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STATE-OF-THE-ART REVIEW

VALVULAR HEART DISEASE

Radiation-Induced Aortic Stenosis

An Update on Treatment Modalities

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ABSTRACT

The adverse effects of radiation therapy for cancer are well described and can include a wide array of cardiac complications. Radiation-induced aortic stenosis (AS) is an increasingly recognized entity that poses particular therapeutic challenges. Several retrospective studies comparing the outcomes after transcatheter aortic valve replacement (TAVR) vs those after surgical aortic valve replacement patients with radiation-induced AS have found a trend toward decreased mortality and fewer major complications with TAVR. Surgical aortic valve replacement is associated with increased mortality in patients with radiation-induced AS compared with patients without a history of prior radiation. TAVR has been shown to be a safe and effective alternative in patients with radiation-induced AS, with safety similar to that for patients who have not received prior radiation. However, rare and unexpected complications may occur after TAVR from the deleterious effects of radiation on mediastinal structures. More studies are needed to identify the optimal way of managing patients with radiation-induced AS, and algorithms are needed for planning these complex interventions. (JACC Adv 2023;2:100163) © 2023 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/).

While radiation therapy has dramatically increased the survival rates of numerous malignancies, its cardiac complications are now well recognized and have been described at length.[1-5] Mediastinal radiation can lead to virtually any cardiac pathology: cardiomyopathy, constrictive pericarditis, coronary artery disease (CAD), diseases of the conduction system, and valvulopathy. Radiation-induced aortic stenosis (AS) is becoming an increasingly recognized pathology. Thirty-seven percent to 81% of patients who have received radiation to the chest will develop valvular heart disease.[6,7] Radiation leads to premature valve leaflet thickening, fibrosis, and calcification.[8] A dose-dependent toxic effect on the heart has been previously demonstrated,[9,10] and immunohistological studies have shown specifically a dose-dependent effect of aortic valve fibrosis.[11] It has been suggested that >30 Gy is considered a high dose of mediastinal radiation.[12] The aortic valve is the most commonly affected the most commonly affected valve with radiation given it is in direct line of the radiation beam.[13] Aortic regurgitation is the most commonly seen pathology although AS most often requires intervention. Echocardiographic images classically demonstrate aortomitral continuity calcifications[14]

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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

CABG = coronary artery bypass graft

CTA = computed tomography angiography

OR = odds ratio

SAVR = surgical aortic valve replacement

STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

(Figure 1). There is usually a latency of 10 to 20 years between the timing of radiation treatments and the appearance of heart disease.[6,16]

The treatment of radiation-induced AS poses particular challenges given the high-risk nature of surgery in these patients. There has been a rising interest regarding transcatheter aortic valve replacement (TAVR) in patients with a history of prior radiation as they may derive more benefit from undergoing percutaneous rather than surgical aortic valve replacement (SAVR). In this article, we review the outcomes and considerations for the surgical approach for correction of radiation-induced AS, the percutaneous approach, and a comparison of the surgical vs percutaneous approach. Finally, we outline a decision-making algorithm for these complex patients.

SURGICAL APPROACH

Patients with a prior history of radiation to the chest are considered to be at high risk for surgery for numerous reasons. Radiation leads to calcification and fibrosis of blood vessels, leading to accelerated atherosclerosis. The aorta was found to be porcelain in up to 60% of patients with previous radiation exposure on a computed tomography angiography (CTA) imaging study, which precludes safe aortic clamping for cardiopulmonary bypass.[17] If a porcelain aorta is clamped, there is an increased risk of stroke and mortality.[18] Radiation leads to mediastinal adhesions and fibrosis that need to be dissected and increase the risk of bleeding and poor wound healing, which is often referred to as a hostile chest.[19] Extensive debridement may increase the cardiopulmonary bypass time. Another complication that may be encountered is the presence of radiation-induced pulmonary fibrosis. The degree of pulmonary fibrosis has been shown to correlate directly with mortality postoperatively.[20] Finally, there may be other concomitant radiation-induced heart diseases (coronary disease, pericardial calcifications, restrictive cardiomyopathy) which can also complicate the postoperative course.

