–12) showed its safety and effectiveness in different scenarios mostly involving the venous system and the right heart chambers, demonstrating its versatility as an option also to treat high-risk patients. More than having complete control of the infection, the first aim of the procedure is to debulk the vegetation size, lowering the embolic risk and the microbic burden with a positive impact on the effect of antibiotic therapy, thereby enhancing its effectiveness and controlling systemic involvement (9).

Treatment of aortic or mitral prosthesis endocarditis with the AngioVac System, though a transapical or transeptal approach, has been previously described with encouraging results (4–6). In this study, we report the first cases of the native mitral valve and combined mitral and aortic prosthesis endocarditis treatment using the AngioVac System in combination with a cerebral embolic protection device.

The presence of a floating mass attached to one of the left-sided valves of the heart is an urgent indication for cardiac surgery because of the high embolic risk (2). Conventional surgery entails the need for a cardiopulmonary bypass (CPB) and cardioplegic arrest which represent a great threat to frail patients like the reported cases. Therefore, a minimally invasive, beating-heart solution to remove the mass represents a valid alternative when there is no significant valve regurgitation or destruction.

Gerosa et al. (4) reported the use of the AngioVac System to treat an endocarditic mass located on the ventricular side of a mitral bioprosthesis through a transapical surgical approach. On the basis of these reports, we decided to extend the use of the AngioVac system to treat infective endocarditis involving the native mitral valve and both aortic and mitral prostheses. Both our patients were discharged with no in-hospital complications and no recurrence of endocarditis. The presence of a PVL at follow-up (FU) in Patient 2 was carefully evaluated since this condition is associated with worse outcomes; however, the decision for conservative management was driven by the patient's prohibitive surgical risk, which was the first reason we preferred to use the AngioVac procedure over conventional surgery. In cases like these, the PVL AngioVac procedure should be reserved for inoperable patients and close clinical FU is necessary. When treating the mitral valve, one drawback is an increased risk of MV subvalvular apparatus damage during LV navigation. Using a totally ventricular approach without crossing the valve under accurate real-time TEE guidance to enable optimal alignment with the MV orifice might lower this risk. Alternatively, a transeptal approach has been described (5, 6). However, after using the transeptal approach, the iatrogenic septal atrial defect might need to be closed with a closure device, but this occurrence is rare. Placement of material inside the heart in patients should, in our opinion, be avoided in patients with bacteremia; therefore, a careful evaluation of the hemodynamic impact of the ASD (significant shunt) must be done before proceeding with its closure. Transapical access, in expert hands, is a safe maneuver with minimal risk of access site complications and no significant impact on ventricular function (13), and the surgical technique to perform it is well established (14).

In the case of double involvement of mitral and aortic prostheses, a transapical approach allows for the corresponding treatment of both valves. In the presence of vegetation on the atrial side of a mitral prosthesis, it may be wise to prefer a 180° AngioVac cannula so that once it crosses the MV it can be angled downward in the direction of the mitral plane. Again, TEE imaging is of utmost importance to guide the operator during LV navigation and valve crossing. In our experience, we found it very useful to direct the AngioVac cannula using the bi-plane view.

Another drawback of this procedure is the risk of stroke due to mass embolization. For this reason, we decided to position a cerebral embolism protection device as reported by other authors (5, 6). This procedure is easy and safe and does not significantly prolong the fluoroscopy time of the procedure. Femoral or radial access can be used depending on the operator's preference and reinfusion cannula position.

Contrary to previous reports, we preferred an arterial reinfusion site (5), and we did not establish a parallel ECMO circuit (4) to support hemodynamics since the patient was not in septic shock and presented good cardiovascular conditions; however, we included an oxygenator that increased the filter

efficacy of the system. For this reason, an ACT > 450 s was achieved with no significant periprocedural bleeding complications. Other groups (5) preferred complete venous access with transeptal aspiration and reinfusion in the femoral vein. Even if this option was safe in reducing the risk of vascular complications, we believe that such a setup might provide inferior hemodynamic support to the patient, overloading the right system. However, in the case of inadequate arterial access for reinfusion, this choice would be preferable.

Conclusions

A minimally invasive approach using the AngioVac system can be safe and effective to treat native mitral valve and aortic and mitral prosthesis endocarditis in selected patients, especially when prohibitive surgical risk is present. The combined use of cerebral embolic protection is of utmost importance.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by CEAVNO Pisa. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

LB wrote and revised the manuscript and supervised data collection. AF collected data, wrote the manuscript and performed figure editing. AC revised the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY
Maximillian A. Rogers,
Moderna Therapeutics, United States

REVIEWED BY
Boris Schmitt,
German Heart Center Berlin, Germany
Nigel Wilson,
Auckland District Health Board, New Zealand

*CORRESPONDENCE
Feng Liu
✉ liufengxiangya@gmail.com
Chengming Fan
✉ fanchengming@csu.edu.cn

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Case report: Surgical valvular pulmonary reconstruction for a previous unreported rheumatic right-sided valve disease with severe pulmonary regurgitation

Zijing Zhou[1], Weijie Tang[2], Xiaokang Tu[2], Feng Li[2], Zhonghua Huang[2], Wancun Jin[2], Qin Wu[2], Feng Liu[2]* and Chengming Fan[2]*

[1]Department of Pulmonary and Critical Care Medicine, The Second Xiangya Hospital, Central South University, Changsha, China, [2]Department of Cardiovascular Surgery, The Second Xiangya Hospital, Central South University, Changsha, China

Rheumatic heart disease (RHD) is a widespread illness in developing countries. RHD causes 99% of mitral stenoses in adults and 25% of aortic regurgitation. However, it only causes 10% of stenoses of the tricuspid valve, and is almost always associated with left-side valvular lesions. Isolated right-side valves are rarely affected, but may result in severe rheumatic pulmonary regurgitation. Herein, we present a case of rheumatic right-sided valve disease with severe pulmonary valve contracture and regurgitation in a symptomatic patient, successfully managed by surgical valvular reconstruction with a tailored bileaflet bovine pericardial patch. The options for surgical approach are also discussed. To our knowledge, the presented rheumatic right-sided valve disease with severe pulmonary regurgitation is the first to be reported in the literature.

