JACC: CASE REPORTS VOL. 2, NO. 10, 2020

EDITORIAL COMMENT

Look, Simulate, Treat

Multimodality Imaging Guiding Bivalve Complex Transcatheter Replacement*

Agustín Fernández Cisnal, MD,[a] Alfredo Redondo Diéguez, MD,[b] Abdel Hakim Moustafa, MD[c]

Since the 1960s, high-dose, extended-field radiotherapy (RT) has played a key role in the treatment of Hodgkin lymphoma (1) and has usually been applied in an anteroposterior/posteroanterior technique irradiating all chest tissues, including the heart, leading to several cardiac complications including cardiomyopathy, arrhythmia, conduction disorders, and pericardial and valvular diseases.

The prevalence of valvulopathies after RT ranges from 2% to 37% (2), of which approximately 17% develop moderate to severe stenosis or regurgitation (3). Although the physiopathology is not widely known, it seems that radiation activates fibrogenic growth factors (4) and induces valve interstitial cell differentiation to an osteogenic phenotype (5). These facts could explain the severe valve thickening and calcification present in these patients. Multivalvular heart disease is a growing condition against which we must make decisions based on expert opinions or previous clinical experiences (6). RT-induced valvulopathies are associated with cardiopulmonary disorders such as mediastinal and pulmonary fibrosis, constrictive pericarditis, coronary disease, porcelain aorta, and extensive valve calcification which incurs an elevated surgical risk that is not predicted by standard surgical risk scoring systems (7). Likewise, the effects of RT on valves are usually extensive, and adjacent structures, such as subvalvular apparatus, annulus, and especially the aortomitral curtain (7), are commonly involved, and higher thickening is a robust predictor of mortality (8). Mitral and aortic valves are usually affected simultaneously, and even if there is only moderate disease in one of them, it is recommended that both valves be replaced because there is a rapid progression and the very high risk of a potential reoperation. There are 2 special issues concerning valve replacement in radiation induced valve disease, the first is severe continuous calcification involvement from the aortic annulus to the aortomitral curtain and the anterior leaflet of the mitral valve (9), which requires extensive debridement and decalcification to expose healthy tissue for suture placement. The second issue is a small aortic and mitral annulus which can result in a mismatch between prosthesis and patient, resulting in inadequate hemodynamics. Both problems tend to be solved by using the Commando operation, in which the mitral annulus, aortomitral curtain, aortic annulus, and aortic valve are repaired with a pericardium or polyethylene terephthalate (Dacron, DuPont, Wilmington, Delaware) patch allowing for better fixation of the prosthesis and an adequate valve sizing. Unfortunately, this surgery presents a high rate of in-hospital mortality (10) and should be reserved for a patient in whom there are no other suitable alternative procedures (11).

Preprocedural planning using multimodality imaging is crucial for the success of this complex procedure, where cardiac computed tomography (CT) with coverage of the entire cardiac cycle provides important static and dynamic information to

*Editorials published in *JACC: Case Reports* reflect the views of the authors and do not necessarily represent the views of *JACC: Case Reports* or the American College of Cardiology.

From the [a]Cardiology Department, Hospital Clínic i Universitari de València, Instituto de Investigación Sanitaria INCLIVA, Valencia, Spain; [b]Interventional Cardiology Unit, Hospital Clínico Universitario de Valladolid, Valladolid, Spain; and the [c]Cardiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. The authors have reported that they have no relationships relevant to the contents of this paper.

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.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.07.002

determine procedure feasibility and device sizing and enhances understanding of the interaction between the patient-specific anatomy and the device by using 3D computational modeling and 3D printing.

Patient-specific 3D computational modeling is increasingly applied in structural heart interventions (transcatheter aortic valve replacement [TAVR] and transcatheter mitral valve replacement [TMVR]), using commercially available software that provides a complete virtual simulation environment for device implantation, to predict the anatomical and physiological consequences of device deformation, paravalvular leakage, obtaining gradients and velocities and flow streamlining within the neo-left ventricular outflow tract (LVOT) using computational fluid dynamics (12).