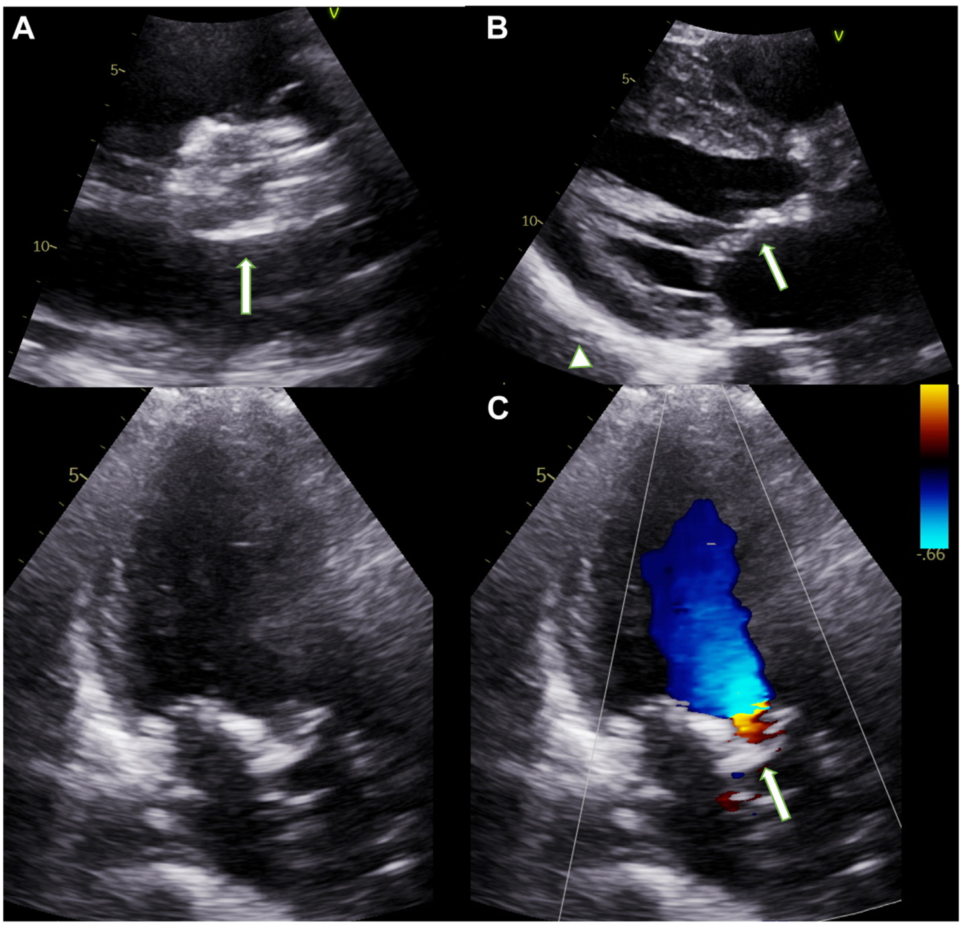
SAVR has been shown to have worse outcomes in patients with a prior history of mediastinal radiation compared to controls. In 2013, Wu et al demonstrated in a retrospective study increased operative mortality at 30 days in patients undergoing a cardiac surgery with a previous history of radiation compared with patients without radiation exposure (4% vs 0.3%, $P = 0.01$). There was also increased long-term mortality at a mean follow-up of 7.6 years (55% vs 28%, $P < 0.001$).[21] These very high long-term mortality rates may be attributed to the fact that approximately two-thirds of patients in both groups were undergoing combination surgical procedures and that the mean EuroSCORE was very elevated (7.8 and 7.4 in patients with and without prior radiation, respectively). Patients are generally considered to be at high risk with a EuroSCORE of 6 or more, with traditionally cited mortality of 11.2%.[22] A more recent matched cohort study in 2017 found that radiation was associated with a statistically significant increase in in-hospital mortality (2% vs 0%, $P = 0.005$) and 6-year mortality (48% vs 7%, $P < 0.001$) after SAVR compared with patients without a radiation history.[23] However, 61% of patients were undergoing SAVR with another concomitant procedure (coronary artery bypass graft [CABG] or aortic surgery). Isolated SAVR has been shown to have better 5-year survival than combined procedures in patients with radiation-induced AS (65% vs 37%, $P = 0.03$).[24] These studies suggest that these surgeries are both technically challenging given increased perioperative mortality and that there is a persisting higher risk of death after a cardiac surgery in patients with a prior history of radiation.

Certain risk factors may render surgery more difficult in patients with radiation-induced AS. In a cohort of 60 patients with previous mediastinal radiation undergoing a cardiac valve surgery, the main predictors of mortality were a history of constrictive pericarditis, longer cardiopulmonary bypass times, and reduced preoperative left ventricular ejection fraction.[25] Prior versions of the Society of Thoracic Surgeons (STS) score did not take into consideration a history of mediastinal radiation. A retrospective analysis of 261 patients undergoing a cardiac surgery for valvular heart disease showed significantly higher mortality in patients with prior radiation than that in nonirradiated matches (3.5% vs 0.8%, $P = 0.004$),

HIGHLIGHTS

- Aortic stenosis is the most common valvulopathy related to radiation that requires correction.
- SAVR has increased complications and mortality in patients with radiation-induced AS.
- TAVR is a promising alternative especially for patients at high risk for surgery.

