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Simultaneous Transcatheter Double Valve Treatment of Mediastinal Radiation-Induced Severe Calcific Aortic and Mitral Stenosis

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ABSTRACT

Mediastinal radiation-induced severe calcific valve disease carries increased operative mortality. Transcatheter therapies are also challenging and potentially hazardous. We used a unique constellation of imaging and planning technologies to successfully plan, simulate, and perform novel combined transcatheter aortic valve replacement and valve in mitral annular calcification in a high-risk patient. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2020;2:1443–7) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

We present a 61-year-old woman with New York Heart Association functional class II to III dyspnea after undergoing lifesaving mantle field radiotherapy and chemotherapy for Hodgkin lymphoma 20 years ago. Notable past medical history included paroxysmal atrial fibrillation. Heart rate was 90 beats/min, blood pressure was 121/60 mm Hg, respiratory rate was 17 breaths/min, and oxygen saturations was 99% on room air. Echocardiography demonstrated good left ventricular function, critical aortic stenosis (mean gradient = 50 mm Hg, valve area = 0.5 cm^2), and severe mitral stenosis (mean gradient = 18 mm Hg, valve area = 0.9 cm^2). Dedicated multiphase cardiac computed tomography angiography (CTA) highlighted extensive calcification throughout the

LEARNING OBJECTIVES

- To discuss the potential long-term cardiorespiratory sequelae of mediastinal radiation.
- To understand the technical challenges to valve intervention imposed by extensive calcific valve disease, particularly involving the aortomitral continuity.
- To understand the potential role of preprocedural modeling informed by multimodality imaging to mitigate these hazards and plan transcatheter interventions.

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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, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

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ABBREVIATIONS AND ACRONYMS

CEP = cerebral embolic protection

CTA = computed tomographic angiography

FEM = finite element modeling

LVOT = left ventricular outflow tract

THV = transcatheter heart valve

aortomitral continuity with severely calcified aortic valve leaflets and circumferential mitral annular calcification (**Figures 1A to 1C**). Coronary angiography indicated eccentric, angiographically mild, biostial left main stem and right coronary artery disease, likely reflecting the underlying radiation-induced pathology.

Despite relatively low perioperative risk scores (European System for Cardiac Operative Risk Evaluation II = 1.8% and Society of Thoracic Surgeons score = 3.6%), the extensively calcified anatomy posed high surgical risk. The consensus across heart teams in multiple international centers was that conventional dual-valve replacement was not technically feasible, and they proposed the "Commando" procedure to reconstruct the aortomitral continuity after mitral annular decalcification in conjunction with mitral and aortic valve replacement (1). The patient declined, citing unacceptable operative risk, thereby prompting consideration of transcatheter options.

DIFFERENTIAL DIAGNOSIS

- Radiation-induced, severe calcific valve disease;
- Degenerative valve disease;
- Noncardiac dyspnea (e.g., pulmonary fibrosis).

INVESTIGATIONS

Extensive planning was performed to predict the procedural outcome. CTA indicated borderline narrow sinuses of Valsalva (27 × 30 × 30 mm) but sufficient coronary heights (left main stem = 16 mm, right coronary artery = 17 mm) to suggest a low risk of coronary obstruction. From the CTA, we performed computer-simulated finite element modeling (FEM) (FEops, Ghent, Belgium) to simulate mitral transcatheter heart valve (THV) implantation to derive a neo-left ventricular outflow tract (LVOT) area and predict the likelihood of paravalvular regurgitation (**Figure 1D**, Video 1) (2). Subsequent computational fluid dynamics modeled the pressure gradient within the neo-LVOT and predicted an acceptable, unobstructed outcome (**Figures 1E and 1F**, Videos 2A and 2B) (3). Finally, a 3-dimensional-printed bespoke heart model aided pre-procedural implant simulation (Mimics Innovation Suite and HeartPrint Flex, Materialise, Leuven, Belgium) (**Figure 1G**, Supplemental Figures 1 and 2).

