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Efficacy and follow-up of transcatheter aortic valve implantation in patients with radiation-induced aortic stenosis

Marina Dijos, Amélie Reynaud, Lionel Leroux, Patricia Réant, Claire Cornolle, Raymond Roudaut, Pierre Dos Santos, Stéphane Lafitte

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Valvular Disease Department and Echocardiography Laboratory, Haut-Lévêque Bordeaux University Hospital–CIC0005–France, Pessac, France

Correspondence to
Dr Stéphane Lafitte; stephane.lafitte@chu-bordeaux.fr

ABSTRACT

Objective: To investigate transcatheter aortic valve implantation (TAVI) feasibility, effectiveness and safety in radiation-induced aortic valve stenosis cases.

Methods: 198 consecutive patients referred for TAVI were prospectively enrolled. They were divided into two groups: patients with a history of chest radiation therapy with suspected radiation-induced valvular disease (RXT) and others with suspected degenerative aortic valve stenosis (NRXT). Procedural, early and mid-term clinical outcomes were compared.

Results: Of the 198 patients enrolled in our study, 9.6% qualified for inclusion in the RXT group. A comparison of baseline characteristics revealed that patients with RXT were younger than patients with NRXT (68.3 vs 82.5 years; p<0.05) and exhibited a lower surgical risk score (Euroscore: 7.1% vs 21.8%; p<0.05) and a higher frequency of hostile thorax and porcelain aorta (52.6% vs 28.5%; p<0.05; 63.2% vs 10.6%; p<0.05, respectively). In both groups, the implantation success rate was high and the 30-day safety end point acceptable (RXT: 94.7% and 83.3%; NRXT: 93.9% and 75.6%, respectively). At 6 months, overall mortality was significantly lower in the RXT group (0% vs 18%; p=0.048).

Conclusions: In patients suffering from radiation-induced aortic valve stenosis and contraindicated for surgery, TAVI is a promising approach, with high feasibility, acceptable risk, low mortality and high clinical effectiveness at mid-term follow-up.

KEY MESSAGES

What is already known about this subject?

- This is the first study to focus on the subgroup of patients with transcatheter aortic valve implantation (TAVI) who present with radiation-induced aortic stenosis.

What does this study add?

- We compared this subgroup of patients with conventional patients with TAVI in order to identify a specific profile in immediate results and during the 6 months follow-up. As a main finding, we observed a reduced mortality rate in the patients with radiation-induced aortic stenosis at 6 months.

How might this impact on clinical practice?

- The impact of this study could be a better selection of this subgroup of patients for TAVI.

INTRODUCTION

Using radiation therapy in thoracic malignancy management has led to significant improvements in survival. However, radiation-induced cardiovascular diseases have been reported to manifest decades after therapy and now represent the most common non-malignant cause of death in survivors of radiation-treated cancer.[1]

Both disease incidence and severity increase with higher radiation doses, larger exposed volumes, younger age at time of exposure and greater time elapsed since treatment. Despite the safety advances achieved over the past decades in radiation therapy, patients with Hodgkin's lymphoma or left breast, lung, oesophageal or gastric cancer still receive as standard either a high dose of radiation to a small part of the heart or a low dose to the whole heart.[2]

Manifestations of radiation-induced heart disease include accelerated atherosclerosis, pericardial and myocardial fibrosis, conduction abnormalities and cardiac valve damage.[2–7]

Radiation-induced valvular diseases affect approximately 6–15% of patients exposed to mediastinal radiation.[8] While aortic or mitral valvular regurgitation is the more commonly seen dysfunction, aortic stenosis is typically the main reason motivating surgical options. On average, valve lesions are diagnosed 11.5 years after radiation therapy, and symptoms occur 5 years later.[9] In comparison to a normal matched population, patients with mediastinal radiation have been reported to exhibit increased risk of requiring valve surgery, with a standard incidence ratio of 9.2.[10]

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Nevertheless, aortic or mitral valve replacement is associated with myocardial dysfunction, severe coronary artery disease, high frequency of extensively calcified ascending aorta, mediastinal fibrosis, lung fibrosis and chest wall deformation. This intervention may therefore lead to high surgical mortality, even in young patients, whether associated with coronary artery bypass or not. For this reason, some of these patients are contraindicated for surgery, which is associated with very poor prognosis.[11 12]