KEYWORDS
cardiac surgery, rheumatic heart disease, pulmonary valve, echocardiography, reconstruction

Introduction

In 65%–70% of patients with rheumatic heart disease (RHD), the mitral valve is the most commonly and severely affected, while the aortic valve accounts for 25% of lesions (1). Rheumatic tricuspid valve lesions occur in only 10% of patients and are almost always left-sided. RHD is a widespread illness in developing countries and causes 99% of mitral stenoses in adults, while the pulmonary valve is rarely affected (2). Pulmonary valve stenosis caused by rheumatic disease is quite rare and, when it occurs, it is almost always accompanied by rheumatic lesions of other heart valves. A few cases of rheumatic pulmonary valve disease were reported in 2016 in children under the age of 15 in the tropical zone of India and most of them presented with various degrees of pulmonary stenosis without the involvement of other cardiac valves (3). Severe isolated primary rheumatic tricuspid and pulmonary insufficiency with normal left-side heart valves is extremely rare and almost always accompanied by endocarditis, carcinoid syndrome and trauma (4, 5). Herein, we present a case of a severe rheumatic right-sided valvular regurgitation in a patient without endocarditis, carcinoid syndrome or trauma that was successfully managed by surgical pulmonary valve and trunk reconstruction with a tailored

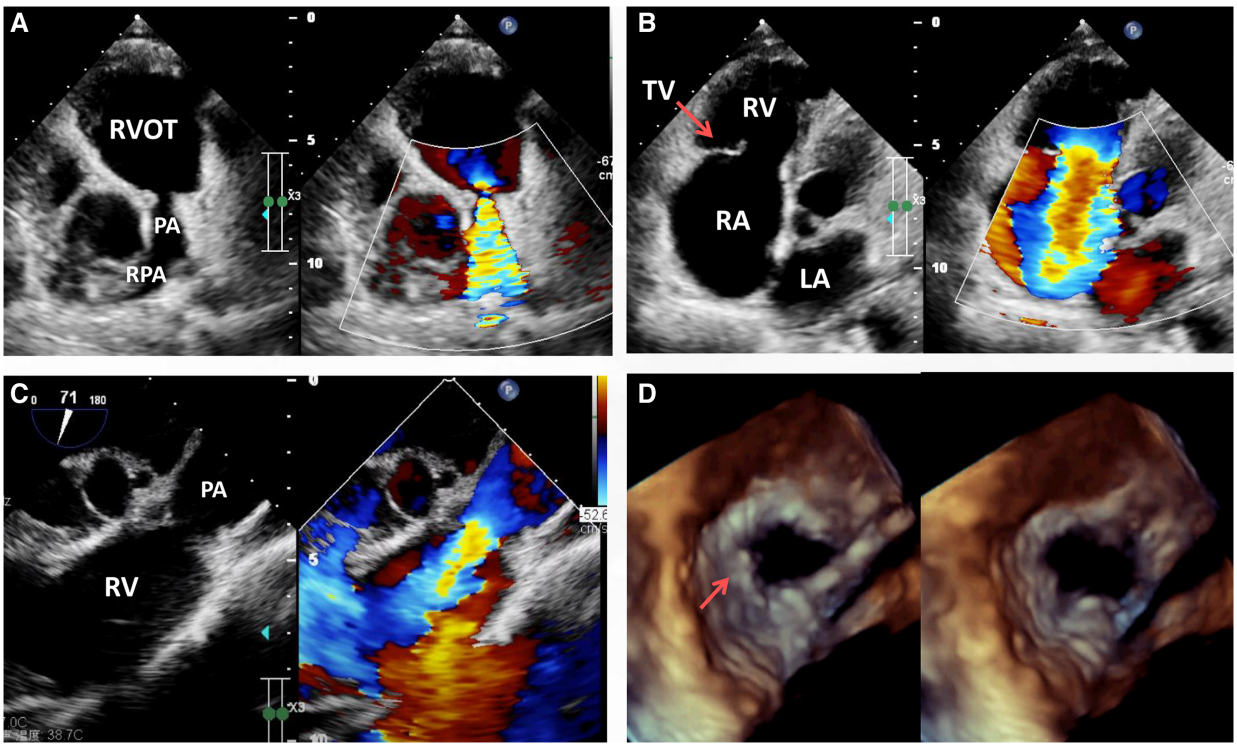

FIGURE 1
Transthoracic echocardiogram (TTE) pre-operation revealing the presence of severe pulmonary stenosis with the contracture of the pulmonary annulus and valves but with no sign of RVOT stenosis (A), RA enlargement, severe tricuspid regurgitation (B, arrow) and pulmonary regurgitation (C). Transesophageal echocardiography (TEE) immediately before surgery revealing severe pulmonary valvular insufficiency in the cardiac end diastolic period and end systolic period (D, arrow). LA, left atrium; PA, pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract; TV, tricuspid valve.

bileaflet bovine pericardial patch. The diagnostic modalities, surgical strategy and choice of operation technique are also discussed.

Case presentation

A 58-year-old female was referred to our cardiac center complaining of dyspnea on exertion and chest tightness over the last few years, which had gradually worsened in the last 2 weeks with lower limb edema. The patient had no previous history of cardiovascular disease and denied a relevant family history or a history of smoking, alcohol intake or drug abuse. She also denied a history of rheumatic fever. On admission, the patient's body mass index (BMI) and body temperature were 23.3 kg/m^2 and 36.5°C, respectively. Her blood pressure was 132/86 mmHg with a heart rate and radial pulse rate of 80 bpm.

Laboratory investigation including routine blood, stool, urine and troponins were all within the normal range. The biochemical examination showed no changes in serum levels of thyroxine, alkaline phosphatase, blood glucose, potassium, sodium, urea, creatinine, transaminase or total bilirubin. NT-pro BNP was 1,372 pg/ml (normal: 25–125 pg/ml) on admission. On physical examination, the patient had good psychomotor development without neurological signs or nystagmus, but peripheral lower limb edema was detected. A severe systolic and diastolic cardiac murmur in the precordial region was audible. ECG showed sinus rhythm with non-specific T-wave abnormalities in the lateral leads. Chest radiograph showed no significant signs of abnormality except for a mild enlarged cardiac silhouette. Coronary arteriography showed normal coronary flow without plaque or stenosis. Transthoracic echocardiogram (TTE) examination revealed the following measurements: left atrium 20 mm, right atrium 56 mm, LV cavity 53 ml (end-diastolic diameter) and 19 ml (end-systolic diameter), aorta 29 mm, pulmonary trunk from 13 to 27 mm with left and right pulmonary artery both 11 mm in diameter (**Figure 1A**). The pulmonary annulus (4 mm) and leaflets showed severe contraction and stenosis, the Vmax with peak and mean gradient were 3.4 m/s and 45 mmHg, respectively (**Figure 1A**). Severe tricuspid regurgitation (**Figure 1B**) and pulmonary regurgitation were also detected (**Figure 1C**, See **Supplementary Video S1**). Transesophageal echocardiography (TEE) confirmed the diagnosis (**Figure 1D**) and showed a short and thick solid ring bulge at the site of the pulmonary annulus (**Figure 1D**, arrow). Rheumatic right-sided valve disease with severe tricuspid and pulmonary regurgitation was diagnosed before surgery.