MANAGEMENT

After placement of a cerebral embolic protection (CEP) device (Sentinel, Boston Scientific, Quincy, Massachusetts) via the right radial artery and systemic heparinization guided by the activated clotting time, a 23-mm Sapien 3 (Edwards Lifesciences, Irvine, California) transcatheter aortic valve replacement was performed via the left femoral artery without complication (**Figure 2A**, Video 3). Atrial transseptal puncture was performed with an electrified Brockenbrough needle via an SL0 sheath (Swart, Abbott Vascular, Santa Clara, California) from the right femoral vein using computed tomography–simulated fluoroscopic guidance (**Figure 2B**) (4). After 18-mm atrial balloon septostomy (**Figure 2C**) (VACS-II, Osypka, Longmont, California), a Safari wire (Boston Scientific, Quincy, Massachusetts) was positioned in the left ventricle via an Agilis steerable sheath (Abbott Vascular). Correct positioning of the 29-mm Sapien 3 valve within the mitral annulus required snaring of the Safari wire into the aorta via the left femoral artery to provide additional support (**Figures 2D and 2E**, Videos 4A and 4B). After successful deployment under rapid left ventricular pacing (120 beats/min), completion of the left ventriculogram demonstrated a well-functioning mitral prosthesis (**Figure 2F**, Video 5) confirmed on Doppler, 4-dimensional imaging, and blood speckle imaging echocardiography (**Figures 2G to 2I**, Video 6). Hemodynamics improved dramatically, and the patient has remained well.

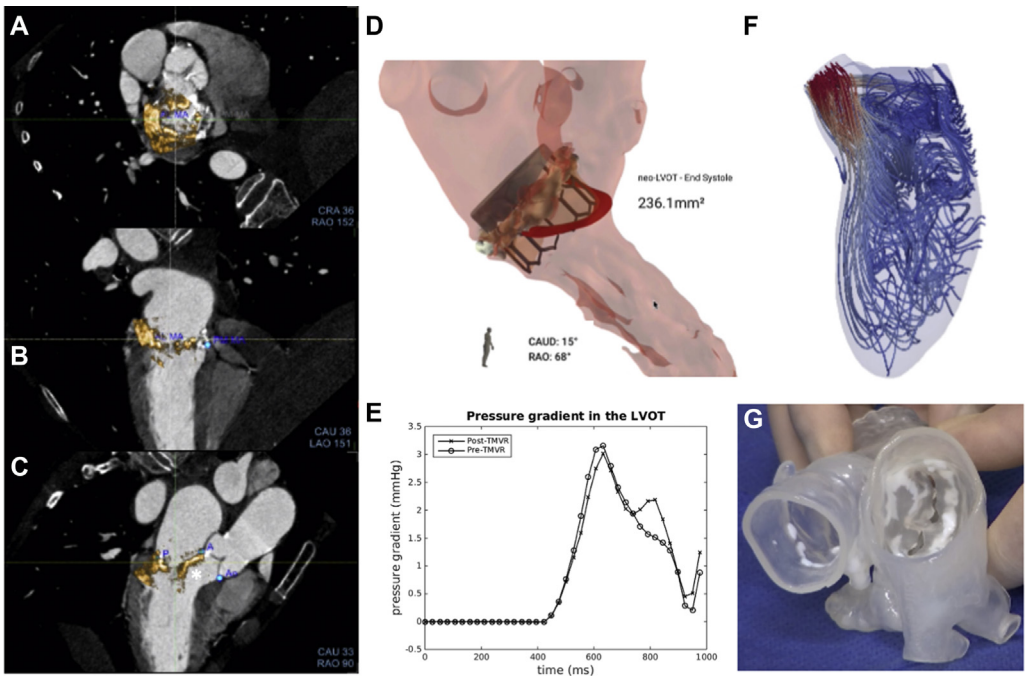
DISCUSSION

Depending on the precise definition used, clinically significant calcific valve disease may develop in up to 37% of patients after mediastinal radiation (5,6). The incidence is dose dependent, and, as in this case, extensive field radiation (e.g., Mantle) and co-administration of chemotherapeutic agents are recognized risk factors (7). Moreover, as survival from malignancies such as Hodgkin lymphoma continues to improve (20-year survival now >80%), the incidence of remote cardiac complications is expected to increase (8).

Patients with radiation-induced valve disease undergoing conventional cardiac surgery are at increased risk of perioperative complications in a manner not reflected in traditional risk stratification models. The potential sequelae of radiation exposure including mediastinal fibrosis/adhesions; pulmonary fibrosis; pericardial constriction; and coronary, cardiac, and aortic calcification confer an increased risk of perioperative bleeding, cardiorespiratory failure, rhythm disturbance, embolic stroke, and death (9,10).