Transcatheter aortic valve implantation (TAVI) has recently emerged as a promising alternative to surgical aortic valve replacement for high-risk patients with severe symptomatic aortic stenosis.[12] In a little over a decade after the first implantation performed by Cribier *et al*, more than 50 000 patients have been treated worldwide by TAVI. This technique has been performed mostly in older frail patients suffering from symptomatic degenerative aortic valve stenosis with comorbidities. Yet it also appears to be an interesting alternative to surgical aortic valve replacement in younger patients presenting with radiation-induced aortic valve stenosis and hostile thorax who are at-risk candidates for conventional surgery. The percutaneous approach (transfemoral, subclavian, transcarotid or transapical) may, in fact, overcome issues of extensively calcified ascending aorta, mediastinal fibrosis, pericardial calcification and chest wall deformation.[13]

Over the past few years, several encouraging case reports have been published concerning TAVI in patients with radiation-induced aortic stenosis.

Our study aimed to make the first ever comparison of the procedural results, clinical symptom status and early to mid-term outcomes of TAVI between patients with radiation-induced aortic stenosis and those with degenerative aortic stenosis.

METHODS

Study population

Consecutive patients diagnosed with severe symptomatic aortic valve stenosis and considered unsuitable for conventional surgery, referred for TAVI between January 2011 and January 2013 at the Cardiologic University Hospital of Bordeaux, were prospectively enrolled in the study. Severe aortic valve stenosis was defined as an aortic valve area <1 cm^2, a mean aortic valve gradient ≥40 mm Hg or a peak aortic jet velocity ≥4 m/s, as determined by echocardiography following the recommendations of the American Society of Echocardiography.[14] Patients with a low-flow, low-gradient aortic stenosis could be included in the study. Each patient was first evaluated by a heart team, including a surgeon, cardiologist and anaesthesiologist. Symptoms, medical history, comorbidities, surgical score, thorax analysis, life expectancy, level of frailty and prescreening examinations (echocardiography, aortic CT scan and coronary angiography) were assessed by the heart team. In accordance with American and European guidelines,[15 16] the heart team selected patients with severe and symptomatic aortic valve stenosis, along with high surgical risk scores (logistic Euroscore >20% or Society of Thoracic Surgeons (STS) score >10%)[17 18] for TAVI, as well as those exhibiting other risk factors not captured by the risk scores, such as hostile thorax, porcelain aorta, severe liver disease or high degree of frailty. Diagnoses of porcelain aorta and hostile chest were established according to the Valve Academic Research Consortium-2 consensus document.[19] Furthermore, on the basis of prescreening results, patients had to have a life expectancy exceeding 1 year and anatomical features compatible with TAVI.

The study population was divided into two groups:

- The first group included radiation-induced valvular disease cases (RXT), consisting of patients who had previously undergone mediastinal or left-chest-wall radiation treatment for cancer more than 10 years before inclusion. Reasons for radiation therapy and year of treatment were recorded.
- The second group included non-radiation-induced valvular disease cases (NRXT), consisting of patients who had never undergone thoracic radiation therapy presenting with suspected degenerative aortic valve stenosis.

TAVI procedure

The TAVI procedure has previously been reported in detail.[12 15 20] In brief, the procedure consists in the following: the preferred access route was the femoral artery; other access sites (subclavian or carotid artery, transaortic, or transapical) were considered when femoral access was not suitable due to severe femoral artery disease; the femoral artery was punctured percutaneously and closed using a suture device, while the other access sites were managed surgically. Two commercially available systems were used: a self-expandable prosthesis, namely the Medtronic CoreValve Revalving System (Medtronic, Minneapolis, Minnesota, USA); a balloon-expandable prosthesis, the Edwards SAPIEN valve (Edwards Lifesciences, Irvine, California, USA). All patients provided written informed consent before the TAVI procedure.