An open-heart operation was performed through a median sternotomy (**Figure 2A**), and cardiopulmonary bypass was established via routine aortic, superior and inferior vena cava

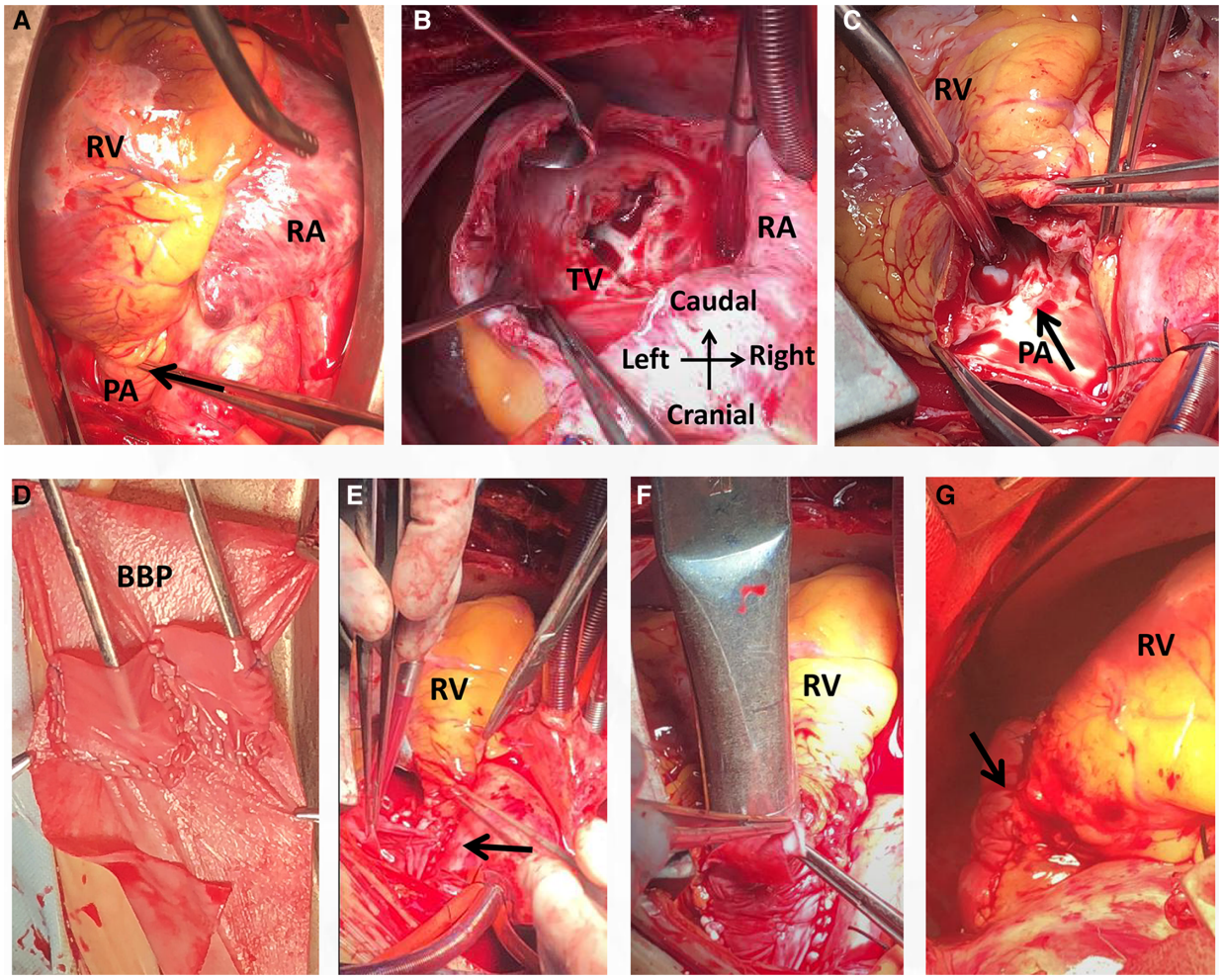

FIGURE 2
Intraoperative view showing a small pulmonary annulus (A), rheumatic tricuspid stenosis with regurgitation (B) and pulmonary regurgitation with valvular contracture (C). A bileaflet bovine pericardial patch was then tailored (D) and used for reconstruction of the pulmonary trunk with the leaflets at the same high level (E, arrow). The diameter of the reconstructed pulmonary was 20 mm (F). The operation was completed (G). BBP, bovine pericardial patch; PA, pulmonary artery; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract; TV, tricuspid valve.

cannulation under mild hypothermia of 30°C. The aortic cross-clamp and theinfusion of any cardioplegic solution were not applied. The tricuspid valve and pulmonary annulus were approached through the right atrium (Figure 2B) and a right ventricular outflow tract (RVOT) incision (Figure 2C), respectively. Valve sizing for tricuspid valve was 37 mm, thus the replacement with a size 29 bioprosthetic valve (Edwards 7300TFX) was performed. Notably, only one residual pulmonary valvular tissue was observed (Figure 2C, arrow), thus a bileaflet (23 mm each) bovine pericardial patch (Figure 2D) was tailored with a running suture and used to reconstruct the pulmonary trunk and the valves (Figure 2E) via a running suture with the leaflets at the same high level (*in situ*, Figure 2E, arrow) using Ozaki's technique (6). Once the reconstructed pulmonary trunk had been enlarged (Figure 2F), the technique was completed (Figure 2G). The reconstructed pulmonary valvular ring was measured with 20 mm in diameter. Hemostasis was then achieved, followed by chest closure. Intraoperative histopathologic examination of the excised specimen revealed fibrous tissue hyperplasia with hyalinosis (Figure 3A), mucoid degeneration (Figure 3B) and a few lymph cells infiltrated without valve calcification, which confirmed the diagnosis of rheumatic valvular heart disease (Figure 3). The operation was uneventful with Cardiopulmonary bypass time of 87 min. The postoperative course was also uneventful. The patient was discharged from the cardiac intensive care unit and from the hospital on the 2nd and 8th postoperative day, respectively. The TTEs performed at discharge detected good functioning of the bioprosthetic valve and the reconstructed pulmonary valves with only mild pulmonary regurgitation (Figure 4). During the 4 months of follow-up, the patient had an uneventful recovery and was symptom-free.