As present in this case, extensive calcification of the aortomitral continuity presents a particularly formidable surgical challenge, with the attendant

FIGURE 1 Pre-Operative Planning: Fusion Imaging, Finite Element Modeling and Computational Fluid Dynamics



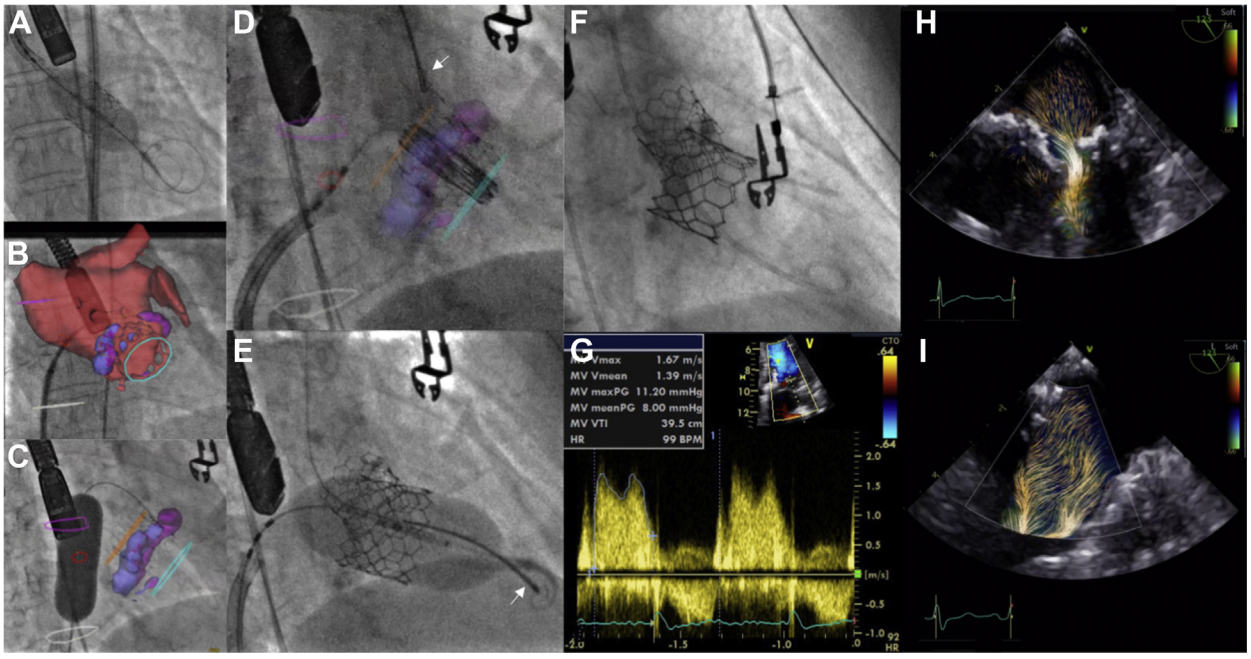
(A to C) Dedicated multiphase cardiac CTA with echocardiographic fusion imaging indicating severe calcific valve disease, with calcification extending throughout the aortomitral continuity (asterisk). **(D)** Mitral THV implant simulation via finite element modeling predicting a safe neo-LVOT area with a 60:40 implant position. **(E and F)** Computational fluid dynamic modeling after virtual mitral THV implant predicting a safe neo-LVOT pressure gradient (maximum = 3 mm Hg). **(G)** Three-dimensional–printed bespoke heart model for implantation rehearsal and planning. CTA = commuted tomographic angiography; LVOT = left ventricular outflow tract; THV = transcatheter heart valve.

risks of intractable hemorrhage, atrioventricular disruption, coronary artery injury, and ventricular rupture. Decalcification followed by reconstruction of the intervalvular fibrous body with either glutaraldehyde-fixed bovine pericardium or Dacron polyester fabric during aortic and mitral valve replacement was first described in this setting over 20 years ago (1), although it remains restricted to a few expert centers worldwide, with technical failures, complications, and operative mortality (>10%) still relatively high, even in experienced hands (11).

In the face of prohibitive or unacceptable surgical risk, transcatheter techniques may offer an alternative, although the treatment of dual radiation-induced valve pathology demonstrated here has not previously been systematically described (12–14). In particular, complex, calcified mitral valve anatomy poses numerous challenges to treatment with a round THV without an anchoring mechanism, with potential complications including paravalvular regurgitation, valve migration, and principally LVOT obstruction through distortion of the subvalvular apparatus. Thus, despite technical advancements, 30-day mortality for transcatheter valve in mitral annular calcification remains unacceptably high (25% to 30%) (15,16). Appropriate patient selection is key to minimizing risk, with cardiac computed tomography to measure the expected neo-LVOT area considered mandatory. However, this approach does not permit modeling of the dynamic interaction of the valve with the host and vice versa (e.g., mitral annulus calcification deformation under conditions of radial stress). As such, the evaluation based on geometric measurements alone is likely insufficient to accurately predict outcome.

