JACC: CASE REPORTS VOL. 2, NO. 3, 2020

CASE REPORT

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

Untreatable Severe Structural Degeneration of a Transcatheter Aortic Heart Valve

A Salutary Tale

Noman Ali, PhD,[a] Christopher J. Malkin, MD,[a] Michael S. Cunnington, MD,[a] Robert J. Lederman, MD,[b] Daniel J. Blackman, MD[a]

JACC: CASE REPORTS CME/MOC/ECME

This article has been selected as this issue's CME/MOC/ECME activity, available online at http://www.acc.org/jacc-journals-cme by selecting the *JACC* Journals CME/MOC/ECME tab.

Accreditation and Designation Statement

The American College of Cardiology Foundation (ACCF) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The ACCF designates this Journal-based CME/MOC/ECME activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*™. Physicians should only claim credit commensurate with the extent of their participation in the activity. Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Untreatable Severe Structural Degeneration of a Transcatheter Aortic Heart Valve: A Salutary Tale will be accredited by the European Board for Accreditation in Cardiology (EBAC) for 1 hour of External CME credits. Each participant should claim only those hours of credit that have actually been spent in the educational activity. The Accreditation Council for Continuing Medical Education (ACCME) and the European Board for Accreditation in Cardiology (EBAC) have recognized each other's accreditation systems as substantially equivalent. Apply for credit through the post-course evaluation. While offering the credits noted above, this program is not intended to provide extensive training or certification in the field.

Method of Participation and Receipt of CME/MOC/ECME Certificate

To obtain credit for this CME/MOC/ECME activity, you must:

1. Be an ACC member or *JACC: Case Reports* subscriber.
2. Carefully read the CME/MOC/ECME-designated article available online and in this issue of the *journal*.
3. Answer the post-test questions. A passing score of at least 70% must be achieved to obtain credit.
4. Complete a brief evaluation.
5. Claim your CME/MOC/ECME credit and receive your certificate electronically by following the instructions given at the conclusion of the activity.

CME/MOC/ECME Objective for This Article: Upon completion of this activity, the learner should be able to: 1) discuss the pathogenesis of SVD and identify recognized risk factors for its development following SAVR; 2 identify the indications for ViV TAVI, as well as the principle challenges associated with it and be able to discuss the rationale behind transcatheter valve selection for ViV TAVI; 3) discuss the risks of coronary obstruction during ViV TAVI and identify methods which can be employed to mitigate these; and 4) discuss the current evidence regarding TAVI durability, including comparisons to bioprosthetic SAVR.

Author Disclosures: Dr. Malkin is a consultant and proctor for Boston Scientific and Medtronic. Dr. Cunnington has received speaker fees from Medtronic. Dr. Lederman is an inventor on National Institute of Health-assigned patents on devices for transcatheter leaflet laceration. Dr. Blackman is a consultant and proctor for Boston Scientific and Medtronic. Dr. Ali has reported that he has no relationships relevant to the contents of this paper to disclose.

Medium of Participation: Online (article and quiz).

CME/MOC/ECME Term of Approval

Issue Date: March 2020
Expiration Date: February 28, 2021

From the [a]Department of Cardiology, Leeds General Infirmary, Leeds, United Kingdom; and the [b]National Heart, Lung, and Blood Institute, Bethesda, Maryland. Dr. Malkin is a consultant and proctor for Boston Scientific and Medtronic. Dr. Cunnington has received speaker fees from Medtronic. Dr. Lederman is an inventor on National Institute of Health-assigned patents on devices for transcatheter leaflet laceration. Dr. Blackman is a consultant and proctor for Boston Scientific and Medtronic. Dr. Ali has reported that he has no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, or patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received November 5, 2019; accepted January 14, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.01.023

JACC: CASE REPORTS, VOL. 2, NO. 3, 2020
MARCH 2020:347–51

Untreatable Severe Structural Degeneration of a Transcatheter Aortic Heart Valve

A Salutary Tale

Noman Ali, PhD,[a] Christopher J. Malkin, MD,[a] Michael S. Cunnington, MD,[a] Robert J. Lederman, MD,[b] Daniel J. Blackman, MD[a]