Discussion and conclusion

Pulmonary valve disease is often congenital, and only rarely do acquired disorders such as carcinoid and rheumatic fever affect the

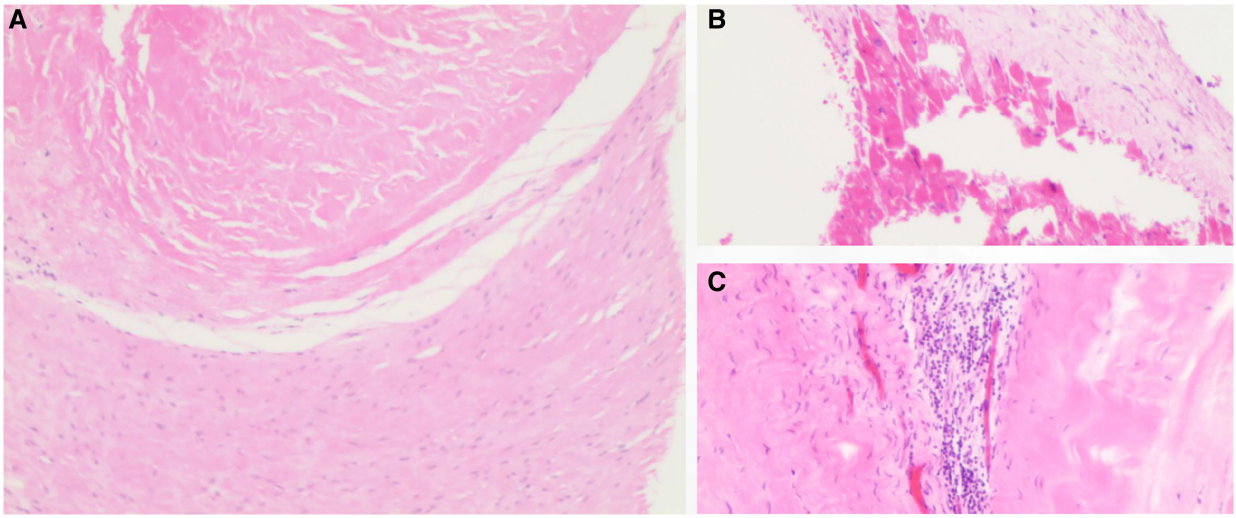

FIGURE 3
Histopathology of the tricuspid valve showed fibrous tissue hyperplasia with hyalinosis (A), mucoid degeneration (B) and the infiltrated lymphocytes (C). H&E staining, ×10 for panel A and ×40 for panel B,C.

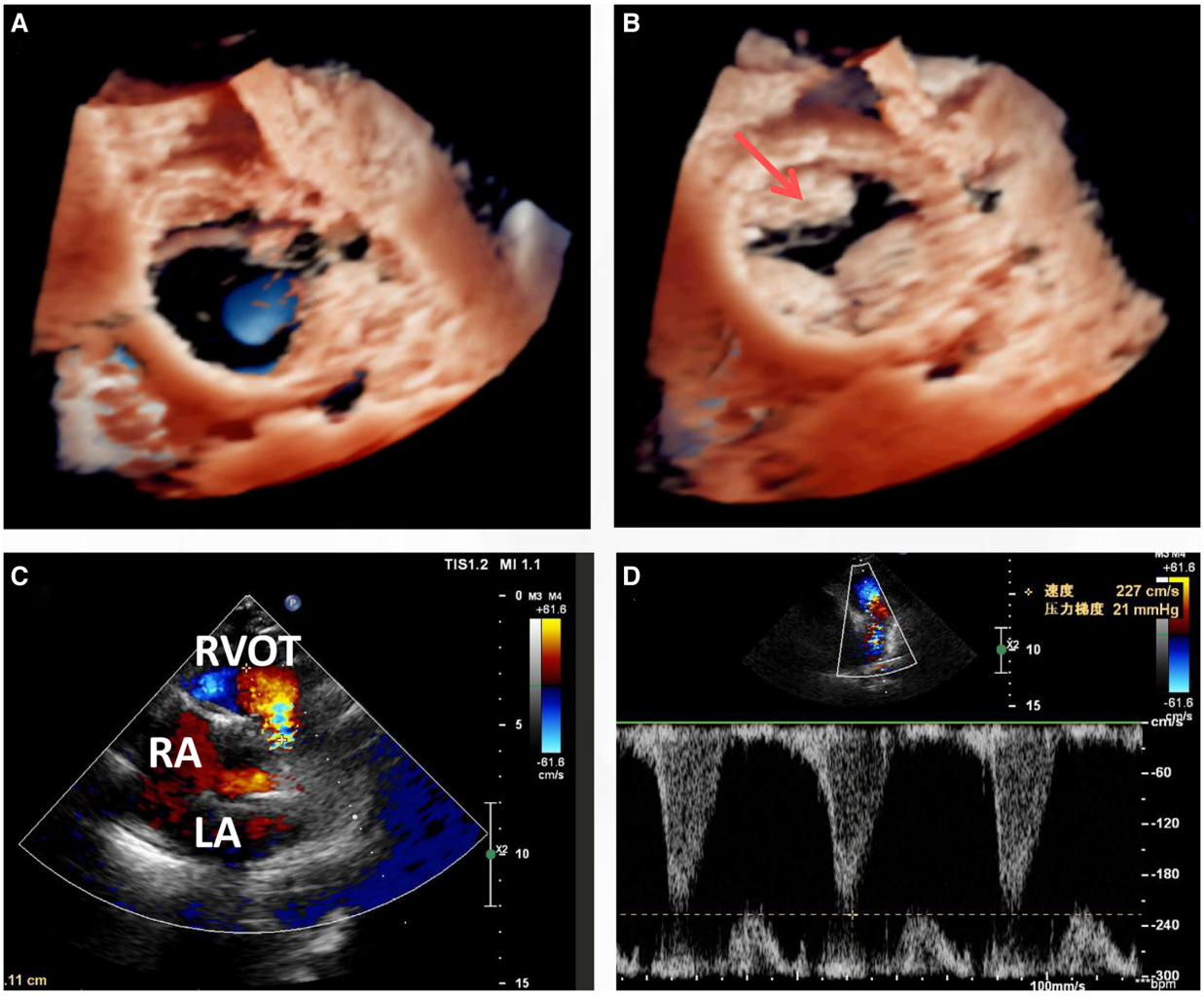

FIGURE 4
Transthoracic echocardiogram (TTE) at discharge (8 days post-surgery) indicated that the leaflets functioned well in both the cardiac phase of end systolic (A) and diastolic (B), with only mild regurgitation (C,D).

pulmonary valve (7). As with other types of valvular regurgitation, pulmonary valve regurgitation is a well-known valvulopathy that involves leakage of the pulmonary valve in the cardiac diastolic phase that leads to reverse blood flow heading from the pulmonary to the right ventricle. Etiologies of pulmonary regurgitation may be due to the valvular pathology, considered as a primary cause, or due to the dilation of the annulus from pulmonary arterial hypertension or pulmonary artery dilation, considered as a secondary cause (8). Rheumatism is a rare primary cause. Additional causes of pulmonary regurgitation include carcinoid heart disease, trauma and endocarditis (7). It was reported that acute rheumatic endocarditis involving the pulmonary valve may be more common than chronic valvular scarring resulting in clinically recognizable disease (9). However, isolated rheumatic right-sided valve disease with severe pulmonary valve contracture and regurgitation as presented in this case is extremely rare.