The patient-specific computer simulation used here enabled virtual implantation of a THV using FEM in which the geometric and mechanical properties of the valve and host are integrated. Simulating deformation of the device after deployment and other interactions of the device with neighboring anatomy improved the predictive power of geometric measurement to permit comprehensive assessment of the likelihood of LVOT obstruction and paravalvular regurgitation. To our knowledge, the only system that

FIGURE 2 Procedural Guidance: Computed Tomography Fluoroscopic Landmark Fusion Imaging



(A) Successful deployment of a 23-mm balloon-expandable valve in the aortic position under rapid LV pacing. **(B)** Transseptal puncture assisted by both simulation and landmark computed tomography–fluoroscopic fusion imaging, indicating left atrial and mitral anatomy, and puncture position target, respectively. **(C)** An 18-mm balloon septostomy. **(D and E)** The stiff Safari wire was snared **(arrowheads)** to increase delivery support, aiding correct positioning and deployment of the 29-mm balloon-expandable mitral THV between the preplanned landmarks indicated on computed tomographic–fluoroscopic fusion imaging. **(F)** Completion imaging demonstrating a well-functioning valve with **(G)** appropriate reduction in transvalvular gradient on continuous wave Doppler. **(H and I)** Corresponding pre- and post-intervention blood speckle imaging echocardiography demonstrating improved flow characteristics. LV = left ventricular; THV = transcatheter heart valve.

is available for performing FEM in this fashion is the platform used here. Computational fluid dynamics further enabled patient-specific modeling of a physiological response to mitral THV implantation to predict the pressure gradient within the neo-LVOT after deployment (17). As a final safety assurance, a 3-dimensional-printed bespoke heart model was manufactured to aid the operator in procedural planning. Further integration of these detailed imaging analyses into periprocedural computed tomography simulation fluoroscopic and computed tomography-transoesophageal echocardiogram fusion imaging guidance with blood speckle imaging flow characterization enhanced the safety and technical success of the procedure.

The dual-filter CEP system (Sentinel) deployed in this case is licensed by the Food and Drug Administration for embolic protection during transcatheter procedures. The aggregate data support a positive effect on clinical stroke reduction, although an appropriately powered randomized efficacy trial is awaited (18). Our institutional practice is to evaluate the requirement for cerebral protection on an individual case basis. The consensus of the heart team discussion was that this young, high-functioning patient had a number of risk factors to increase embolic potential, including known atrial fibrillation, extreme valvular/LVOT calcification, and procedural complexity/time, which supported the use of CEP in this case.

We selected a balloon-expandable prosthesis for the mitral position, reflecting the majority of experience worldwide in this setting (15). We also opted for a balloon-expandable prosthesis in the aortic position because, although there is a degree of clinical equipoise in the setting of LVOT calcification, in our experience a carefully sized balloon prosthesis can achieve excellent results at low risk. Moreover, in the presence of high procedural complexity and increased risk, we have found that selecting the device with which we have the greatest experience has, as in this case, enhanced procedural safety. The low-profile, intra-annular nature of the device could also have the added benefit of permitting more routine coronary reaccess. The durability of THVs remains an area of active research in need of further long-term

data. Accepting the patient's young age, the potential requirement for subsequent reintervention was considered. Based on the patient's anatomy and size and position of the prostheses, we were able to first simulate and then implant; we were satisfied that a redo transcatheter procedure(s) would be technically feasible in the future.

FOLLOW-UP

The patient underwent an uneventful postprocedure recovery and was discharged after 24 h. She was re-established on long-term warfarin anticoagulation and has progressed remarkably well through the 30-day and 6-month follow-ups, enjoying an excellent symptomatic improvement.

CONCLUSIONS

Transcatheter heart interventions continue to provide new treatment options for patients unsuitable/high risk for conventional surgery. The unique constellation of imaging and planning technologies used to orchestrate a successful outcome in this case illustrate a potential framework to enhance safety and provide greater certainty for procedures that otherwise may be deemed unfeasible.

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KEY WORDS computational fluid dynamics, finite element simulation, mitral annular calcification, transcatheter aortic valve replacement, transcatheter mitral valve replacement

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