FIGURE 1 **Echocardiography Findings of Radiation-Induced Cardiotoxicity in a 54-Year-Old Woman Presenting to Our Center With Dyspnea**



She had a history of Hodgkin's lymphoma treated with chemotherapy and mediastinal radiation 36 years prior. **(A)** Short-axis view of the aortic valve showing significant calcification of all leaflets **(arrow)**. **(B)** Aorto-mitral continuity calcifications, typical of radiation-induced cardiotoxicity **(arrow)** and pericardial thickening and calcifications **(arrowhead)**. **(C)** Color Doppler assessment of the aortic valve in an apical 3-chamber view showing turbulent flow through a calcified and stenotic valve **(arrow)**. Adapted from Belzile-Dugas et al.[15]

despite similar STS scores (2.57 vs 2.51, $P = 0.337$). Observed-to-expected mortality ratio was 1.48 in patients with prior radiation compared to 0.32 in patients without prior radiation.[26] Another study demonstrated qualitatively similar results with an observed-to-expected mortality ratio of 5 (95% CI: 1.62-11.67, $P = 0.005$) with SAVR in patients with radiation-induced AS compared to controls.[27] Hence, a history of prior chest radiation is now included in the STS risk score before a cardiac surgery given its significant effect on surgical mortality.[28] Finally, it has to be reiterated that a repeat cardiac surgery (reoperation) in these patients involves extremely high risk with operative mortality of 17% vs 2.3% in nonirradiated matches ($P = 0.001$). Operative mortality is 17% vs 3.7% ($P = 0.003$) in reoperation vs first operation of patients with a history of mediastinal radiation, with a HR of 3.19 for long-term mortality compared with nonirradiated controls (95% CI: 1.95-5.21).[26] In our experience, most centers will refuse to do these cases, even in the hands of experienced teams and surgeons. While SAVR may be appropriate for certain low-risk patients, its associated morbidity and mortality have led to an increasing interest for TAVR in patients with radiation-induced AS.

PERCUTANEOUS APPROACH

TAVR is an increasingly performed procedure and may be an important treatment avenue for patients with radiation-induced AS. A case-control study in 2015 compared 19 patients with radiation-induced AS to 179 patients without a history of prior radiation. TAVR was safe in patients with radiation-induced AS compared to controls, with a high implantation success rate (94.7% vs 93.9%, respectively, $P = 0.90$) and no significant difference in 30-day mortality (0% vs 11.6%, respectively, $P = 0.23$) and 6-month mortality (0% vs 18%, respectively, $P = 0.048$).[29] Zafar et al[30] showed in a 2020 systematic review and meta-analysis (which included the previously mentioned study) that TAVR was a safe option for patients with radiation-induced AS. Four studies were included with a total of 2,010 patients with severe AS. There was no statistically significant difference in 30-day mortality in patients with prior radiation compared to controls (OR: 1.29; CI: 0.64-2.58; $P = 0.48$). However, significantly higher rates of 1-year mortality were observed in patients with prior radiation (OR: 1.97; CI: 1.15-3.39; $P = 0.01$). There was no difference in rates of stroke, major bleed, need for pacemaker implantation, or access-related vascular complication, but there were significantly more heart failure exacerbations in the radiation group (OR: 2.03; CI: 1.36-3.04; $P = 0.0006$). Finally, safety and efficacy endpoints (left ventricular ejection fraction and mean aortic valve gradient after the procedure) were similar between patients with prior radiation and controls.[30]

TAVR, however, may have some limitations in patients with radiation-induced AS. A concern that may arise with TAVR is the durability of the implant in those cancer survivors, who are typically younger than patients in the studies regarding safety of TAVR. In one of the studies previously mentioned, the mean age of patients with radiation-induced AS undergoing TAVR was 68.3 years, compared to 82.5 years for the patients without a history of prior radiation.[29] Long-term durability of TAVR is unknown, but studies in the general population have suggested that the durability of TAVR is better than that initially expected. A small study of 129 patients younger than 70 years undergoing TAVR has shown to have excellent implantation success rates and very low rates of valve reintervention (2.3% at 3-year follow-up).[31] In the SURTAVI (Surgical Replacement and Transcatheter Aortic Valve Implantation) trial, intermediate-risk patients were randomized to undergoing TAVR (n = 864) or SAVR (n = 796). There was no reintervention in the TAVR group at 24 months.[32] TAVR was associated with a superior hemodynamic valve performance compared to SAVR but slightly higher rates of reintervention at 5-year follow-up (3.5% vs 1.9%, $P = 0.02$).[33] In the NOTION trial (Nordic aortic valve intervention clinical trial), 145 low-risk patients were randomized to undergo TAVR, and the reintervention rate was only 2.1% at 5 years[34] and 3.6% at 8 years of follow-up.[35] However, long-term studies are needed to assess prosthesis function years to decades after implantation specifically for patients who have received mediastinal radiation. In a simulation model study, life expectancy was reduced when TAVR durability was 30%, 40%, and 50% shorter than the durability of surgical valves in 40-, 50-, and 60-year-old patients.[36] Hence, the improved periprocedural risk of TAVR needs to be balanced with the durability of the implanted valve in young cancer survivors.