The application of 3D printing technology in cardiology has grown in the last decade, and it has emerged as a planning tool for complex structural heart disease (13). 3D printing allows creating patient-specific biomodels that replicate accurately the real anatomy. Multimaterial printing techniques allow simulating the physical properties of different tissues. This is of special interest in cases where calcium of fibrous tissue determines the indication for prosthetic devices such as TAVR or valve-in-mitral annular calcification (MAC) procedures. Recently the use of metamaterials has been reported; this is a special multimaterial printing technique that takes into account spatial orientation of reinforcements, allowing to best mimic the strain and stress behavior of certain tissues.

These models allow for not only better understanding of the anatomy but also simulation of the procedures and implantation of the device and even evaluation of the physiologic response to the implant. Several cases have been reported using 3D print for TAVR and TMVR (14), mostly used for preoperative planning.

In this issue of *JACC: Case Reports*, Allen et al. (15) present a case of a 61-year-old female who had been treated 20 years previously with mantle field RT for Hodgkin lymphoma and presented with severe and symptomatic mitral and aortic stenosis (Video 1). After multiple heart teams at different centers evaluated her case, all of them proposed a surgical solution using the Commando procedure. The patient was informed about the high operative risk and considered it was unacceptable and declined the surgical choice.

This is a challenging case for many reasons. First, there is a lack of evidence-based recommendations for multivalvular heart disease (6); second, transcatheter mitral valve therapies are one of the most challenge procedures due the complex mitral valve anatomic relationship and potential complications; and third, there is little or no experience with transcatheter simultaneous aortic mitral valve replacement, so planning the procedure should be done carefully in order to avoid potential, predictable complications and take into account similar diseases, anatomies, and techniques.

Allen et al. (15) performed an extensive multimodality analysis, anticipating predicted and potential complications. CT scanning is crucial for preplanning TMVR and other advanced image techniques (3D printing, finite element analysis).

The main concerns of TMVR in a severely calcified annulus (also known as valve-in-MAC) are, first, valve sizing and device stability. The mitral annulus is a noncircular structure that offers limited prosthetic anchorage with a considerable risk for paravalvular leakage and even embolization. Those concerns cannot be predicted based only on morphological data acquired from CT scans or ultrasonography images, on which the device-patient interplay depends, including not only anatomy but also properties of the physical tissues. The authors faced this situation by reproducing the implantation of aortic and mitral valves using finite element modeling that combined anatomy, physical properties of the tissues, and virtual valve prosthetic models to predict the interactions between all elements, simulating deformations and achieving a reliable model for the procedure which would be able to predict paravalvular leakage and measure the neo-LVOT area.

The second concern is neo-LVOT obstruction. During mitral prosthesis implantation, the anterior mitral leaflet is shifted anteriorly toward the basal septum creating a so-called neo-LVOT (16) that is likely to be obstructive depending on valve sizing, basal septum anatomy, and mitroaortic angle. Guerrero et al. (17) reported an incidence of neo-LVOT obstruction of 9.3% with poor outcomes. A neo-LVOT cross-sectional minimal area cutoff of 1.7 cm^2 has been described to rule out a significant neo-LVOT obstruction (18). Nevertheless, this has theoretical limitation because in the neo-LVOT 3D configuration, neither flow is taken into account. Interestingly authors have used the 3D biomodel to evaluate the physiological response in terms of gradients and pressures especially within the neo-LVOT, using computational fluid dynamic systems. Finally,

JACC: CASE REPORTS, VOL. 2, NO. 10, 2020
AUGUST 2020:1448-50

a biomodel of both valves was 3D printed by using a multimaterial technology with elastic and rigid materials mimicking the real patient's anatomy and allowing the operator to have a touchable and out-of-screen assessment.

This case illustrates how innovative and diverse imaging modalities are essential tools for selecting candidate patients and guiding complex transcatheter procedures and how they can be used in combination to successfully carry out such complex interventions.

