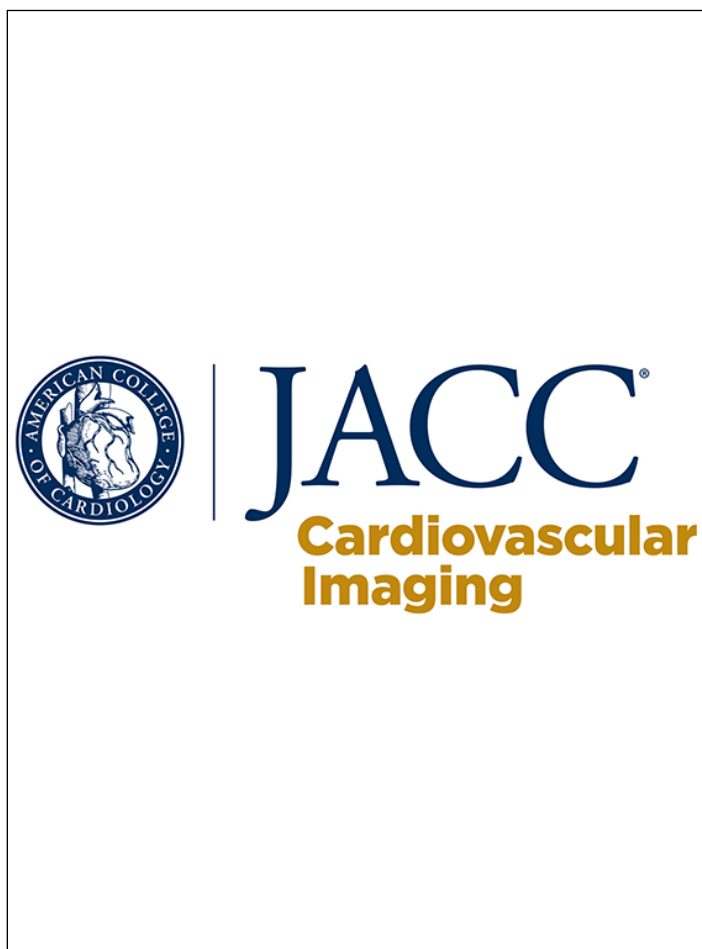


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representing deformation of myofibers during systole, is more reproducible and has previously been shown to provide superior risk prediction compared with LVEF in patients with both symptomatic and asymptomatic severe AS (3).

The rationale for aortic valve intervention in patients with moderate AS and LV dysfunction stems from the high event rate in these patients. Our study shows that patients with the highest risk for mortality are those with more abnormal GLS. The TAVR UNLOAD (Transcatheter Aortic Valve Replacement to Unload the Left Ventricle in Patients With Advanced Heart Failure) study is a randomized study investigating whether symptomatic patients with moderate AS and LVEF <50% benefit from TAVR compared with medical therapy (4). The hypothesis is that relieving the excess afterload of moderate AS in patients with LV impairment may alleviate symptoms and improve prognosis. A hypothesis generated from our data is that intervention may more likely benefit those patients at greatest risk with more abnormal GLS.

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Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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: Cardiovascular Imaging* [author instructions page](#).

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Myocardial Function in Patients With Radiation-Associated Aortic Stenosis Undergoing Transcatheter Aortic Valve Replacement