Another concern that may arise with TAVR in patients with radiation-induced AS is that the presence of friable and calcified cardiac tissues may lead to unusual complications. A patient underwent an uncomplicated TAVR for radiation-induced AS but was found later to have a left-to-right shunt between the aorta and the right ventricle, originating behind the aortic prosthesis. It was treated conservatively; unfortunately, the patient died suddenly a few months later.[37] A case of iatrogenic ventricular septal defect after transapical TAVR was reported in a patient with radiation-induced AS. The patient underwent successful percutaneous closure of the defect.[38] Finally, a case of aortic valve leaflet rupture was reported after valvuloplasty preceding the TAVR in a patient with radiation-induced AS. This led to severe aortic regurgitation and left main ostial obstruction, which were corrected with implantation of the valve capturing the ruptured leaflet and a left main stent.[39] While TAVR is usually safe in patients with radiation-induced AS, these cases illustrate that tissues having received radiation are often very calcified, and unusual complications such as fistulization and tissue rupture may arise. More research is needed to assess complications of TAVR specific to patients having previously received radiation therapy to the chest.

SURGICAL VS PERCUTANEOUS APPROACH

Four studies have retrospectively compared outcomes after TAVR vs SAVR in patients with radiation-induced AS (**Tables 1 and 2**). Zhang et al[27] were the first to show in a 2019 retrospective study of 110 patients a significant mortality benefit in TAVR compared to SAVR in patients with radiation-induced

TABLE 1 Summary of Studies Comparing Mortality After TAVR vs SAVR in Radiation-Induced AS

First Author	Design	Population	Follow-Up	Main Survival Findings
Zhang et al[27]	Single center, retrospective study	TAVR (n = 55) SAVR (n = 55)	30 d 1 y	After inverse probability treatment weighting adjusting for STS score, 30-d and 1-y mortality decreased with TAVR vs SAVR ($P < 0.0001$). Observed-to-expected 30-d mortality lower with TAVR (0.33; 95% CI: 0.01-1.86) than SAVR (5.00; 95% CI: 1.62-11.67) $P = 0.005$.
Elbadawi et al[40]	NIS database,[a] retrospective study	TAVR (n = 2,170) SAVR (n = 1,505)	In-hospital	On multivariable analysis, in-hospital mortality lower in TAVR vs SAVR (1.2% vs 2.0%; $P = 0.02$).
Nauffal et al[41]	STS database, retrospective study	TAVR (n = 1,668) SAVR (n = 2,611)	30 d	After adjustment for baseline covariates in multivariable analysis, TAVR had 40% reduction in all-cause mortality vs SAVR (1.9% vs 3.2%, $P = 0.03$).
Yazdchi et al[42]	Single-center, retrospective study	TAVR (n = 69) SAVR (n = 117)	Operative 30 d, midterm[b] (average 37 mo)	Operative mortality 4.3% for SAVR vs 1.4% for TAVR ($P = 0.41$). No significant difference in midterm survival between TAVR and SAVR (HR: 1.12; 95% CI: 0.51-2.47; $P = 0.27$). Intermediate-/high-risk SAVR patients had significantly worse midterm survival than TAVR patients (HR: 2.94; 95% CI: 1.57-5.55; $P < 0.001$).

[a]NIS database includes data from all states participating in the Healthcare Cost and Utilization Project, covering 97% of the US population, which makes it the largest inpatient database in the United States. [b]Midterm survival: patients identified retrospectively from January 2012 to December 2018; follow-up time was calculated from the date of procedure to the date of death or study end (June 30, 2019) if alive.

AS = aortic stenosis; NIS = National Inpatient Sample; SAVR = surgical aortic valve replacement; STS = Society of Cardiovascular Surgeons; TAVR = transcatheter aortic valve replacement.

AS. The mortality benefit was seen both at 30 days and 1 year of follow-up ($P < 0.0001$). However, 25.5% of the SAVR patients underwent concomitant CABG, which may explain the increased mortality seen with surgery. TAVR patients had a higher STS score than SAVR patients (5.1 vs 1.6, $P < 0.001$), and there was a significant decrease in postoperative atrial fibrillation and length of hospital stay in the TAVR group. However, there was a higher rate of readmission in the TAVR group at 90 days (30.9% vs 5.5%, $P = 0.001$), mostly attributed to heart failure.

