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Letters

RESEARCH LETTER

Predictive Value of CTA-Derived Extracellular Volume for Pacemaker Implantation Post-TAVR in Low-Flow Low-Gradient Aortic Stenosis

Transcatheter aortic valve replacement (TAVR) has quickly revolutionized the management paradigm of aortic stenosis (AS). Nevertheless, the prevalence of permanent pacemaker implantation (PPM) following TAVR ranges between 9% and 26%.[1] Post-TAVR PPM risk factors include preprocedural conduction abnormalities such as right bundle branch block (RBBB), deep valve implantation, larger device size, and a high number of comorbidities.

Extracellular volume fraction (ECV), a marker of interstitial fibrosis, is associated with cardiac dysfunction and increased risk of death and heart failure hospitalization after TAVR.[2] Although traditionally measured by magnetic resonance imaging, iodinated contrast agents and an equilibrium technique can be used for ECV quantification by computed tomography angiography (CTA). CTA-derived ECV accurately reflects extracellular matrix and replacement fibrosis. We evaluated the association between myocardial fibrosis assessed by CTA-derived ECV and PPM in patients with low-flow, low-gradient (LFLG) AS who underwent TAVR.

The current study was approved by the Cedars-Sinai Medical Center Institutional Review Board. Using a dual-source computed tomography (CT) platform (SOMATOM Definition Flash, Siemens Healthineers), precontrast and delayed postcontrast at 3 to 5 minutes after contrast injection, prospectively electrocardiogram-triggered acquisitions were performed at diastole with a tube voltage of 120 kVp. CT attenuation in HU was measured in regions of interest in the septum and lateral wall in the mid left ventricle and in the left ventricle cavity for blood pool attenuation. Myocardial ECV was calculated as: $ECV_{CT} = (1 - \text{hematocrit}) \times (\Delta HU_{myocardium}/\Delta HU_{blood})$, where $\Delta HU_{myocardium}$ and ΔHU_{blood} are given by $(HU_{delayed} - HU_{early})$. Mean ECV was calculated as: (septal ECV + lateral ECV)/2. Backward stepwise multivariable logistic regression analysis, including age, sex, prior history of myocardial infarction, Society of Thoracic Surgeons score, left ventricular ejection fraction, aortic valve (AV) mean pressure gradient, AV calcium score, baseline 1′ or 2′ atrioventricular block, left bundle branch block (LBBB), RBBB, new-onset LBBB after TAVR, TAVR valve type and size, and mean ECV, was performed. A P value cutoff of 0.1 was used for initial selection in stepwise regression with backward elimination.

From a total of 208 patients with LFLG who underwent TAVR from August 2016 to December 2017 at a single institution, 122 patients (age 80 ± 10 years, 73 [60%] male) without prior PPM who underwent precontrast and delayed postcontrast CT at the time of their CTA for procedural planning of TAVR were included in the study. PPM was required in 15 patients (9.3%; median 1 day [range 0-7 days]; 14 patients due to complete heart block and 1 patient due to sinus pause) after the TAVR procedure. New LBBB after TAVR occurred in 7 patients but was not the reason for PPM. There was no significant difference in age or frequency of risk factors between groups. Patients with prior myocardial infarction tended to have higher ECV compared with those without (34.3 ± 11.7 vs 31.2 ± 8.6; $P = 0.204$). PPM vs non-PPM patients also had similar baseline ejection fraction, aortic valvular pressure gradient, valvular area, and valvular calcium. There were significant differences in the prevalence of baseline RBBB (53.3% vs 8.4%; $P < 0.001$) and first- or second-degree atrioventricular block (33.3% vs 13.1%; $P = 0.043$). The PPM rate tended to be higher in patients with CoreValve compared with Sapien (21.7% vs 10.1%; $P = 0.126$). Mean valve size was larger in the PPM group vs the non-PPM group (27.9 ± 2.8 vs 26.1 ± 2.6; $P = 0.013$). Mean ECV was elevated in the PPM group vs the non-PPM group (38.2% ± 11.8% vs 30.7% ± 0.8%; $P = 0.003$). In multivariable analysis (**Table 1**), baseline RBBB (OR: 21.34 [95% CI: 4.64-98.21]; $P < 0.001$) and ECV (OR: 1.10 [95% CI: 1.03-1.17]; $P = 0.007$) are independent predictors for post-TAVR PPM.

Myocardial and interstitial fibrosis is believed to disrupt conduction signal generation and anisotropic conduction, inducing slowing of electrical conduction velocities. In patients with sinus node dysfunction, sinoatrial nodal fibrosis is frequently evident in

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TABLE 1 Predictors of PPM Insertion After TAVR in LFLG AS Patients

	Univariable			Multivariable		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age	1.02	0.96-1.07	0.575			
Male	2.00	0.60-6.67	0.262			
Body mass index	0.99	0.91-1.09	0.948			
Prior myocardial infarction	1.02	0.21-5.02	0.979			
STS score	1.06	0.99-1.13	0.082			
LVEF (per 5%)	1.02	0.88-1.80	0.812			
AV mean PG	0.99	0.92-1.06	0.715			
AV calcium (log transformed)	0.85	0.42-1.75	0.660			
1° or 2° AV block	3.32	0.99-11.16	0.052			
LBBB	0.52	0.63-4.26	0.539			
RBBB	12.4	3.66-42.27	<0.001	21.34	4.64-98.21	<0.001
New-onset LBBB	1.20	0.14-10.7	0.869			
CoreValve (vs Edward Sapien)	2.47	0.75-8.10	0.135			
TAVR size (per 3 mm)	2.45	1.08-5.58	0.032	2.33	0.88-6.15	0.089
Mean ECV, %	1.09	1.03-1.53	0.005	1.10	1.03-1.17	0.007
Septal ECV, %	1.06	1.01-1.12	0.042			
Lateral ECV, %	1.06	1.01-1.10	0.009			

AV = aortic valve; ECV = extracellular volume; LBBB = left bundle branch block; LFLG = low-flow, low-gradient; LVEF = left ventricular ejection fraction; PG = pressure gradient; PPM = permanent pacemaker insertion; RBBB = right bundle branch block; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

pathologic specimens. Kawara et al[3] examined the presence of activation delay caused by interstitial fibrosis in hypertrophic cardiomyopathy. Moreover, the impact of interstitial and replacement fibrosis is notable in cardiac sarcoidosis: patients with evidence of interstitial fibrosis exhibited a higher event rate, including need for PPM.[4]

In cases of severe AS, chronic pressure overload in the myocardium results in an advanced state of extracellular expansion and replacement fibrosis of the conduction system. Other pre-existing factors such as aging and atherosclerosis can exacerbate cardiac conduction defects commonly observed in patients with AS.[5] In our study, the independent association between CTA-derived ECV and PPM indicates the iatrogenic injury from TAVR on fibrotic myocardium, which can lead to reduced resistance against mechanical forces or fibrosis within the conducting system, may result in an increased likelihood of PPM. Therefore, ECV may serve as a potential imaging marker indicative of a compromised conduction system prone to advanced conduction abnormalities necessitating PPM following TAVR. Future studies are warranted to explore potential mechanisms that can elucidate the findings of our current study.

A relatively small sample at a single center and restricted to a subset of AS patients with LFLG limits generalizability of our finding. In addition, the potential for unmeasured confounding factor including coexisting myocardial disease or procedural factors might have influenced the need for PPM in this study.

Increased CTA-derived ECV is independently associated with post-TAVR PPM. ECV quantification, which can be easily performed during routine pre-procedural CTA with an additional delayed scan, may thus improve the identification of patients at high risk of post-TAVR PPM.

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