ABSTRACT

We describe a patient who presented with heart failure 7 years post-transcatheter aortic valve implantation (TAVI) as a result of severe structural valve degeneration. Anatomic challenges, combined with the type of transcatheter heart valve used initially, meant that TAVI-in-TAVI risked obstructing the coronary arteries, even if preceded by bioprosthetic aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction. The patient was treated with balloon aortic valvuloplasty. (J Am Coll Cardiol Case Rep 2020;2:347–51)

A 67-year-old female patient with a background of chronic obstructive pulmonary disease and relapsing polychondritis initially presented to the cardiology outpatient department in 2010 with progressively worsening exertional dyspnea. Echocardiography demonstrated severe aortic stenosis and normal left ventricular systolic function, whereas coronary angiography showed normal coronary arteries. She was considered for surgical aortic valve replacement (SAVR) but was deemed to be at extreme risk because of her comorbidities; in particular, the requirement for long-term immunosuppressive therapy with prednisolone and azathioprine for treatment of her relapsing polychondritis raised concerns regarding post-surgical wound healing. Transcatheter aortic valve implantation (TAVI) was performed with deployment of a 29-mm CoreValve (Medtronic, Minneapolis, Minnesota), with a good procedural result. She was asymptomatic following the TAVI and remained so until 2017, when she presented to the emergency department with dyspnea on minimal exertion, orthopnea, and paroxysmal nocturnal dyspnea. Clinical examination demonstrated features of pulmonary edema, with bilateral lower zone crepitations audible on auscultation of her lungs, hypoxia, and tachycardia. Auscultation of her heart sounds elicited ejection systolic and early diastolic murmurs. Her jugular venous pressure was not elevated, and there was no peripheral edema. A chest radiograph confirmed the presence of pulmonary edema, with bilateral pleural effusions and central pulmonary vascular congestion. Blood tests demonstrated a significant rise in N-terminal pro-B-type natriuretic peptide, but results were otherwise unremarkable. Her electrocardiogram showed sinus rhythm with mild left ventricular hypertrophy.

LEARNING OBJECTIVES

- To understand the importance of SVD as a differential diagnosis in patients who present with signs and symptoms of heart failure, angina, or exertional syncope in the years following TAVI.
- To appreciate SVD as a problem that affects a proportion of patients post-TAVI and that will likely become more prevalent as we expand into treating younger patients.
- To understand the need for the heart team to consider not only the suitability of the native anatomy for first-time TAVI, but also the anatomic feasibility of TAVI-in-TAVI for SVD if and when it occurs.

Question 1: What is the differential diagnosis, and which next test would be the most useful?

Answer 1: For a patient with a history of previous TAVI who presents with pulmonary edema, the 2 main differential diagnoses are the development of left ventricular systolic dysfunction or valvular dysfunction. The potential causes of dysfunction in a transcatheter aortic valve include leaflet thrombosis, structural degeneration, and infective endocarditis. The most useful next test to help distinguish among these differential diagnoses is a transthoracic echocardiogram.

Transthoracic echocardiography demonstrated preserved left ventricular systolic function but marked thickening of the transcatheter aortic valve leaflets, with severe stenosis (peak velocity of 4.6 m/s, mean gradient of 46 mm Hg, valve area of 0.5cm^2) and moderate regurgitation. On the basis of this initial imaging it was difficult to distinguish between structural valve degeneration (SVD) and leaflet thrombosis. As such, transesophageal echocardiography was performed. It demonstrated significant calcification of the thickened valve leaflets, a finding most consistent with severe SVD (Video 2).

Question 2: What is SVD, and how great a problem is it for TAVI?

Answer 2: A comprehensive review into the topic has described SVD as "an acquired intrinsic bioprosthetic valve abnormality defined as deterioration of the leaflets or supporting structures resulting in thickening, calcification, tearing, or disruption of the prosthetic valve materials with eventual associated valve hemodynamic dysfunction, manifested as stenosis or regurgitation" (1). SVD has traditionally been associated with bioprosthetic SAVR. However, it has been recognized following TAVI, and it has been highlighted as an area of concern with respect to long-term durability.