Elbadawi et al[40] showed similar results in a large retrospective study from the National Inpatient Sample database, with 3,675 patients with

TABLE 2 Summary of Studies Comparing Outcomes After TAVR vs SAVR in Radiation-Induced AS

First Author	Population	Mean Age, y	Mean STS Score	Female	Significant Complications (TAVR vs SAVR)
Zhang et al[27]	TAVR (n = 55) SAVR (n = 55)	72.0 60.0	5.1 1.6	61.8% 61.8%	Length of hospital stay 4 vs 6 d ($P < 0.001$) Postoperative AF 3.6% vs 32.7% ($P < 0.001$) 90 d rehospitalization 30.9% vs 5.5% ($P = 0.001$)
Elbadawi et al[40]	TAVR (n = 2,170) SAVR (n = 1,505)	76.28 68.77	N/A N/A	77.2% 83.7%	Major bleeding 12.9% vs 34.7% ($P < 0.001$) Mechanical support 0% vs 1.7% ($P = 0.03$) Blood transfusion 12% vs 28.2% 9 ($P < 0.001$) Respiratory complication 1.4% vs 4.3% ($P = 0.01$) Complete heart block 12.7% vs 5.3% ($P < 0.001$) Pacemaker insertion 10.8% vs 4.3% ($P < 0.001$) Discharge to a nursing facility 12.9% vs 25.6% ($P < 0.001$) Length of hospital stay 3 vs 6 d ($P < 0.001$)
Nauffal et al[41]	TAVR (n = 1,668) SAVR (n = 2,611)	76.2 68.9	5.0 2.2	75.5% 75%	Postoperative AF 8.8% vs 32.6% ($P < 0.001$) Pneumonia 3.1% vs 3.5% ($P = 0.002$) Pleural effusion 3.9% vs 9% ($P < 0.001$) Renal failure 2.5% vs 3.1% ($P = 0.002$) Bleeding complication 15.6% vs 31.5% ($P < 0.001$) Stroke 2.3% vs 1.3% ($P = 0.03$) Pacemaker insertion 11.3% vs 5.6% ($P = 0.001$)
Yazdchi et al[42]	TAVR (n = 69) SAVR (n = 117)	75.3 64.8	5.73 2.53	66.7% 69.2%	Blood transfusion 8.7% vs 35% ($P = 0.001$) Length of hospital stay 2 vs 7 d ($P = 0.001$)

AF = atrial fibrillation; AS = aortic stenosis; N/A = not available; SAVR = surgical aortic valve replacement; STS = Society of Cardiovascular Surgeons; TAVR = transcatheter aortic valve replacement.

radiation-induced AS who underwent either TAVR or isolated SAVR from 2012 to 2017. TAVR was found to be increasingly performed over time. TAVR was associated with significantly lower in-hospital mortality than SAVR (1.2% vs 2%, $P = 0.02$). TAVR was associated with significantly lower rates of kidney injury, use of mechanical circulatory support, major bleeding, blood transfusion, respiratory complications, discharge to nursing facility, and shorter length of stay. However, the TAVR group had significantly higher rates of pacemaker implantation (10.8% vs 4.3%, $P = 0.01$).[40]

Nauffal et al[41] showed similar short-term outcomes. A total of 1,668 patients who underwent TAVR were compared with 2,611 patients who underwent isolated SAVR for radiation-induced AS from the STS United States national database. TAVR was associated with significantly reduced 30-day mortality compared with SAVR in the matched case-control analysis (1.9% vs 3.2%, $P = 0.03$). Postoperative atrial fibrillation, pneumonia, renal failure, pleural effusion, and bleeding occurred less often with TAVR. However, stroke and pacemaker implantation were higher in the TAVR group. In the propensity-matched analysis, the 30-day mortality benefit in TAVR was only seen in the contemporary era of the procedure from 2015 to 2018 (OR: 0.31; 95% CI: 0.14-0.65; $P = 0.02$), but not in the early era of the procedure from 2011 to 2014 (OR: 0.78; 95% CI: 0.48-1.28; $P = 0.33$).[41]