Study end points

The primary end points were:

- Device implantation success: composite end point defined as the absence of procedural mortality, positioning of a single prosthetic heart valve into the correct anatomical location, and appropriate prosthetic valve function;
- Thirty-day combined safety: composite end point defined as the absence of all-cause mortality, stroke (disabling and non-disabling), life-threatening bleeding, acute kidney damage, coronary artery obstruction requiring surgery, major vascular complication or valve-related dysfunction requiring repeat procedure;

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- Six-month cardiovascular and overall mortality;
- Six-month clinical efficacy: composite end point defined as the absence of all-cause mortality, stroke (disabling and non-disabling), hospitalisation for valve-related symptoms or worsening congestive heart failure, New York Heart Association (NYHA) Class III or IV, or valve-related dysfunction.

The secondary end points were procedural complications:

- Thirty-day cardiovascular and overall mortality;
- Bleeding complications classified as 'life-threatening', 'major' or 'minor';
- Vascular complications classified as 'major' or 'minor';
- All strokes (disabling and non-disabling);
- Acute kidney injury;
- Conduction disturbances leading to pacemaker implantation;
- Six-month performance of the bioprosthesis, as assessed by echocardiography (mean gradient, aortic valve area and presence of aortic valve regurgitation).

Composite end points and procedural complications were defined in accordance with Valve Academic Research Consortium 2 (VARC2) criteria.[19]

Data collection

All data selected for analysis in this study were obtained from patient medical files. These included medical history, baseline clinical findings, patient characteristics, coronary angiography findings, as well as aortic CT, transthoracic or transoesophageal echocardiography findings, and periprocedural parameters, such as bioprosthesis type, access route and adverse events. The data also included 30-day and 6-month patient survival, clinical status and echocardiographic findings. This information was obtained and recorded in each patient's medical file during dedicated consultations at 30 days and 6 months, or by telephone if the patient could not attend consultations. Clinical symptom status was evaluated at baseline using the NYHA classification system for all patients. The survivors were also assessed 6 months after TAVI, during the consultation. Each patient underwent a transthoracic echocardiography at baseline, prior to discharge, and at 6-month follow-up. Echocardiographic examinations were all performed in our echocardiography laboratory by experienced sonographers, with the results stored on digital workstations (EchoPAC PC, GE Vingmed Ultrasound SA). Left-ventricular volumes and ejection fraction were calculated using the biplane disk method (modified Simpson's rule). The degree of aortic valve stenosis was evaluated on the basis of the mean aortic valve gradient, calculated using continuous-wave Doppler and a continuity equation-based assessment of the aortic valve area. The degree of calcification of the aortic valve was scored as follows: 1, no calcification; 2, mildly calcified (small isolated spots); 3, moderately calcified (multiple larger spots) and 4, heavily calcified (extensive thickening and calcification of all cusps).[21]

The severity of preprocedural aortic valve regurgitation (grades 0–4) and preprocedural or postprocedural mitral regurgitation (grades 0–4) was assessed according to current guidelines and based on the presence of mitral valve stenosis.[14 22–24] The degree of postprocedural aortic valve regurgitation (grades 0–4), including central or paravalvular leak, was assessed according to the VARC2 document recommendations.[19]

Statistical analysis

All statistical analyses were carried out using the Statel software (AdScience, Paris, France). Continuous variables were expressed as mean± SD, and categorical data values were expressed as percentages. Comparisons between the two groups were performed using the unpaired Student t test, Mann-Whitney test, χ^2 test or Fisher's exact test as appropriate. All statistical tests were two-sided, and a p value <0.05 was considered statistically significant.

RESULTS

Patient baseline characteristics

Of the 202 patients accepted for TAVI procedure between January 2011 and January 2013, four patients with a history of radiation therapy were excluded: two had undergone radiation therapy less than 10 years ago while the remaining two had received right chest radiation therapy for right breast cancer.

Thus, 198 patients were enrolled in our study. 19 patients (9.6%) were assigned to the radiation-induced valvular disease (RXT) group and 179 (90.4%) to the non-radiation-induced valvular disease (NRXT) group. Hodgkin's lymphoma was the most common reason for radiation therapy (42.5%), followed by left breast cancer (36.8%), and then lung cancer (10.5%). Mean age was lower in the RXT group than in the NRXT group (68.3 vs 82.5 years; p=0.00001) and traditional cardiovascular risk factors were less represented in the RXT group, with lower proportions of hypertension (47.3% vs 77.6%; p=0.0095), diabetes mellitus (5.3% vs 31.3%; p=0.017) and peripheral artery disease (10.5% vs 33.5%; p=0.04) observed. Renal function was significantly better in the RXT group, with an estimated glomerular filtration rate (according to the Cockcroft-Gault formula) of 107.2 vs 52.4 mL/mn in the NRXT group (p=0.00001).