Echocardiography, which can be used to observe the valvular shape, size, effect on diastolic cardiac function, relationship with the adjacent tissues, and severity of the valve noninvasively, is currently the preferred diagnostic tool for patients with a suspected valvular disease (10). Mild pulmonary regurgitation detected via echocardiography is quite common and present in up to 78% of people (10). Notably, transthoracic echocardiography (TTE) is deficient in distinguishing the detailed features of various tissues, which was also apparent in the presented case. Thus, transesophageal echocardiography (TEE), which allows better visualization than TTE, is widely used during surgery. In the presented case, the lack of a pulmonary valve was misdiagnosed via TTE; however, the residual valvular tissue was observed via TEE and intraoperatively (**Figure 1D** arrow and **Figure 2C** arrow).

Valvular replacement is a traditional strategy for patients with severe rheumatic right-sided valve disease (7, 9). However, there are often anatomic challenges within the RVOT, including a small annulus, that limit replacement options (6). Nonvalved transannular patches are still frequently used because availability of the conduit remains problematic in some countries. This nonvalved patch technique may lead to severe pulmonary regurgitation and volume overload of the right ventricle, leading to right ventricular dilation, dysfunction and finally failure, arrhythmias, and sudden death. Conversely, due to valvular calcification, dysfunction and lack of growth potential, valved conduits are prone to stenosis and insufficiency, especially in young patients (6). Pulmonary valve replacement with polytetrafluoroethylene single leaflet, polytetrafluoroethylene bileaflet and trileaflet valves has been described but generally has not been broadly reproducible and has shown limited long-term competence (11, 12). In the presented case, residual valvular tissue was observed (**Figure 1D** arrow and **Figure 3C** arrow), and due to the small annulus, a tailored bileaflet (instead of trileaflet) bovine pericardial patch was used to reconstruct the pulmonary valve and trunk. Given the good functioning of the tailored bileaflet and the residual valvular tissue (**Figure 4B**), only mild regurgitation was detected during the follow-up period.

Although early technical success of the pulmonary valvular reconstruction with a tailored bileaflet bovine pericardial patch was achieved, the optimal leaflet material remains under debate. A larger sample size and long-term follow-up are needed.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of the Second Xiangya Hospital of Central South University. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

ZZ drafted the manuscript. CF and FLiu designed the study. FLi, ZH and QW revised the manuscript. WT, XT and WJ were responsible for the collection of data or analysis. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2023.1129529/full#supplementary-material.

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EDITED BY
Verena Veulemans,
University Hospital of Düsseldorf, Germany

REVIEWED BY
Francesco Giannini,
Maria Cecilia Hospital, Italy
Rutger-Jan Nuis,
Erasmus Medical Center, Netherlands

*CORRESPONDENCE
Oliver Reuthebuch
✉ oliver.reuthebuch@usb.ch

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Severe structural valve deterioration after TAVR with ACURATE Neo: report of two cases

Thibault Schaeffer[1], Luca Koechlin[1], Raban Jeger[2], Gregor Leibundgut[2] and Oliver Reuthebuch[1]*

[1]Department of Cardiac Surgery, University Hospital Basel, University of Basel, Basel, Switzerland, [2]Department of Cardiology, University Hospital Basel, University of Basel, Basel, Switzerland

Structural valve deterioration (SVD) of transcatheter implanted aortic valve (TAVR) prostheses leading to prosthesis dysfunction is an uncommon yet increasingly described complication. Literature is scarce on specific mechanisms and clinical presentation of SVD after TAVR, notably on self-expanding valve ACURATE Neo. We report on two cases with severe bioprosthetic failure after ACURATE Neo implantation due to leaflet disruption, and we treated them with surgical aortic valve replacement. Based on the literature, we further discuss the incidence of SVD after TAVR, the durability of ACURATE NEO, and the modes of failure of biological valve prostheses.

KEYWORDS

ACURATE Neo, TAVR explantation, structural valve deterioration (SVD), bioprosthesis failure, surgical aortic replacement

1. Introduction

Structural valve deterioration (SVD) refers to intrinsic alterations of bioprosthetic heart valves such as leaflet fibrosis and/or calcification, leaflet tear, and pannus that eventually lead to their hemodynamic dysfunction. Bioprosthetic failure (BVF) defines any clinically expressive valve dysfunction related to SVD or other conditions, such as endocarditis and prosthetic valve thrombosis, that eventually requires valve reoperation or reintervention (1). The clinical manifestation of bioprosthetic failure varies according to the severity of valve dysfunction. Literature is scarce on specific mechanisms and clinical presentation of SVD after TAVR, notably on self-expanding valve ACURATE Neo (Boston Scientific, Ecublens, Switzerland). We herein report on two cases with distinct mechanisms of SVD after ACURATE Neo implantation leading to BVF.

Abbreviations
SVD, structural valve deterioration; BVF, bioprosthetic valve failure; TAVR, transcathter aortic valve replacement; TTE, transthoracic echocardiography; AR, aortic valve regurgitation; TEE, transesophageal echocardiography; SAVR, surgical aortic valve replacement; EAPCI, European Association of Percutaneous Cardiovascular Interventions.

2. Case description

2.1. Case 1

A 70-year-old man was implanted with ACURATE Neo (size M) for symptomatic, severe aortic valve stenosis. The procedure was unremarkable, and transthoracic echocardiography (TTE) at discharge showed a mean aortic transvalvular aortic gradient of 7 mmHg and trivial paravalvular regurgitation. Approximately 4 years (54 months) later, he presented to his regional hospital with rapidly progressive dyspnea. TTE revealed severe aortic valve regurgitation (AR). After transfer to our tertiary center, transesophageal echocardiography (TEE) demonstrated a well-seated TAVR prosthesis with severe intraprosthetic, eccentric AR (see **Figures 1A,B**). Transvalvular aortic gradients were slightly elevated (mean pressure gradient 18 mmHg). Blood cultures were negative. Considering the intermediate surgical risk of the patient, we opted for an emergent TAVR explant and surgical aortic valve replacement (SAVR). Intraoperative inspection of the prosthesis revealed a leaflet disruption with its adjacent strut in the noncoronary position (see **Figure 1C**). There were no signs of endocarditis. Extraction of the prosthesis was complicated due to extensive pannus arising from the heavily calcified native aortic valve. Due to subsequent lacerations of the aortic annulus, the aortomitral junction was reconstructed with a bovine pericardial patch, and a 23-mm stented bioprosthesis was implanted in the aortic position. The postoperative course was uneventful, and the patient was promptly discharged. After an internal review, the manufacturer was unable to identify the cause of prosthesis dysfunction. According to the manufacturer's archive, the referenced device had passed all tests during manufacturing and met all required specifications before approval for final distribution and sale.