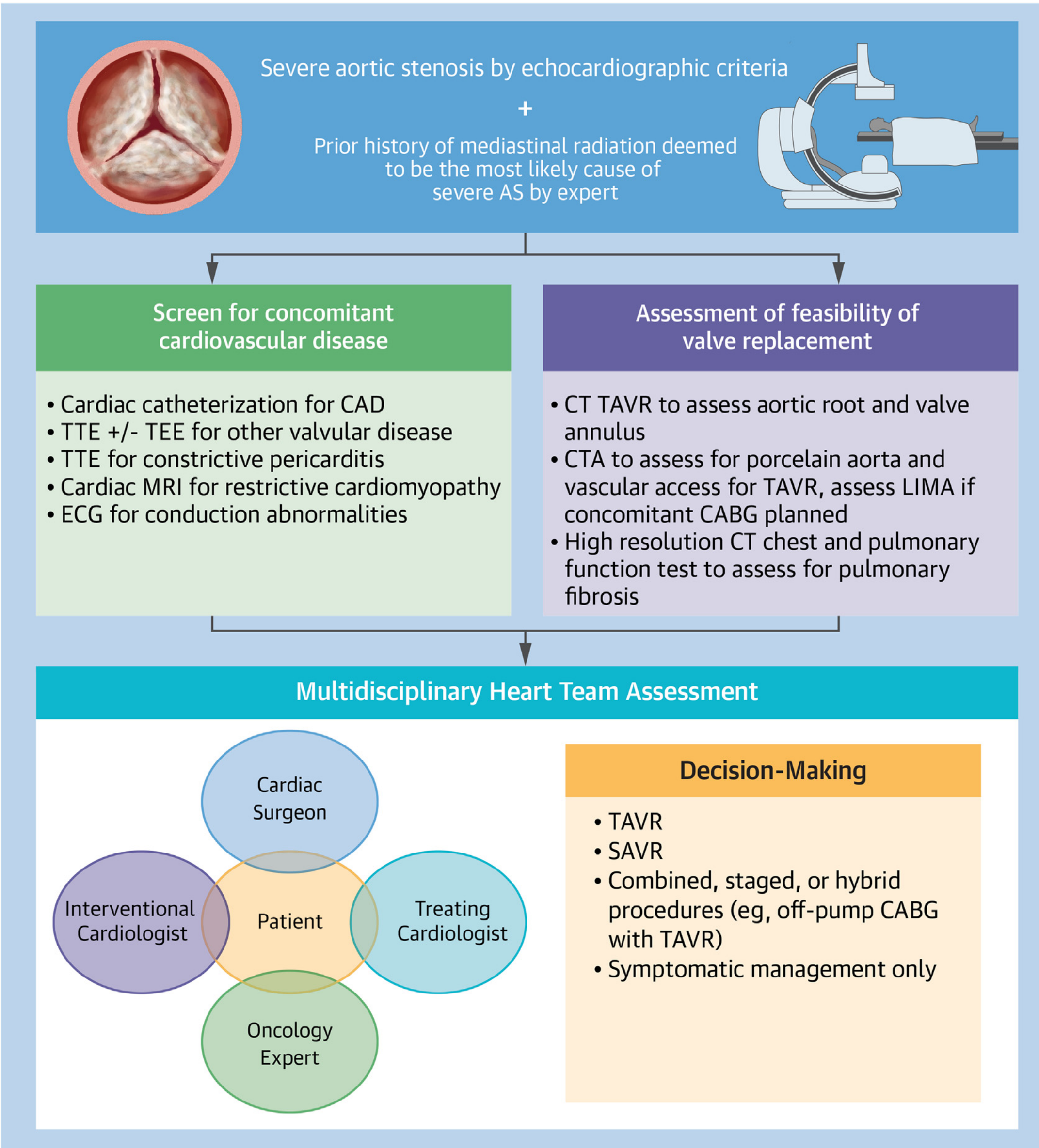
Finally, Yazdchi et al[42] looked retrospectively at 69 patients who underwent TAVR and 117 patients who underwent isolated SAVR for radiation-induced AS. TAVR patients were older and had more comorbidities. Operative mortality was 4.3% for SAVR and 1.4% for TAVR ($P = 0.41$). Most SAVR deaths occurred in the intermediate- to high-risk STS group. Observed-to-expected mortality was better for TAVR and low-risk SAVR patients (0.72; 95% CI: 0.59-0.86, and 0.24; 95% CI: 0.05-0.51, respectively) than it was for high-risk SAVR patients (2.52; 95% CI: 0.26-4.13). SAVR patients had significantly longer length of stay in the intensive care unit and higher blood transfusion requirements but similar rates of stroke and pacemaker implantation.[42]