The mean logistic Euroscore was low in the RXT group (7.1%±4.5%), whereas it exceeded 20% in the NRXT group (21.8%±12.5%), resulting in statistical difference between the two groups (p=0.00001). Mean Euroscore 2 was 2.7% in the RXT group and 10.3% in the NRXT group.

On the other hand, hostile thorax and porcelain aorta were more common in the RXT group (52.6% vs 28.5%; p=0.03; 63.2% vs 10.6%; p=0.00001, respectively). Baseline patient characteristics have been listed in table 1.

With regard to echocardiographic findings before TAVI, there was no statistical difference noted between the RXT and NRXT groups in terms of ejection fraction (57%±11.3% vs 53.8%±14.4%; p=0.36), mean aortic

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Table 1 Baseline patient characteristics

Variable	Total (n=198)	RXT (n=19)	NRXT (n=179)	p Value
Age (years)	81.1±8.4	68.3±11.7	82.5±6.6	<0.00001
Women	90 (45.4%)	12 (63.2%)	78 (43.6%)	0.1
Body mass index (kg/m^2)	27±5.6	25.9±5.1	27.1±5.7	0.37
NYHA 3 or 4 (%)	169 (85.3%)	14 (73.6%)	155 (86.6%)	0.17
Peripheral artery disease	62 (31.3%)	2 (10.5%)	60 (33.5%)	0.04
Previous heart failure	105 (53.0%)	8 (42.1%)	97 (54.1%)	0.32
Coronary artery disease	113 (57.1%)	9 (47.3%)	104 (58.1%)	0.37
Previous cerebrovascular event	11 (5.6%)	0 (0%)	11 (6.1%)	0.6
Diabetes mellitus	57 (28.8%)	1 (5.3%)	56 (31.3%)	0.017
Hypertension	148 (74.7%)	9 (47.3%)	139 (77.6%)	0.0095
Chronic pulmonary disease	75 (37.9%)	9 (47.3%)	66 (36.9%)	0.37
Logistic Euroscore (%)	20.3±12.7	7.1±4.5	21.8±12.5	<0.00 001
Estimated glomerular filtration rate (mL/min) with Cockroft formula	57.7±32.5	107.2±35.2	52.4±27.4	<0.00001
Previous cardiac surgery	53 (26.8%)	2 (10.5%)	51 (28.5%)	0.093
Hostile thorax	61 (30.1%)	10 (52.6%)	51 (28.5%)	0.03
Porcelain aorta	31 (15.7%)	12 (63.2%)	19 (10.6%)	<0.00001
History of atrial fibrillation	73 (36.9%)	2 (10.5%)	71 (39.7%)	0.012
Pacemaker	41 (20.7%)	4 (21%)	37 (20.6%)	1

Values are expressed as mean±SD or n (%).
NRXT, non-radiation-induced valvular disease; NYHA, New York Heart Association; RXT, radiation-induced valvular disease.

valve gradient (47.9±15.5 vs 45.9±15.8 mm Hg; p=0.92) or aortic valve area (0.60±0.18 vs 0.68±0.23 cm^2; p=0.22). On the other hand, mitral valve stenosis and aortic valve regurgitation were more frequently observed in the RXT group (57.9% vs 9.5%; p=0.00001 and 47.3% vs 16.9%; p=0.0038, respectively), though no statistical difference was found concerning systolic pulmonary artery pressure (41.7±9.7 vs 38.8±13.2 mm Hg; p=0.16).

With regard to the aortic valve calcium score, we found statistical difference between the two groups with a mean value of 2.4±0.7 in the RXT group and 3.2±0.4 in the NRXT group (p<0.0001).

Echographic findings at baseline have been outlined in table 2.

Procedural characteristics

The type of bioprosthesis and distribution of access routes did not significantly differ between the two groups. The implantation success rate was high in both groups, as shown by device implantation success composite end points of 94.7% and 93.9% in the RXT and NRXT groups, respectively (p=0.9). Only one device implantation failed in the RXT group due to left coronary obstruction by TAVI, requiring the procedure to be stopped. The mean duration of the procedure was 55±9 min in the RXT group and 59±12 min in the NRXT group (p=0.3).

