Is Low CACs Really Different From Zero…

A Report From the CACTI Study

The use of small Agatston scores to indicate the presence of coronary artery calcium (CAC) as a marker of atherosclerosis is controversial and may depend on the study population. Two studies found increased associations with all-cause mortality and incident cardiovascular events with low CAC (>0 to 10 AU) compared with none; however, the study populations were older (mean ages of 58 and 54 years, respectively) (1,2). In contrast, another study found no significant association between low CAC (>0 to 10 AU) and incident cardiovascular events in a younger population (mean age 43 years) (3). The significance of low CAC scores in younger populations is unclear. Therefore, we examined whether progression of CAC over 6 years was increased in participants with low CAC compared with individuals with zero CAC in the CACTI (Coronary Artery Calcification in Type 1 Diabetes) study. The CACTI study is a prospective cohort study of the prevalence and progression of CAC in a young population of adults with and without type 1 diabetes mellitus (T1DM).

Study participants were 19 to 56 years of age with T1DM (n = 442) or without diabetes (n = 506) who enrolled in the CACTI study in 2000 to 2002 and completed follow-up after 6 years. All participants reported no diagnosis of cardiovascular disease and were asymptomatic at enrollment. The protocol was reviewed and approved by the Colorado Multiple Institutional Review Board, and informed consent was obtained. The study has been described in detail elsewhere (4).

CAC was obtained using an ultrafast Imatron C-150XL electron beam computed tomography scanner (Imatron, San Francisco, California). Progression was defined as an increase in volume of CAC between baseline and follow-up of ≥2.5 square root-transformed units (5).

Baseline CAC was categorized as 0, >0 to 10, >10 to 100, and >100 AU. Multivariate logistic regression was used to determine the association of baseline CAC on progression of CAC. All analyses were performed using SAS/STAT software version 9.3 (SAS Institute, Inc., Cary, North Carolina).

The study population was relatively young at baseline, with 48.8% of participants <40 years of age. Participants with T1DM were significantly younger than participants without diabetes (37 vs. 41 years; p < 0.001), had lower total cholesterol (172 vs. 194 mg/dl; p < 0.001), lower low-density lipoprotein cholesterol (98 mg/dl vs. 117 mg/dl; p < 0.001), higher systolic blood pressure (117 mm Hg vs. 115 mm Hg; p < 0.001), and a higher urine albumin creatinine ratio (71 µg/mg vs. 9 µg/mg;...
Mechanism of Aortic Valve Opening: Beyond the Pressure Gradient

Regurgitation across cardiac valves is driven by the presence and size of a regurgitant orifice and transvalvular pressure gradient. Thus, under normal circulatory conditions, aortic regurgitation is a diastolic phenomenon that occurs in the setting of an incompetent aortic valve when pressure in the aorta exceeds that of the left ventricle. The paradoxical phenomenon of systolic aortic regurgitation (SAR) has been previously identified in patients with arrhythmias, after palliative operations for congenital heart disease, and in patients with left ventricular assist devices (LVADs) (1–3).

Herein, we describe a series of 3 cases of SAR in the setting of continuous flow LVAD (2 patients with the HeartMate II device [Thoratec Corporation, Pleasanton, California]), and 1 patient with a HeartWare device (HeartWare International Inc., Framingham, Massachusetts). Parasternal echocardiographic imaging in the first patient demonstrated trivial systolic aortic valve movement while purely SAR appears during every heart cycle (Fig. 1A, Online Video 1). There was no regurgitation during diastole as evidenced by both parasternal color M-mode (Fig. 1B, arrows) and pulsed-wave Doppler of the outflow tract just below the aortic valve plane (Fig. 1C, arrows showing SAR but not diastolic aortic regurgitation). In the second patient, aortic regurgitation was trivial but continuous (Fig. 1D, Online Video 2); color M-mode captured only SAR (Fig. 1E, arrows). There was continuous regurgitation on pulsed-wave Doppler, with reduced gradient (lower velocity) but increased Doppler density in late systole (Fig. 1F, arrows). Finally, the third patient had continuous aortic regurgitation, with significant increase in aortic regurgitation vena contracta during systole (Figs. 1G and 1H, Online Video 3).

SAR occurred in all 3 patients long after device implanta-tion (130, 134, and 438 days, respectively). There was no evidence of device malfunction according to clinical (no change in effort ability) and echocardiographic (neutral position of the interventricular septum, laminar flow with normal velocities in inflow and outflow cannulae) criteria. Cardiac output (estimated from the right ventricular outflow tract diameter and time-velocity integral) was at the low end of normal (4.8, 4.9, and 5.3 l/min, respectively) and was unchanged compared with previous echocardiographic studies.

Presence of SAR in this series of patients with LVADs offers unique insights into valvular physiology. In all patients, systolic increase in left ventricular pressure was demonstrated by mitral valve closure (Online Videos 4, 5 and 6). Conversely, aortic systolic pressure clearly exceeded ventricular pressure, a fact demonstrated by the presence of SAR at the time of systolic opening of the aortic valve. Given that left ventricular pressure cannot induce conventional “valvular opening,” a mechanism other than pressure gradient must be involved.