Hence, there is a trend with TAVR towards improved short-term outcomes and fewer complications (except for pacemaker insertion) compared to SAVR in patients with radiation-induced AS. While surgery may still be an option in low-risk patients, TAVR should strongly be considered in patients at high risk for surgery. Limitations to these studies include their nonrandomized and observational nature where results can be affected by confounding factors. The studies by Zhang et al[27] and Yazdchi et al[42] had small cohorts from which it is difficult to draw conclusions. In the studies by Zhang et al,[27] Nauffal et al,[41] and Yazdchi et al,[42] patients undergoing TAVR had higher STS scores and, hence, were more likely to be redirected toward a percutaneous approach rather than a surgical one, creating a selection bias from treatment assignment. Analysis was done adjusting for patient factors and confounders, but residual confounding cannot be excluded. Elbadawi et al[40] used data from the National Inpatient Sample database, which are derived from billing data. While this is a large database providing information about thousands of patients, critical information such as comorbidities, concomitant CAD, and patient risk factors is missing, which does not allow for calculation of the baseline STS risk score. On the other hand, Nauffal et al[41] used the STS database, which is much more robust and contains data regarding patient risk factors and comorbidities, but the data are limited to 30-day follow-up. Furthermore, the longest follow-up duration for complications in these studies was 37 months. Longer follow-up is needed to compare long-term safety of TAVR and SAVR in patients with radiation-induced AS. Finally, for reasons that are still unclear, women seem to be disproportionately affected by radiation-induced heart diseases, as the proportion of women requiring an intervention for radiation-induced AS was largely superior to that of men in all 4 studies. This has been demonstrated in other studies where women have significantly higher cardiovascular events and mortality than men in relation to radiation therapy.[43]

DECISION-MAKING

The decision-making of treatment modality for radiation-induced AS should ultimately be a multidisciplinary decision that is targeted for the patient's specific characteristics and needs. The multidisciplinary heart team approach is formally recommended in the American Heart Association 2021 guidelines for the decision-making of treatment modality of severe cases of AS,[44] which is especially relevant in the treatment of patients with radiation-induced AS given the complexity of their anatomy and disease history. This multidisciplinary discussion involves the treating cardiologist, interventional cardiologist, cardiac surgeon, and, at the center of the

CENTRAL ILLUSTRATION Algorithm for Planning of Intervention for Radiation-Induced Aortic Stenosis



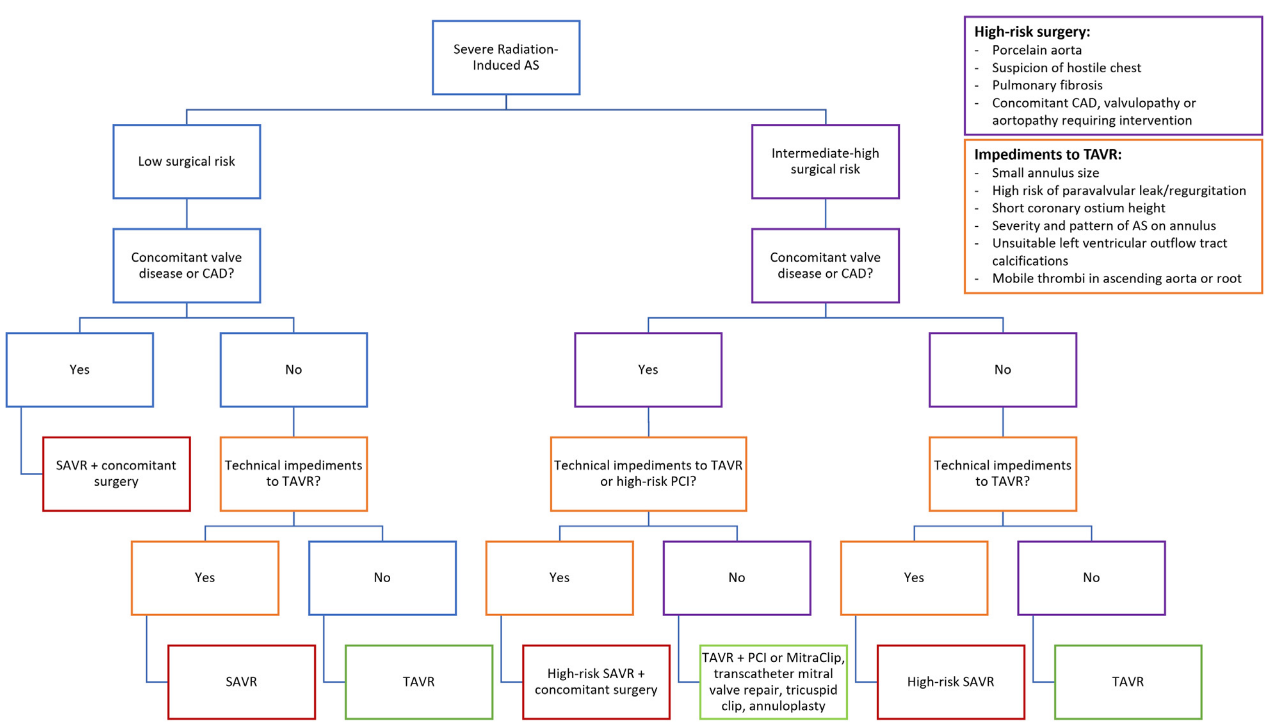
Belzile-Dugas E, et al. JACC Adv. 2023;2(1):100163.