Five patients from the NRXT group who were transferred to another institution were lost to follow-up.

Table 2 Baseline echographic variables

Variable	Total (n=198)	RXT (n=19)	NRXT (n=179)	p Value
Ejection fraction (%)	54.1±14.2	57±11.3	53.8±14.4	0.36
Ejection fraction <35%	24 (12.1%)	1 (5.3%)	23 (12.8%)	0.46
Aortic valve area (cm^2)	0.66±0.18	0.60±0.18	0.66±0.23	0.22
Mean gradient (mm Hg)	46.1±15.7	47.9±15.5	45.9±15.8	0.92
Aortic regurgitation ≥2	39 (19.8%)	9(47.3%)	30 (16.9%)	0.0038
Mitral regurgitation ≥2	50 (25.6%)	3 (15.7%)	47 (26.7%)	0.41
Mitral stenosis	28(14.2%)	11 (57.9%)	17 (9.5%)	<0.00001
Pulmonary artery pressure (mm Hg)	39.1±12.9	41.7±9.7	38.8±13.2	0.16
Pulmonary artery pressure ≥50 mm Hg	41 (20.7%)	6 (31.6%)	35 (19.5%)	0.24

Values are expressed as mean±SD or n (%).
NRXT, non-radiation-induced valvular disease; RXT, radiation-induced valvular disease.

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In terms of early complications, no statistical difference was noted between the two groups. The 30-day combined safety end point was, in fact, 83.3% in the RXT group and 75.6% in the NRXT group (p=0.57). Vascular and bleeding complications did not significantly differ. The following two major vascular complications occurred in the RXT group: a fistula between the aorta and right ventricle in one patient and a left carotid artery obstruction requiring a right-to-left carotid bypass in the other.

None of the patients in the RXT group presented with a disabling or non-disabling stroke, while 10 (5.81%) of those in the NRXT group suffered from cerebrovascular events, though this difference did not reach statistical significance (p=0.6). Procedural characteristics have been listed in table 3.

Six-month follow-up

All in all, 10 patients from the NRXT group were lost to follow-up at 6 months. The overall mortality at 6 months was significantly higher in the NRXT group than in the RXT group (18% vs 0%; p=0048). None of the patients in the RXT group died during follow-up. Cardiovascular mortality did not differ significantly between the two groups (RXT: 0%, NRXT: 11.4%, p=0.22). There was a trend towards better clinical efficacy in the RXT group, as shown by the 6-month clinical efficacy composite end point that reached 88.9% in this group, as compared with 69.5% in the NRXT group (p=0.08). The 6-month follow-up results have been presented in table 3.

Echocardiographic follow-up at 6 months revealed favourable haemodynamic results in both groups. No intravalvular or paravalvular aortic regurgitation exceeding grade 1 was observed in the RXT group, while this was reported in 9.8% of the patients in the NRXT group, with the difference not statistically significant (p=0.36). Echocardiographic findings at 6 months have been outlined in table 4.

DISCUSSION

In our study, patients exhibiting radiation-induced aortic stenosis represented almost 10% of the patients referred for TAVI, equating to approximately the same proportion found in national registries.[12 13 20]

First of all, our findings highlighted that this patient population exhibits characteristics that differ from those of patients with degenerative aortic valve stenosis. Patients with radiation-induced aortic valve stenosis do, in fact, present with less comorbidities, less cardiovascular risk factors and less peripheral vascular diseases, are younger, and their renal function is, for the greater part, unimpaired. These patients display a low logistic Euroscore that does not constitute a motivation for choosing TAVI instead of conventional surgery. This is in contrast to the population with degenerative aortic valve stenosis where a logistic Euroscore above 20% is the main reason for TAVI (49% of patients in our study). Our primary reasons for choosing the percutaneous procedure in patients with RXT included the presence of a porcelain aorta for approximately two-thirds of them, or a hostile thorax (skin burns, thoracic deformation, lung fibrosis or prior coronary artery bypass) for the remaining patients. On the other hand, these two reasons only applied to 15% of patients in the NRXT group. Baseline echocardiographic findings also revealed over half of the patients with radiation-induced aortic stenosis to be suffering from mitral valve stenosis, as compared with only 10% of patients with degenerative aortic valve stenosis. Interestingly, baseline aortic valve regurgitation, as detected by echocardiography, was more frequent in the RXT group, suggesting that valvular retraction is more marked in this population.