2.2. Case 2

An 80-year-old woman was implanted with ACURATE Neo (size S) for symptomatic aortic valve stenosis. Moderate residual AR after valve deployment was immediately addressed with single balloon dilatation. TTE at discharge and at the 1-year routine control showed no significant regurgitation and low transaortic gradients. After barely 2 years (23 months), the patient complained of sudden dyspnea and medication-refractory elevated blood pressure. TTE performed by her cardiologist revealed a severe AR. TEE after admission at our center

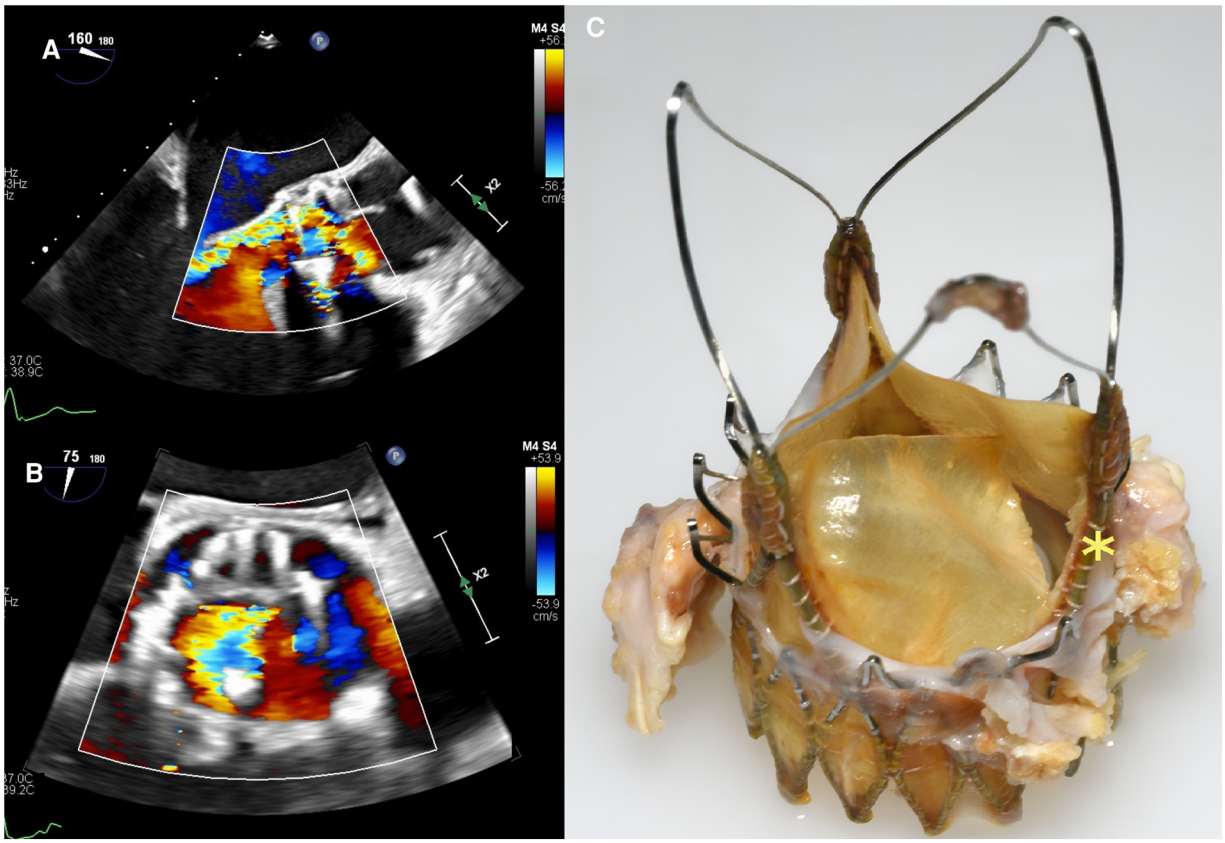

FIGURE 1
Case 1: transesophageal echocardiography three-chamber view with color-flow Doppler (**A**) and aortic valve-centered short-axis view with color-flow Doppler (**B**) showing an eccentric, severe intraprosthetic regurgitation. (**C**) Explanted ACURATE Neo prosthesis with leaflet disruption with its adjacent strut in the noncoronary position (yellow asterisk).