A Layer-Specific Strain Analysis Study

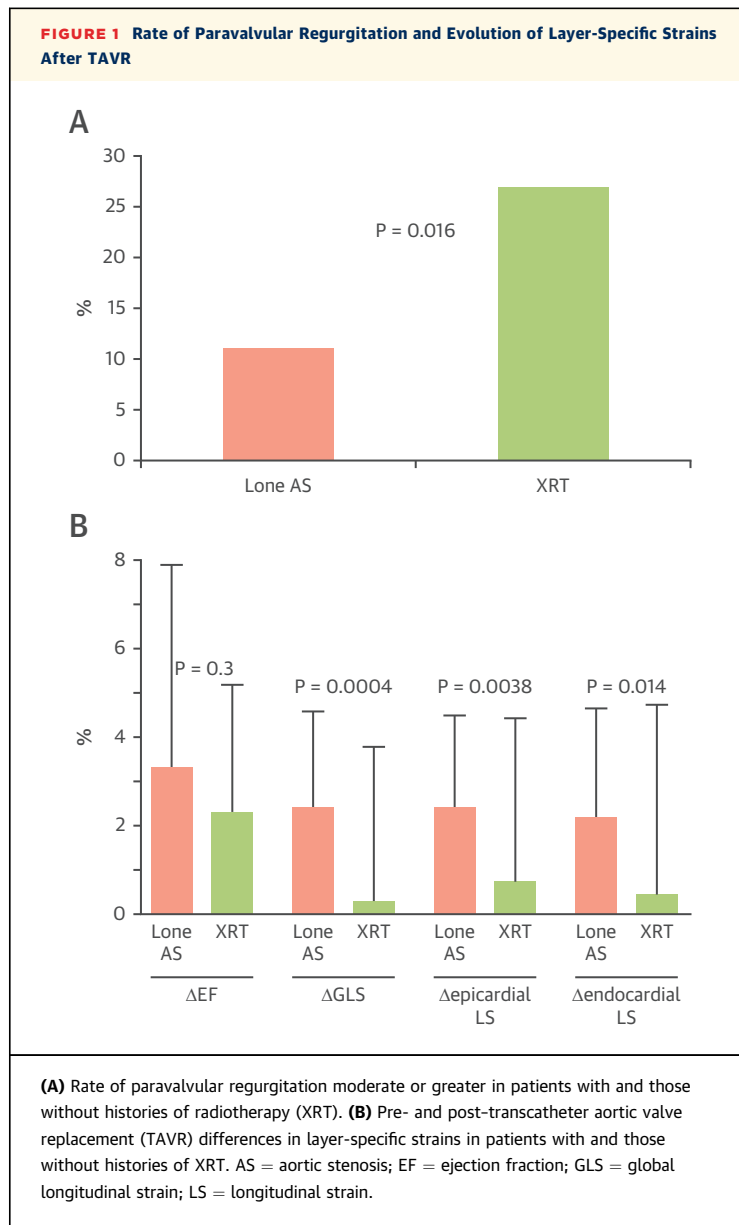
Patients with aortic stenosis (AS) and prior mediastinal radiotherapy (XRT) represent a challenging group (1-3). The detrimental effects due to the pressure overload associated with AS may be compounded by the presence of radiation heart disease. Echocardiographic speckle-tracking strain analysis can reliably estimate left ventricular (LV) systolic function and the subtle changes in LV performance after transcatheter aortic valve replacement (TAVR) (4). Because of the different vulnerability to pressure overload of the 3 myocardial layers, multilayer strain analysis can better characterize the extent of damage in AS (3). No studies have assessed the effect of XRT on myocardial function in patients with AS and whether elimination of AS may lead to improvement of LV systolic function. The aim of the present retrospective study was to investigate the impact of prior XRT on layer-specific strains and on post-TAVR early outcomes and recovery of myocardial function in patients with AS.

Of 227 patients with severe AS (aortic valve area ≤ 0.6 cm²/m²) who underwent TAVR between January 2013 and February 2018, 58 patients were excluded because of suboptimal quality of speckle-tracking image analysis, unclear radiation status, nonsinus rhythm, or valve-in-valve TAVR. The study was approved by the university hospital local ethics committee of Liège, Belgium.

Of the remaining 169 patients (Society of Thoracic Surgeons risk score $6.9 \pm 4.1\%$), 33 (20%) had histories of XRT. All TAVR procedures were performed with CoreValve self-expandable biologic prostheses (Medtronic, Minneapolis, Minnesota) via the transfemoral (n = 146) or transaxillary (n = 23) approach. Clinical endpoints were independently adjudicated according to the Valve Academic Research Consortium-2 criteria. Post-TAVR echocardiographic assessment was performed immediately before discharge and at 6 ± 1.5 month follow-up.

Patients with XRT did not differ from those with lone AS in terms of clinical data (age, sex, cardiovascular risk factors, presence of cardiovascular disease, baseline brain natriuretic peptide level) and baseline conventional echocardiography data (aortic valve area and pressure gradients) except for mitral calcifications (69% vs. 27%; $p < 0.001$) and stenosis (greater than mild, 15% vs. 3.6%; $p < 0.035$). Five patients (15%) in the XRT group presented with porcelain aorta ($p < 0.05$). ST2 level was significantly higher in patients with XRT ($p = 0.026$). Conversely to LV ejection fraction (LVEF) ($53 \pm 11\%$ vs. $56 \pm 11\%$; $p = 0.26$), longitudinal strains (LS) (epicardial LS $13.8 \pm 4.2\%$ vs. $12.2 \pm 4.04\%$ [$p = 0.04$], endocardial LS $18.04 \pm 5.5\%$ vs. $15.8 \pm 4.9\%$ [$p = 0.036$], and global LS $15.6 \pm 4.7\%$ vs. $14.1 \pm 4.2\%$ [$p = 0.07$]) were significantly decreased in patients with XRT. The rates of stroke (1 [0.7%] vs. 3 [9%]; $p = 0.024$) and delirium (5 [3.7%] vs. 7 [21%]; $p = 0.0023$) after TAVR were higher in patients with XRT, whereas in-hospital death (11 [8.1%] vs. 2 [6.1%]; $p = 0.51$) and major vascular complications (12 [8.9%] vs. 6 [18%]; $p = 0.11$) were similarly distributed between groups. The rate of paravalvular aortic regurgitation was also higher in patients with histories of XRT after TAVR (15 [11%] vs. 9 [27%] for greater than moderate; $p = 0.016$) (Figure 1A). Follow-up echocardiography was performed in 103 patients (30 of 33 [91%] of the XRT group). At follow-up, post-TAVR LV systolic function had improved significantly, with increases in LVEF, transmural global LS, and epicardial and endocardial LS ($p < 0.05$ for all). However, except for LVEF, the rate of change was significant only in patients without histories of XRT (Δ LVEF $3.3 \pm 4.6\%$ vs. $2.3 \pm 2.9\%$ [$p = 0.30$], Δ global LS $2.4 \pm 2.19\%$ vs. $0.29 \pm 3.5\%$ [$p = 0.0004$], Δ epicardial LS $2.4 \pm 2.1\%$ vs. $0.73 \pm 3.7\%$ [$p = 0.0038$], and Δ endocardial LS $2.16 \pm 2.5\%$ vs. $0.44 \pm 4.3\%$ [$p = 0.014$]) (Figure 1B).