Our study revealed that patients with radiation-induced aortic valve stenosis had lower 6-month overall mortality following TAVI than those with degenerative aortic valve stenosis. According to our interpretation, this decreased postprocedural mortality is multifactorial. First of all, it may be accounted for by more favourable baseline patient characteristics (younger patients with less comorbidities), and second by lower native valve calcifications, leading to a lower risk of paravalvular leak and stroke. With regard to the aortic valve structure itself, we hypothesised that radiation-induced aortic valve stenosis might be less calcified than degenerative stenosis. In patients with prior radiation therapy, observations made during surgery revealed that aortic valve nodular thickening and fibrosis were at least in part responsible for stenosis, whereas calcification was the main form of valvular damage in the context of degenerative aortic valve stenosis.[25–28] In this sense, we have noticed in this study that the baseline echographic calcium score was lower in the RXT group. Recent studies have demonstrated that severe native valve calcifications (calcium mass score), as measured by a CT scan, were a significant predictor of a post-TAVI relevant paravalvular leak,[29] and more generally of 30-day major adverse cardiovascular events and 1-year mortality. As a matter of fact, patients with severe periprocedural complications (death, acute myocardial infarction or stroke) exhibited significantly more aortic valve calcium than those without any complications.[30] These studies concluded that such a parameter was extremely valuable for improving our ability to select and risk stratify candidates for TAVI. This parameter did not attain statistical significance in our study, most likely due to the small sample size of the RXT group. Nevertheless, the RXT patients suffered no postprocedural stroke, and no significant paravalvular aortic regurgitation was revealed on the 6-month echocardiography examination.

Our study also demonstrated that no specific complication appeared to be linked to the history of radiation therapy. The early postprocedural safety end point did not significantly differ between the two groups. Only one patient from the RXT group developed aortic root

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Table 3 Procedural and postprocedural results

Variable Periprocedural	Total (n=198)	RXT (n=19)	NRXT (n=179)	p Value
Type of bioprosthesis				
Medtronic corevalve	97 (49%)	9 (47.4%)	88 (49.2%)	0.88
Edwards sapien	98 (49.5%)	9 (47.4%)	89 (49.7%)	0.85
Implantation failure (no valve implanted)	3 (1.5%)	1 (5.3%)	2 (1.1%)	0.26
Access route				
Transfemoral	153 (77.3%)	17 (89.5%)	136 (76%)	0.25
Transapical	25 (12.6%)	1 (5.3%)	24 (13.4%)	0.48
Subclavian	13 (6.6%)	1 (5.3%)	12 (6.7%)	1
Transaortic	4 (2.0%)	0 (0%)	4 (2.2%)	1
Transcarotid	3 (1.5%)	0 (0%)	3 (1.7%)	1
Device implantation success composite end point	186 (94%)	18 (94.7%)	168 (93.9%)	0.9
Postprocedural—30 days	**(n=190)**	**(n=18)**	**(n=172)**	
30-day mortality	20 (10.5%)	0 (0%)	20 (11.6%)	0.23
CV mortality	13 (6.8%)	0 (0%)	13 (7.6%)	0.62
Non-CV mortality	7 (3.7%)	0 (0%)	7 (4.1%)	1
Early safety composite end point	145 (76.3%)	15 (83.3%)	130 (75.6%)	0.57
Stroke (all types)	10 (5.3%)	0 (0%)	10 (5.81%)	0.6
Life-threatening or major bleeding	23 (12.1%)	0 (0%)	23 (13.4%)	0.14
Major vascular complication	12 (6.3%)	2 (11.1%)	10 (5.8%)	0.32
Acute kidney injury	21 (11.1%)	1 (5.6%)	20 (11.6%)	0.7
Minor vascular complication	17 (8.9%)	3 (16.7%)	14 (8.1%)	0.21
Minor bleeding	21 (11.1%)	2 (11.1%)	19 (11%)	1
New pacemaker implantation	36 (18.9%)	5 (27.8%)	31 (18%)	0.34
Postprocedural—6 months				
6-month mortality	30/185 (16.2%)	0 (0%)	30/167 (18%)	0.048
CV mortality	19/185 (10.3%)	0 (0%)	19/167 (11.4%)	0.22
Non-CV mortality	11/185 (5.9%)	0 (0%)	11/167 (6.6%)	0.6
6-month clinical efficacy composite end point	132/185 (71.3%)	16 (88.9%)	116/167 (69.5%)	0.083
NYHA class 3 or 4 at 6 months	23/155 (14.8%)	2 (11.1%)	21/137 (15.3%)	1
Rehospitalisation for valve-related symptoms	28/155 (18.1%)	2 (11.1%)	26/137 (19%)	0.53