AS = aortic stenosis; CABG = coronary artery bypass graft; CAD = coronary artery disease; CT = computed tomography; CTA = computed tomography angiography; ECG = electrocardiogram; LIMA = left internal mammary artery; MRI = magnetic resonance imaging; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram.

discussions, the patient. It takes into consideration the patient's cardiac and general comorbidities, their specific anatomy, and ultimately the patient's values and preferences.

The International Cardio-Oncology Society has also made formal recommendations in 2021 for the multidisciplinary evaluation of patients with radiation exposure before a cardiac intervention. They

FIGURE 2 Algorithm for Decision-Making of Treatment Modality for Radiation-Induced Aortic Stenosis



AS = aortic stenosis; CAD = coronary artery disease; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement. Adapted with permission from Yazdchi et al.[42]

suggest TAVR as the preferred treatment modality for radiation-induced AS, especially in patients with higher radiation doses to the mediastinum or prior cardiac surgery.[3] The dose of radiation received may influence the decision-making; however, it is often hard to quantify as many of these patients received radiation decades prior to presentation for a cardiac disease. With these recommendations in mind and the findings described in the prior sections, we suggest an algorithm for the planning of these complex procedures with the investigations to be performed before deciding on a treatment modality for patients with radiation-induced AS (**Central Illustration**). We also suggest an algorithm for the decision-making of the treatment modality of radiation-induced AS (**Figure 2**).

First, the patient should be assessed for a concomitant heart disease, specifically CAD and other valve diseases. Second, it should be assessed if the CAD or other valvulopathy is clinically important enough to require intervention. If that is the case, the feasibility of percutaneous coronary intervention and CABG should be assessed by the heart team. The left internal mammary artery should be assessed for patency by CTA given the potential for stenosis and calcification from radiation. If TAVR is considered, the patient should undergo CT-TAVR to assess vascular access, aortic root, and aortic annulus size.[45] Finally, the risk of surgery should be assessed and individualized for each patient and then discussed with the patient. For example, if there is severe AS and significant CAD in a patient at low risk for a surgery, SAVR + CABG would be recommended.[42] A patient with severe AS and significant CAD at intermediate risk for a surgery who has technical impediments to TAVR should also be considered for SAVR + CABG. On the other hand, if there is a porcelain aorta on CTA and the patient is deemed to be at very high risk for surgery, the patient should be considered for TAVR + percutaneous coronary intervention if feasible. If the patient is at high risk for surgery but TAVR is not technically feasible, high-risk

SAVR + CABG could be offered after discussion with the multidisciplinary heart team if the patient understands and accepts the risks of surgery.

Combined, staged, and hybrid procedures should also be considered such as off-pump CABG with TAVR.[15] If both the mitral and aortic valves need replacement, the commando procedure should be considered (aortic and mitral valve replacement with aorto-mitral curtain reconstruction).[46] The MitraClip (Abbott) has also been described as an option for radiation-induced mitral regurgitation in a small study of 15 patients where there was symptomatic improvement in most patients.[47] There are also case reports of transcatheter mitral valve replacement in patients with significant mitral stenosis related to radiation.[48] While this is still an area for ongoing advancements, the best approach for these complex patients with a radiation-induced heart disease is a meticulous and multidisciplinary heart team approach with the patient at the center of all discussions.

CONCLUSIONS

Mediastinal radiation can lead to a wide array of cardiac complications. AS is the most common valvulopathy related to radiation that requires correction. It is well established that patients with radiation-induced AS who undergo SAVR have higher rates of complications and mortality than nonirradiated patients. TAVR has been shown to be a safe and efficacious alternative. Several recent studies comparing outcomes in patients with radiation-induced AS after TAVR vs SAVR show a trend toward increased survival and fewer complications with TAVR, with the exception of pacemaker insertion. Hence, in the face of high and unacceptable surgical risk, percutaneous approaches may be an alternative to traditional surgical options.

As the survival rate of cancer continues to improve with modern treatments, the number of survivors with radiation-related complications is expected to increase.[6] Prevention may be the key to reducing the incidence of radiation-induced heart disease. Modern radiation techniques can decrease the amount of radiation delivered to the heart—simple techniques such as breath holding can reduce the delivery of radiation to the heart by 50%.[49,50] In terms of screening, the International Cardio-Oncology Society recommends obtaining routine transthoracic echocardiogram in all patients who are planned to undergo thoracic radiation and every 5 years thereafter to screen for radiation-induced valvulopathy.[3] However, this recommendation has yet to be integrated into routine clinical practice. Raising physician awareness about radiation-induced cardiovascular disease will be one of the most important steps toward improving patient outcomes. Radiation-induced cardiovascular diseases will be an interesting area of ongoing research in the next few years.

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