Patients with histories of chest radiation for cancer and severe symptomatic AS have more marked impairment of LV systolic function than those with lone AS. Such alteration mainly concerns a decrease in longitudinal function as assessed by layer-specific strains and is underestimated by the study of LVEF. After TAVR, recovery of heart function is better in patients with lone AS. Conversely, in the presence of radiation cardiomyopathy, myocardial recovery is significantly impaired, with no post-procedural improvement in LS. History of chest radiation is associated with more paravalvular aortic regurgitation and may increase the risk for neurologic events during the hospital stay. A larger cohort of patients, along with longer follow-up, would be necessary to



evaluate the impact of our observations on long-term outcomes.

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Please note: Drs. Martinez and Cicenía contributed equally to this work and are joint first authors. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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: Cardiovascular Imaging* author instructions page.

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Adding Alirocumab to Rosuvastatin Helps Reduce the Vulnerability of Thin-Cap Fibroatheroma

An ALTAIR Trial Report



Large randomized controlled trials demonstrated that adding anti-protein convertase subtilisin/kexin type 9 (PCSK9) inhibitors to statins improved clinical outcomes. Compared with statin monotherapy, the use of PCSK9 inhibitors with statins significantly reduced the incidence of acute myocardial infarction, which can result from coronary plaque destabilization. However, how vulnerable plaque is influenced by more aggressive lipid-lowering therapy with

PCSK9 inhibitors plus statins remains unclear. Therefore, we designed the ALTAIR (Alirocumab for Thin-Cap Fibroatheroma in Patients With Coronary Artery Disease Estimated by Optical Coherence Tomography) study to assess the effect of adding the PCSK9 inhibitor alirocumab to rosuvastatin in patients with thin-cap fibroatheroma who underwent coronary stent implantation.

ALTAIR is an open-label, prospective, randomized, single-center study enrolling 24 patients (12 per group) with low-density lipoprotein cholesterol (LDL-C) levels >70 mg/dl despite statin treatment, randomized to either the alirocumab group (alirocumab 75 mg every 2 weeks and 10 mg/dl rosuvastatin) or the standard-of-care group (10 mg/dl rosuvastatin). The study protocol was approved by the Institutional Review Board of Kobe University Hospital. Optical coherence tomography (OCT) and blood sample analyses (serum LDL-C, matrix metalloproteinase 9, high-sensitivity C-reactive protein, interleukin-6, and vascular cell adhesion molecule-1 levels) were performed at baseline and at 36 weeks. The primary endpoint was the increase in fibrous cap thickness (FCT). Baseline and post-treatment OCT was analyzed at an independent imaging core laboratory (Kobe University Core Analysis Laboratory, Kobe, Japan) blinded to treatment group allocation (1). The fibrous cap was identified as a signal-rich band overlying the lipid core. In each patient, the minimum thickness of the fibrous-cap, defined as the thickness of the signal-rich layer overlying the lipid-rich plaque (2), was measured at the thinnest part of the fibrous cap in 3 candidate frames selected upon visual screening of all contiguous frames; the smallest of the 3 values was retained.

Baseline characteristics and laboratory parameters did not differ between the groups. Rosuvastatin and alirocumab were not interrupted, and concomitant use of ezetimibe or polyunsaturated fatty acids was not started or altered during the study period. At 36 weeks, serum LDL-C levels were significantly lower in the alirocumab group than in the standard-of-care group (27 mg/dl [23 to 55 mg/dl] vs. 71 mg/dl [64 to 77 mg/dl]; $p < 0.0001$), with a significantly greater percentage change in the alirocumab group (-64.6% [-71.2% to -60.2%] vs. -17.4% [-28.7% to 1.6%]; $p < 0.0001$). The percentage change in matrix metalloproteinase 9 was significantly greater in the alirocumab group than in the standard-of-care group (-39.9% [-50.2% to -11.0%] vs. -15.7% [-26.6% to 30.0%]; $p = 0.024$).

There was no difference between the groups regarding findings on baseline OCT. Although FCT