Recent data with both the Sapien 3 (Edwards Lifesciences, Irvine, California) and the CoreValve/Evolut (Medtronic) valves have shown superior or noninferior outcomes with TAVI compared with SAVR in low-risk patients with a mean age of 73 to 74 years (2,3). Since these results will lead to an inevitable expansion of TAVI into younger patients with life expectancies of decades, SVD and its management will become of primary importance. There is accumulating evidence regarding the long-term durability of TAVI prostheses. The 6-year follow-up data from the NOTION (Nordic Aortic Valve Intervention) trial demonstrated that only 4.8% of TAVI-treated patients had evidence of moderate or severe SVD, compared with 24% of patients who had undergone SAVR ($p < 0.001$) (4). Although these results are encouraging, valve performance beyond 10 years remains unknown. Furthermore, follow-up data with bioprosthetic SAVR have demonstrated younger age to be associated with earlier structural deterioration. It is thought that, in addition to a passive degenerative process, there is also an active mechanism that triggers an inflammatory response, which may be more potent in younger patients who are more immunologically active (5). Although it is too early to be certain whether the same applies to TAVI prostheses, it would be intuitive to draw parallels.

Question 3: What are the treatment options for severe SVD following TAVI?

Answer 3: The 2 recognized treatment options are surgical explantation of the transcatheter aortic valve followed by valve replacement, or TAVI-in-TAVI.

Having diagnosed SVD, the next step was to perform computed tomography (CT) angiography to guide further management options. CT scanning demonstrated a low sinotubular junction (STJ) (height above annulus 15.9 mm). Furthermore, the STJ was small (diameter 22.7 mm), and the CoreValve frame was closely opposed to the walls of the STJ (Figure 1A). Because the CoreValve is a supra-annular valve, displacement of the bioprosthetic leaflets following TAVI-in-TAVI will result in a continuous "tube" of tissue extending within the valve frame to a height of approximately 24 mm above its base. In this case, CT clearly showed that this would result in "jailing" at the level of the STJ, so that there would be no blood flow to the coronary ostia, thereby prohibiting consideration of TAVI-in-TAVI. Surgical explantation of the CoreValve followed by valve replacement was rejected because of the adherence of the CoreValve to the STJ and possibly the ascending aorta, thus mandating aortic root replacement in addition to valve replacement. This was considered prohibitively high risk in a 75-year-old patient receiving long-term immunosuppressive therapy, who had already been deemed to be a high surgical risk 7 years earlier.

Question 4: Are there any techniques that could potentially facilitate TAVI-in-TAVI in cases where coronary obstruction is a concern?

Answer 4: The patient was assessed for a possible BASILICA (bioprosthetic aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction) procedure. This technique aims to prevent coronary obstruction at the level of the coronary ostia or STJ during TAVI by performing laceration of the native or surgical bioprosthetic valve leaflets using electrocautery (6–8).

BASILICA has not yet been performed in the setting of TAVI-in-TAVI, and it is not clear whether the lacerated leaflets will separate within the constraining TAVI frame to preserve coronary flow. Furthermore, in this case further analysis of the CT images demonstrated that the commissures of the CoreValve were sitting opposite the left and right coronary ostia,

ABBREVIATIONS AND ACRONYMS

BASILICA = bioprosthetic aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction

BAV = balloon aortic valvuloplasty

CT = computed tomography

NYHA = New York Heart Association

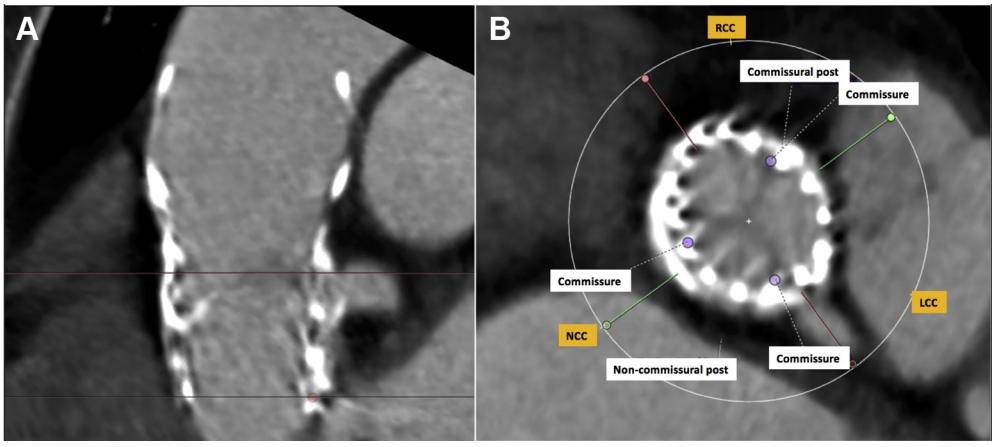
SAVR = surgical aortic valve replacement

