JACC: CASE REPORTS VOL. 8, 2023

EDITORIAL COMMENT

The Complex Treatment of Postradiation Valvular Heart Disease*

Vuyisile T. Nkomo, MD, MPH, Edward A. El-Am, MD

Radiation therapy is widely used and has shown a clear survival benefit in the treatment of certain malignancies. At sufficient doses, however, radiation of the mediastinum can damage the pericardium, coronary arteries, myocardium, valves, and the conduction system.[1] Radiation-associated cardiotoxicity can be acute but is usually delayed, typically 10 to 30 years after radiation therapy. Although complications can be seen with any dose, there is a linear increase in risk of valvular heart disease with total dose of radiation >30 Gy/m^2. In addition to cardiac toxicity, radiation can lead to fibrotic changes in the mediastinum, restrictive lung disease, and to a calcified "porcelain" thoracic aorta, a set-up for a hostile chest when attempting cardiac surgery.

Percutaneous approaches for the correction of valvular heart disease have gained phenomenal traction, and in patients with prior mediastinal radiation have emerged as an attractive alternative, as they circumvent many of the potential complications of open-heart surgery and offer potentially life-saving treatment options for patients who are high risk or otherwise inoperable. However, the percutaneous approaches are not without risk, and choosing between them and surgery in the treatment of post-radiation valvular heart disease can be akin to choosing between Scylla and Charybdis.

*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 Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, USA.

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 Author Center.

In this issue of *JACC: Case Reports*, Schwarzman et al[2] describe a very complex case of a 49-year-old man with symptomatic severe aortic stenosis (AS) and mitral stenosis. The etiology of his condition was elusive until appreciation and recognition of the typical echocardiographic findings of widespread and contiguous calcification of the aortic root, aortic valve, aortomitral curtain, mitral annulus, and mitral leaflets with sparing of the mitral leaflet tips characteristic of radiation-induced valvular heart disease. Indeed, the patient had undergone thoracic radiation for giant cell tumor 25 years prior, putting him at high risk of postradiation heart disease given his young age at the time of radiation. It is not uncommon for cardiac radiation sequalae to be evident first by echocardiography. Screening for radiation-induced cardiovascular disease with transthoracic echocardiogram, cardiac magnetic resonance imaging, or computed tomography in patients who have received >35 Gy/m^2 of radiation; screening either 10 years after radiation exposure or 5 years after radiation therapy in higher risk patients is recommended, with repeat echocardiograms every 5 years.[3] The prevalence of valvular heart disease is up to 26% at 10 years and 60% at 20 years after radiation.[1] Left-sided valves are typically affected,[1] but abnormalities of the tricuspid valve have also been reported. The differential involvement of the left-sided over the right-sided valves is believed to be related to the stress of higher left-sided pressures.

The patient described in this report by Schwarzman et al[2] was faced with the prospect of very-high-risk double valve surgery. Surgical aortic valve replacement (SAVR) in patients with prior mediastinal radiation has shown worse outcomes compared with control subjects without prior mediastinal radiation,[4,5] especially in those undergoing concomitant cardiac surgeries (eg, mitral valve replacement

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2022.09.019

[MVR]). Patients with a history of chest radiation undergoing SAVR require more inotropic support and blood transfusions, have longer intensive care unit and overall hospital length of stay, more frequently undergo pacemaker therapy, and experience a higher rate of atrial fibrillation, stroke, and mortality related to cardiopulmonary disease or multiorgan failure compared with age- and sex-matched control subjects undergoing similar procedures.[4] Despite low in-hospital mortality, the 5-year survival rate after isolated MVR (± coronary bypass) is 55% in patients with radiation-associated cardiac disease vs 80% in those without prior radiation.[5]

There are rare reports of complex hybrid approaches for complex radiation-induced severe AS and mitral stenosis that consist of transcatheter aortic valve replacement (TAVR) for severe AS and left atrial-left ventricular conduit placement through a left thoracotomy to bypass mitral stenosis and avoid severe mitral annulus calcification (MAC); MAC makes it difficult to anchor a mitral valve prosthesis without risk of paravalvular regurgitation or dehiscence or injury to adjacent structures.[6] However, high risk of thrombosis makes left atrial-left ventricular conduits less appealing.