ADDRESS FOR CORRESPONDENCE: Dr. Agustín Fernández Cisnal, Hospital Clínic i Universitari de València, Avenida Blasco Ibáñez, 17, 46010 Valencia, Spain. E-mail: fecia82@gmail.com. Twitter: @afcisnal.

REFERENCES

1. Eichenauer DA, Aleman BMP, Andre M, et al. Hodgkin lymphoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018;29 Suppl 4:iv19–29.

2. Gujral DM, Lloyd G, Bhattacharyya S. Radiation-induced valvular heart disease. Heart 2016;102:269–76.

3. van Nimwegen FA, Schaapveld M, Janus CP, et al. Cardiovascular disease after Hodgkin lymphoma treatment: 40-year disease risk. JAMA Intern Med 2015;175:1007–17.

4. Yarnold J, Brotons MC. Pathogenetic mechanisms in radiation fibrosis. Radiother Oncol 2010;97:149–61.

5. Nadlonek NA, Weyant MJ, Yu JA, et al. Radiation induces osteogenesis in human aortic valve interstitial cells. J Thorac Cardiovasc Surg 2012;144:1466–70.

6. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 aha/acc guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017;135:e1159–95.

7. Kamdar AR, Meadows TA, Roselli EE, et al. Multidetector computed tomographic angiography in planning of reoperative cardiothoracic surgery. Ann Thorac Surg 2008;85:1239–45.

8. Dolmaci OB, Farag ES, Boekholdt SM, van Boven WJP, Kaya A. Outcomes of cardiac surgery after mediastinal radiation therapy: a single-center experience. J Card Surg 2020;35:612–9.

9. Desai MY, Wu W, Masri A, et al. Increased aorto-mitral curtain thickness independently predicts mortality in patients with radiation-associated cardiac disease undergoing cardiac surgery. Ann Thorac Surg 2014;97:1348–55.

10. Forteza A, Centeno J, Ospina V, et al. Outcomes in aortic and mitral valve replacement with intervalvular fibrous body reconstruction. Ann Thorac Surg 2015;99:838–45.

11. De Oliveira NC, David TE, Armstrong S, Ivanov J. Aortic and mitral valve replacement with reconstruction of the intervalvular fibrous body: an analysis of clinical outcomes. J Thorac Cardiovasc Surg 2005;129:286–90.

12. Vukicevic M, Mosadegh B, Min JK, Little SH. Cardiac 3D printing and its future directions. J Am Coll Cardiol Img 2017;10:171–84.

13. De Oliveira-Santos M, Oliveira-Santos E, Gonçalves L, Silva Marques J. Cardiovascular three-dimensional printing in non-congenital percutaneous interventions. Heart Lung Circ 2019;28:1525–34.

14. Tuncay V, van Ooijen PMA. 3D printing for heart valve disease: a systematic review. Eur Radiol Exp 2019;3:9.

15. Allen CH, Patterson T, Prendergast B, et al. Simultaneous transcatheter double valve treatment of mediastinal radiation-induced severe calcific aortic and mitral stenosis. J Am Coll Cardiol Case Rep 2020;2:1443–7.

16. Blanke P, Naoum C, Dvir D, et al. Predicting LVOT obstruction in transcatheter mitral valve implantation: concept of the neo-LVOT. J Am Coll Cardiol Img 2017;10:482–5.

17. Guerrero M, Dvir D, Himbert D, et al. Transcatheter mitral valve replacement in native mitral valve disease with severe mitral annular calcification: results from the first multicenter global registry. J Am Coll Cardiol Intv 2016;9:1361–71.

18. Yoon S-H, Bleiziffer S, Latib A, et al. Predictors of left ventricular outflow tract obstruction after transcatheter mitral valve replacement. J Am Coll Cardiol Intv 2019;12:182–93.

KEY WORDS 3D print, finite elements analysis, multimodality imaging, transcatheter aortic valve replacement, transcatheter mitral valve replacement

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