STJ = sinotubular junction

SVD = structural valve degeneration

TAVI = transcatheter aortic valve implantation

FIGURE 1 CT Analysis of Degenerated Transcatheter Heart Valve Undertaken to Plan Potential BASILICA and TAVI-in-TAVI



(A) Long-axis computed tomography (CT) image showing the frame of the CoreValve CoreValve (Medtronic, Minneapolis, Minnesota) to be adherent to the left ventricular outflow tract, sinotubular junction, and part of the ascending aorta. **(B)** Short-axis computed tomography image showing 1 of the CoreValve commissures to be lined up in front of the origin of the left coronary artery (represented by the **purple dots**). BASILICA = bioprosthetic aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction; LCC = left coronary cusp; NCC = noncoronary cusp; RCC = right coronary cusp; TAVI = transcatheter aortic valve implantation.

such that occlusion would likely occur even if the leaflets were successfully lacerated (Figure 1B). As such, it was deemed that BASILICA would be unhelpful in our patient's case.

Question 5: How was the patient managed?

Answer 5: Despite optimal medical therapy she developed progressive New York Heart Association (NYHA) functional class III exertional dyspnea and pre-syncope, necessitating further intervention. Ultimately, balloon aortic valvuloplasty (BAV) was performed.

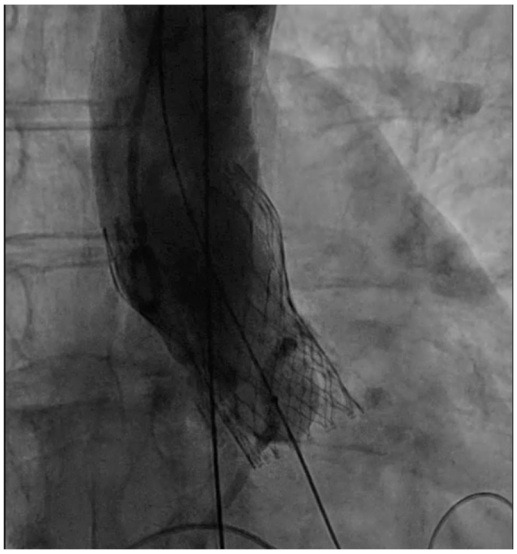
BAV of a failed transcatheter heart valve has several risks, including stroke, avulsion of the leaflets, or valve embolization, any of which may be fatal. However, given the absence of alternative treatments and the progressive clinical decline of the patient, BAV was carried out and resulted in a substantial reduction in the invasive transvalvular gradient from 121 mm Hg to 24 mm Hg, with no increase in aortic regurgitation. Simultaneous aortograms during BAV clearly demonstrated obstruction of coronary flow by the CoreValve leaflets (Figure 2). Symptoms improved markedly to NYHA functional class I post-procedure. We reviewed our patient in the outpatient clinic 4 months later, and she remained symptomatically well. However, repeat echocardiography has shown evidence of restenosis with a peak velocity of 4.96 m/s, a mean gradient of 65 mm Hg, and an aortic valve area of 0.7 cm^2. Repeat BAV will be considered if and when required.

Question 6: What are the learning points from this case?