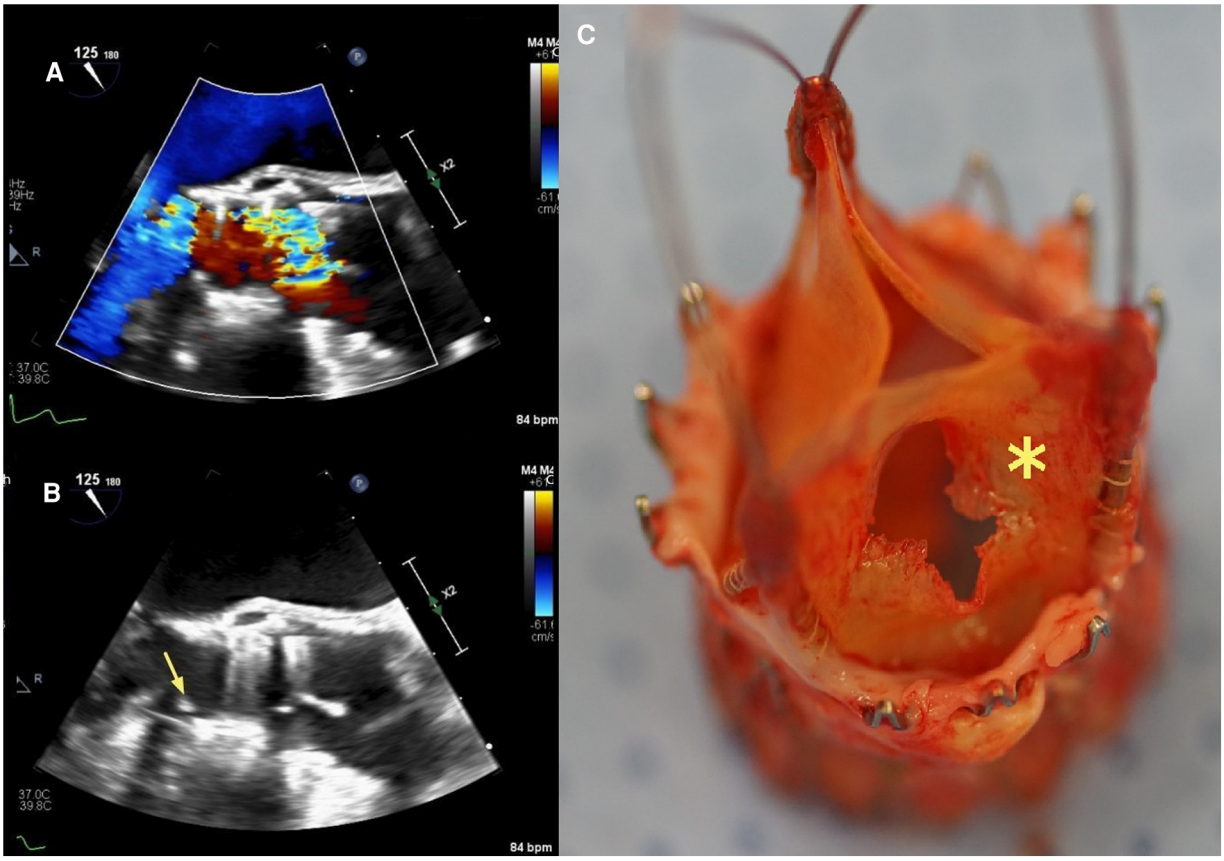

FIGURE 2
Case 2: transesophageal echocardiography three-chamber view with color-flow Doppler (**A**) and aortic valve-centered short-axis view with color-flow Doppler (**B**) showing severe intraprosthetic regurgitation and partial cusp prolapse (yellow arrow) on the right coronary side, respectively. (**C**) Explanted ACURATE Neo prosthesis with a central tear in the leaflet in the right-coronary position (yellow asterisk).

demonstrated a partial cusp prolapse on the right-coronary position associated with severe, eccentric AR (see **Figures 2A,B**). Blood cultures were negative. Given the intermediate surgical risk and to prevent coronary obstruction with limited coronary ostium height (13 mm on both sides), we opted for a TAVR explant and SAVR. Intraoperative inspection of the prosthesis revealed a central tear in the leaflet in the right-coronary position (see **Figure 2C**). There were no local signs of endocarditis. The extraction of the prosthesis was complicated due to an extensive pannus and endothelialization of the axial stabilization arches anchored in the aortic wall. After prosthesis removal, we implanted a 21-mm surgical bioprosthesis in the aortic position. The postoperative course was besides transitory acute-on-chronic renal failure uneventful, and the patient was discharged after 10 days. Cases summary as timeline is provided in **Table 2**.

3. Discussion

Data on specific mechanisms of SVD affecting TAVR prostheses, their incidence, and clinical presentation are limited.

The PARTNER-1 (Placement of Aortic Transcatheter Valves) trial ($n = 1057$) and CoreValve High-Risk Pivotal trial ($n = 795$) reported extremely low rates of severe SVD with 0% and 0.8% after 5 years for SAPIEN (Edwards Lifesciences, Irvine, CA, USA) and CoreValve (Medtronic, Minneapolis, MN, USA), respectively (2, 3). However, interpretation of these findings is limited due to the small number of survivors at 5 years, as predictable with typically elderly and frail patients included in these historical cohorts. With the introduction of standardized criteria for SVD, longer follow-up, and inclusion of younger, lower-risk patients in prospective TAVR trials in recent years, higher rates of SVD were reported. The NOTION (Nordic Aortic Valve Intervention) trial ($n = 139$), referring to the European Association of Percutaneous Cardiovascular Interventions (EAPCI), reported SVD risk after CoreValve implantation as high as 4.8% at 6 years (4). Analyzing data from the PARTNER-2A trial ($n = 1438$) and PARTNER-2/SAPIEN-3 Intermediate-Risk registry ($n = 891$) and referring to the Valve Academic Research Consortium 3 definitions, Pibarot et al. reported SVD risks of 3.9% and 9.5% at 5 years after implantation of Edwards SAPIEN 3 and Edwards SAPIEN XT, respectively (5). However, the rates of BVF were rather low (1.1% and 3.7% for Edwards SAPIEN 3 and Edwards SAPIEN XT, respectively). Also, large European retrospective cohort studies on multiple TAVR devices reported 5-year rates of SVD ranging from 2.5% to 4.2% and low

TABLE 1 Overview of SVD rates reported by the major historical randomized control trials and retrospective cohort studies focusing on TAVR durability.

Author	Year	Trial/referred trial/register	Type of study	*n*	TAVR prosthesis	Follow-up (years)	SVD[a] (%)	BVF (%)	All-cause mortality (%)	Definition of SVD
Kapadia et al.	2015	PARTNER-1	RCT	1,057	SAPIEN	5	0.00	*NA*	71.80	*NA*
Gleason et al.	2018	CoreValve High-Risk Pivotal	RCT	391	CoreValve	5	0.8	*NA*	55.00	EAPCI
Søndergaard et al.	2019	NOTION	RCT	139	CoreValve	6	4.8	6.70%	42.50	EAPCI
Didier et al.	2018	FRANCE-2	Retrospective	4,201	CoreValve SAPIEN SAPIEN XT	5	2.50	NA	60.80	EAPCI
Durand et al.	2019	NA	Retrospective	1,403	SAPIEN SAPIEN XT CoreValve Jena	5	4.2	1.90	69.00	EAPCI
Pibarot et al.	2020	PARTNER-2A PARTNER-2/ SAPIEN-3	Retrospective	774	SAPIEN 3	5	3.90	1.1[b]	NA	VARC-3
				891	SAPIEN XT		9.50	3.7[b]	NA	VARC-3
Testa et al.	2020	NA	Retrospective	990	CoreValve	8	1.6	2.50	78.30	EAPCI
Tamburino et al.	2020	SCOPE-2	RCT	398	ACURATE Neo	1	10.00	0.25[b]	13.00	VARC-2
				398	CoreValve Evolut		14.00	1[b]	9.00	VARC-2
Siquiera et al.	2021	NA	Retrospective	104	ACURATE Neo	3	1.00	1[b]	20.70	VARC-2

TAVR, transcatheter aortic valve replacement; SVD, structural valve deterioration; BVF, bioprosthetic valve failure; RCT, randomized controlled trial; VARC, Valve Academic Research Consortium; EAPCI, European Association of Percutaneous Cardiovascular Interventions; NA, not available.
[a]For study referring to the EAPCI definition, only severe SVD is reported.
[b]Specifically, SVD-related bioprosthetic failure.

rates of SVD-related BVF according to the EAPCI guidelines (6, 7). The heterogeneity of the above-mentioned rates of SVD makes their interpretation difficult and can be explained by at least two factors: first, the underestimation of the incidence of SVD given the substantial competitive risk of death in cohorts with a high mortality on short term (e.g., PARTNER-1), and second, the variability of SVD criteria according to the definitions used. An overview of SVD rates reported by the major historical randomized control trials and retrospective cohort studies focusing on TAVR durability is given in **Table 1**.