TAVR is now the treatment modality of choice for severe AS, unless a patient has other factors that favor SAVR such as severe coronary artery disease requiring surgery, which the study patient fortunately did not have.[2] In a propensity-matched cohort of patients with severe AS after chest radiation, TAVR was associated with lower incident postoperative atrial fibrillation, shorter hospital length of stay, and lower 30-day all-cause mortality compared with SAVR.[7] However, the postoperative complications of paravalvular regurgitation, stroke, atrial fibrillation, and high-grade heart block, as well as overall mortality, remain higher in patients with prior chest radiation compared with control subjects, irrespective of mode of AVR.[7]

The advent of transcatheter mitral valve replacement (TMVR) was spurred on by the successes in TAVR but is still investigational, hence the off-label use of TMVR in this patient.[2] However, TMVR is much more challenging given the complexity of the mitral valve apparatus; the shape of the mitral annulus, which occupies multiple planes; and the variable distribution of calcification, which makes it difficult to obtain a perfect seal with the currently available transcatheter valves. Although there are some comparative observational data of TAVR vs SAVR in postradiation AS, TMVR experience is drawn mainly from transcatheter valve-in-MAC observational studies with variable etiology of MAC, some being postradiation MAC. Valve-in-MAC procedures are challenging because of high rates of left ventricular outflow tract (LVOT) obstruction (requiring pre-TMVR LVOT modification/alcohol septal ablation or anterior mitral valve leaflet laceration), paravalvular leaks, and potential for valve embolization.[8,9] In addition, hemolysis (from paravalvular leak or LVOT obstruction) is not an uncommon complication and sometimes requires blood transfusion or re-intervention, and it can be associated with acute kidney injury. Current short-term outcomes suggest a 4-year survival of <20% for patients undergoing valve-in-MAC,[8] which is worse compared with use of TMVR for treating mitral prostheses (tissue protheses or rings).

With the help of a multidisciplinary heart team and very careful preprocedural planning with multimodality imaging, the patient underwent uncomplicated successful TAVR and off-label TMVR with each using a 29-mm SAPIEN 3 valve (Edwards Lifesciences).[2] The procedural results were excellent, with dramatic symptomatic improvement. A left and right heart catheterization would be indicated to look for underlying restriction or constriction (even when the pericardium is normal thickness and not calcified) if there was persistence or recurrence of symptoms in the setting of normally functioning aortic and mitral valve prostheses.

Newer radiation protocols allow for more precise and efficient delivery of smaller doses of radiation and reduce the volume of heart exposed; however, radiation-induced cardiovascular disease remains a problem among cancer survivors whose population continues to grow. This impressive case from Schwarzman et al[2] is illustrative of the changing paradigms and possibilities at the intersection of transcatheter therapies and complex postradiation structural heart disease.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Vuyisile T. Nkomo, Mayo Clinic, Department of Cardiovascular Medicine, 200 First Street SW, Rochester, Minnesota 55905, USA. E-mail: nkomo.vuyisile@mayo.edu.

REFERENCES

1. Chang HM, Okwuosa TM, Scarabelli T, Moudgil R, Yeh ETH. Cardiovascular complications of cancer therapy: best practices in diagnosis, prevention, and management: part 2. *J Am Coll Cardiol*. 2017;70:2552–2565.

2. Schwarzman LS, Megowan N, Manubolu VS, Shah SU. A rare case of radiation-associated aortic and mitral valve stenosis treated with transcatheter valve replacements. *J Am Coll Cardiol Case Rep*. 2023;8:101646.

3. Lancellotti P, Nkomo VT, Badano LP, et al. Expert consensus for multi-modality imaging evaluation of cardiovascular complications of radiotherapy in adults: a report from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2013;26:1013–1032.

4. Donnellan E, Masri A, Johnston DR, et al. Long-term outcomes of patients with mediastinal radiation-associated severe aortic stenosis and subsequent surgical aortic valve replacement: a matched cohort study. *J Am Heart Assoc*. 2017;6:e005396.

5. Donnellan E, Alashi A, Johnston DR, et al. Outcomes of patients with mediastinal radiation-associated mitral valve disease undergoing cardiac surgery. *Circulation*. 2019;140:1288–1290.

6. Dionne PO, Eleid MF, Schaff HV, Maltais S. Hybrid alternate approach for complex radiation-induced valvular disease. *J Thorac Cardiovasc Surg*. 2018;156:e147–e149.

7. Zhang D, Guo W, Al-Hijji MA, et al. Outcomes of patients with severe symptomatic aortic valve stenosis after chest radiation: transcatheter versus surgical aortic valve replacement. *J Am Heart Assoc*. 2019;8:e012110.

8. Eng MH, Kargoli F, Wang DD, et al. Short- and mid-term outcomes in percutaneous mitral valve replacement using balloon expandable valves. *Catheter Cardiovasc Interv*. 2021;98:1193–1203.

9. El-Sabawi B, Guerrero ME, Eleid MF, Nkomo VT, Pislaru SV, Rihal CS. Hemolysis after transcatheter mitral valve replacement in degenerated bioprostheses, annuloplasty rings, and mitral annular calcification: incidence, patient characteristics, and clinical outcomes. *Catheter Cardiovasc Interv*. 2021;98:776–785.

KEY WORDS aortic valve, mitral valve, radiation, valve replacement