Answer 6: This case illustrates the potential difficulties of managing structural valve degeneration affecting transcatheter aortic valves, and in particular the anatomic challenges of TAVI-in-TAVI. The principal challenge in performing TAVI-in-TAVI to treat SVD is the risk of coronary obstruction. This is most likely to result from displacement of the bioprosthetic transcatheter aortic valve leaflets causing jailing at the level of the STJ. This risk is highest with the use of a device with a long frame extending above the STJ, such as the CoreValve/Evolut used in this case, as well as the Portico (Abbott Vascular, Inc., Santa Clara, California), Acurate Neo (Boston Scientific, Marlborough, Massachusetts), and even potentially the Sapien 3, valves. Supra-annular valve leaflets, as used in the CoreValve/Evolut and Acurate Neo devices, will also elevate risk by increasing the likelihood that the displaced leaflets will reach the level of the STJ after TAVI-in-TAVI.

This case highlights a new paradigm in case preparation and valve selection in younger patients undergoing TAVI, that is, the need to

FIGURE 2 Aortogram Performed During Balloon Aortic Valvuloplasty of the Degenerated Transcatheter Heart Valve



This image demonstrates flow down the right coronary artery but occlusion of flow down the left coronary artery because of the displacement of the CoreValve (Medtronic, Minneapolis, Minnesota) leaflets. This observation correlated with computed tomography findings that predicted coronary obstruction following transcatheter aortic valve implantation–in–transcatheter aortic valve implantation. See Video 1.

consider not only the suitability of the native anatomy for first-time TAVI, but also the anatomic feasibility of TAVI-in-TAVI for SVD if and when it occurs. Specific attention should be paid to the height of the sinuses and the dimensions of the STJ. If the STJ is capacious, then there should be adequate space around the transcatheter aortic valve frame to permit TAVI-in-TAVI without causing obstruction to flow into the sinuses and coronary arteries, regardless of which valve type is used. Similarly, if the STJ is high above the annulus, then the displaced bioprosthetic leaflets may not reach the level of the STJ, particularly if an intra-annular valve is used. However, in patients with a small and low STJ, as seen in our case, TAVI-in-TAVI may be hazardous or even impossible. In these cases, operators should consider the use of a transcatheter aortic valve with a low frame and an intra-annular valve, such as the Sapien, Lotus (Boston Scientific), or Centera (Edwards Lifesciences) devices, and should aim to implant the valve at a depth that keeps the top of the frame below the STJ and, if possible, below the coronary ostia. In addition, valve manufacturers should aim to develop devices that facilitate TAVI-in-TAVI, with short frames, intra-annular leaflets, and the ability to align the valve commissures during deployment so that they can be placed away from the coronary ostia. This would help to avoid the scenario this case presented, in which a patient with late SVD of a transcatheter aortic prosthesis was left with no effective treatment option.

ADDRESS FOR CORRESPONDENCE: Dr. Noman Ali, Department of Cardiology, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, United Kingdom. E-mail: nomanali456@doctors.org.uk.

REFERENCES

1. Dvir D, Bourguignon T, Otto CM, et al. Standardized definition of structural valve degeneration for surgical and transcatheter bioprosthetic aortic valves. Circulation 2018;137:388–99.

2. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380:1695–705.

3. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med 2019;380:1706–15.

4. Søndergaard L, Ihlemann N, Capodanno D, et al. Durability of transcatheter and surgical bioprosthetic aortic valves in patients at lower surgical risk. J Am Coll Cardiol 2019;73:546–53.

5. Rodriguez-Gabella T, Voisine P, Puri R, et al. Aortic bioprosthetic valve durability: incidence, mechanisms, predictors, and management of surgical and transcatheter valve degeneration. J Am Coll Cardiol 2017;70:1013–28.

6. Khan JM, Dvir D, Greenbaum AB, et al. Transcatheter laceration of aortic leaflets to prevent coronary obstruction during transcatheter aortic valve implantation: concept to first-in-human. J Am Coll Cardiol Intv 2018;11:677–89.

7. Khan JM, Greenbaum AB, Babaliaros VC, et al. The BASILICA trial: a prospective multi-center cohort study of intentional leaflet laceration before TAVR to prevent coronary obstruction. J Am Coll Cardiol Intv 2019;12:1240–52.

8. Lederman RJ, Babaliaros VC, Rogers T, et al. State of the art. Preventing coronary obstruction during TAVR, from CT to BASILICA. J Am Coll Cardiol Intv 2019;12:1197–216.

KEY WORDS aortic valve, computed tomography, valve replacement

APPENDIX For supplemental videos, please see the online version of this paper.