When looking at surgical registries of SAVR after TAVR ($n = 123$ and $n = 46$), SVD accounted for 10%–15% of indications for TAVR explant in two recent retrospective studies (8, 9).

Since ACURATE Neo is a more recent and less implanted model of the TAVR era, less information is available about long-term outcomes and specific failure mechanisms of this device.

In the SCOPE-2 (Safety and Efficacy Comparison of Two TAVR Systems in a Prospective Randomized Evaluation 2) trial ($n = 796$), ACURATE Neo was challenged with its self-expandable concurrent Medtronic CoreValve Evolut (10). The authors observed more frequent cardiac deaths at 1 year (8.4% vs. 3.9%; $p = 0.01$), more frequent severe aortic regurgitation in the short term (10% vs. 3%, $p = 0.002$), and more frequent structural valve deterioration in the short term (14% vs. 6%, $p = 0.004$) with ACURATE Neo. However, structural valve deterioration was no more statistically different after 1 year (10% vs. 14%, $p = 0.25$) and the valve-related dysfunction requiring repeat procedure was similarly low in both devices (1%, $p = 0.99$). Reporting on mid- and long-term results after ACURATE Neo implantation ($n = 104$), Siquiera et al. mentioned a single case of SVD-related failure addressed with a *valve-in-valve* procedure (11). The authors concluded with overall reassuring mid- to long-term outcomes with this device. Findings of the SCOPE-2 trial at 1 year and those of Siquiera et al. are summarized in **Table 1**. In our institution, we observed a rate of SVD-related BVF of 0.84%, accounting for the two present cases over the past 5 years, which was similar

TABLE 2 Timeline.

Case 1		Case 2	
Time	Event	Time	Event
T_0	TAVR with ACURATE Neo	T_0	TAVR with ACURATE Neo
$T_1 = T_0 + 54$ months	Hospital admission for rapidly progressive dyspnea/ pulmonary edema	$T_1 = T_0 + 23$ months	Cardiological workup for acute dyspnea and medication-refractory elevated blood pressure
$T_1 + 7$ days	TEE reveals eccentric, severe intraprosthetic AR	$T_1 + 15$ days	TEE reveals severe intraprosthetic AR and partial cusp prolapse
$T_1 + 9$ days	Surgical explant of ACURATE Neo, SAVR	$T_1 + 19$ days	Surgical explant of ACURATE Neo, SAVR
$T_1 + 22$ days	Hospital discharge	$T_1 + 29$ days	Hospital discharge

TAVR, transcathter aortic valve replacement; TTE, transthoracic echocardiography; AR, aortic regurgitation; SAVR: surgical valve replacement.

to the previously mentioned studies. Finally, reviewing the international EXPLANT-TAVR registry ($n = 269$), Bapat et al. noticed six surgical explants of ACURATE Neo (4.5% of all self-/mechanically expandable devices), but neither the causes for explant nor the durability of the failed prostheses was specified (12).

As the number of TAVR in even younger patients increases, the need to manage late complications with TAVR will increase. The number of former implanted and available TAVR models is also increasing. As such, a better understanding of the specific mechanisms of SVD affecting TAVR prostheses is mandatory. Our two cases contribute to increasing knowledge in this area by illustrating two close but specific modes of SVD leading to acute bioprosthetic failure of the ACURATE Neo. A macroscopic examination of the valves revealed no signs of active endocarditis, and the blood cultures were negative. Eubacterial PCR from leaflet samples was not performed to exclude previous endocarditis. Leaflet tear/disruption is a rare yet well-documented mechanism of SVD of surgical bioprostheses, especially those with externally mounted leaflets (13–16). Leaflet disruption in aortic bioprosthesis occurs abruptly, and the affected patient typically presents with acute, clinically poorly tolerated aortic regurgitation, as in the two present cases. In the absence of endocarditis criteria, we assumed that the rupture of the leaflet was due to mechanical fatigue by an analogous mechanism to that affecting surgical bioprostheses. To the best of our knowledge, this issue with ACURATE Neo has never been reported.

As for therapy, we opted for TAVR explant and SAVR. Our strategy was driven in both cases by the limited experience reported with *valve-in-valve* procedures in failed ACURATE Neo, in the second case by the rather shallow aortic root with subsequent risk of coronary obstruction. Indeed, recent works highlighted the increased risk of coronary obstruction following redo-TAVR with high-profile index bioprosthetic valves such as ACURATE Neo (17). Further studies are warranted to define the best approach to failed TAVR prostheses with respect to the index model, mode of failure, and patient´s anatomy.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: Data are available on reasonable request to the corresponding author. Requests to access these datasets should be directed to oliver.reuthebuch@usb.ch.

Ethics statement

Written informed consent was obtained from both participants for the publication of this case report.

Author contributions

TS drafted the manuscript and created the figures. All authors were involved in the conceptualization, analysis, and interpretation of the diagnostic data and the management strategy described in the manuscript and approved and co-edited the manuscript for submission in its current form. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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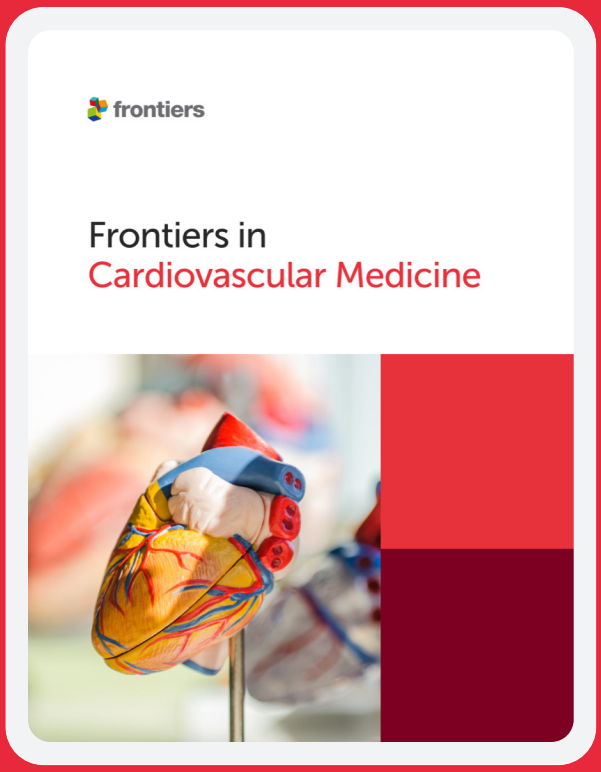

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