Values are expressed as mean±SD or n (%).
CV, cardiovascular; NRXT, non-radiation-induced valvular disease; NYHA, New York Heart Association; RXT, radiation-induced valvular disease.

damage (aorta-right ventricle fistula), which was similar to a small aortic root dissection. This severe but rare complication is not specific to irradiated patients and may occur in any context.[31]

Lastly, this study proved TAVI capable of achieving high clinical effectiveness in radiation-induced valvular disease, as demonstrated by the statistically significant trend of its increased clinical efficacy observed in the RXT group compared to that of the NRXT group. Close to 90% of patients were categorised as NYHA Class 1 or 2 at 6-month follow-up, with no need for a valve-related hospitalisation. This is an interesting result, given that 73% of the patients in the RXT group also exhibited mitral valve stenosis, or at least moderate mitral valve

Table 4 Echographic findings at 6 months

Variable	Total	RXT	NRXT	p Value
Ejection fraction (%)	59.1±11.3	58±12.5	59.3±11.3	0.67
Ejection fraction <35%	5/141 (3.5%)	0/18 (0%)	5/123 (4.1%)	1
Aortic valve area (cm^2)	1.63±0.39	1.58±0.26	1.64±0.41	0.77
Mean gradient (mm Hg)	9.8±5.3	8.9±3.9	10±5.4	0.55
Aortic regurgitation ≥2	12/141 (8.5%)	0/18 (0%)	12/123 (9.8%)	0.36
Mitral regurgitation ≥2	27/141 (19.1%)	2/18 (11.1%)	25/123 (20.3%)	0.53
Mitral stenosis	24/141 (17.0%)	10/18 (55.6%)	14/123 (11.4%)	0.00006
Pulmonary artery pressure (mm Hg)	39.2±13.1	36.8±11.4	40.2±14.5	0.44
Pulmonary artery pressure ≥50 mm Hg	31/138 (22.5%)	4/18 (22.2%)	27/120 (22.5%)	1

NRXT, non-radiation-induced valvular disease; RXT, radiation-induced valvular disease.

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regurgitation associated with aortic valve stenosis. The clinical impact of associated mitral valve disease seems to be lower than that of advanced age and comorbidities.

Study limitations

The main limitation of our study was the small size of the RXT group compared with the population of implanted patients. A larger multicentre study, along with a longer follow-up, would be necessary to confirm our results. Nevertheless, we obtained significant results regarding 6-month mortality.

Another limitation was the difficulty we experienced in unequivocally correlating aortic valve stenosis with prior radiation exposure for patients in the RXT group. As it is, there were no truly specific echocardiographic signs, and we can only assume that aortic valve stenosis was linked to radiation damage.

An additional limitation was that the CT scan calcium score could not be measured at the end of the study, as the required specific CT imaging was not performed systematically. Further investigations would be necessary to compare the CT scan calcium score between radiation-induced and degenerative aortic valve stenosis.

CONCLUSION

In patients suffering from radiation-induced aortic valve stenosis and contraindicated for conventional surgery, TAVI appears to be a highly promising procedure showing high feasibility, no specific early complications, favourable postprocedural haemodynamic results evaluated by echocardiography, and lower mid-term mortality compared with patients with degenerative aortic valve stenosis. TAVI demonstrated high clinical effectiveness, with more than 85% of patients categorised as NYHA class 1 or 2 at 6 months and with no need for valve-related rehospitalisation.

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