JACC: CARDIOVASCULAR IMAGING
VOL. 10, NO. 11, 2017

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
https://doi.org/10.1016/j.jcmg.2017.10.003

iVIEW

EDITOR'S PAGE

ECV for Patients With Aortic Stenosis

Which Patient Will Benefit?

Raymond Y. Kwong, MD, MPH,[a] Christopher M. Kramer, MD,[b] Y. Chandrashekhar, MD[c]

Progressive and advanced wear and tear of the aortic valve (AV) leads to accumulation of calcification that can eventually result in aortic stenosis (AS). The stenotic AV imposes chronic pressure overload onto the left ventricle, which leads to left ventricular (LV) remodeling (initial LV cellular hypertrophy and increased wall thickness and later deposition of interstitial fibrosis). The increased wall thickness is initially compensatory, allowing normalization of wall stress so that LV contractile function can be maintained. However, the increased myocardial cell mass and wall thickness lead to impaired early diastolic relaxation, decreased LV compliance, and resultant diastolic dysfunction. As chronic pressure overload continues beyond the compensatory reserve of the left ventricle, interstitial fibrosis becomes extensive, and ventricular stiffness progressively worsens. In many cases, despite relief of pressure gradient from AV replacement, concentric LV hypertrophy and myocardial fibrosis (to a lesser extent) will regress, but symptoms and markers of diastolic dysfunction often persist for years, denoting the importance of timely delivery of AV replacement. Finding that right moment before transition from protective myocardial compensation to adverse decompensation remains a holy grail for imaging in AS.

Current clinical decision making on the timing of AV replacement relies primarily on the echocardiographic severity of AS and patients' symptom status (1). The use of subjective reporting of symptoms is often nonspecific, life-style dependent, and limited by a short time window between the onset of symptoms and major cardiac events. The severity of diastolic dysfunction, perhaps the result of fibrosis, is the key surrogate of long-term patient mortality and morbidity and remains operative even after successful AV replacement (2). Yet currently, estimates of diastolic dysfunction from chronic AS pressure overload do not play a direct role in determining the timing of AV replacement. The reasons are multiple: the definition of diastolic dysfunction remains vague and incompletely understood given its inconsistent classification schemes, dependence on loading conditions affecting the technical robustness in its grading, and a deficiency of large-scale longitudinal data guiding its clinical use. With continual improvement in surgical AV replacement and the expanding role of transcatheter AV replacement, there is an urgent need to expand and tailor the selection of patients

From the [a]Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [b]Departments of Medicine and Radiology and the Cardiovascular Imaging Center, University of Virginia Health System, Charlottesville, Virginia; and the [c]University of Minnesota and VA Medical Center, Minneapolis, Minnesota. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

with AS who can benefit from either of these evolving treatment options.

Cardiac magnetic resonance, with its multiparametric information, is emerging as an important tool to understand the pathophysiology of AS and perhaps help time intervention. In this issue of *iJACC*, Chin et al. (3) shed more light on the benefits of using cardiac magnetic resonance for traditional as well as newer indexes (serial T1 mapping, extracellular volume [ECV], and extracellular volume index [iECV]) of cardiac structure and function in patients with AS. The investigators propose a new metric of global iECV by estimating the proportion of global LV mass index that belongs to the extracellular compartment. They found a progressive increase of iECV across patients with increasing severity of AS, and it predicted adverse cardiac remodeling (LV mass index, worse longitudinal shortening, and left atrial size) and correlated with traditional indexes of LV structure and biomarkers. Compared with iECV, ECV fraction did not achieve a significant association with the severity of AS (by either transvalvular gradient or AV area). The investigators conclude that iECV more fully characterizes the pathophysiologic myocardial derangement from AS-related chronic pressure overload compared with either ECV or LV mass index. They propose a new 3-group clinical strategy for the early detection of LV decompensation (normal myocardium, ECV expansion, and replacement fibrosis), with the goal of guiding the timing of AV replacement in patients with subclinical disease.

The application of this new marker, iECV, is intriguing given its quantitative capability, ease of calculation, and relevance to a vast number of cardiac conditions. iECV provides a footprint record of fibrosis from progressive wall stress from AS over time. iECV can provide adjunctive information to valvuloarterial impedance, which estimates instantaneous global LV afterload. Pressure overload expands both extracellular compartment and cell size. Indeed, by accounting for total LV mass, iECV may represent a more sensitive metric than ECV fraction in characterizing the global burden of extracellular expansion due to LV remodeling. Chin et al. (3) should be commended for their extensive work validating novel metrics against meaningful clinical markers of AS. As with any pilot study, this one too has limitations, and adequately powered studies with long follow-up comparing various strategies will be needed to inform clinical decisions. The most important questions in the management of patients with AS will need answers: which AS patients benefit from iECV to guide the timing of AV replacement, and whether it is incremental to the current practice guideline recommendations (4). Perhaps in a patient with severe AS without clear symptoms but with clear LV hypertrophy, abnormal iECV or late gadolinium enhancement without other confounding etiology should raise suspicion of subclinical fibrosis secondary to valvular obstruction and should warrant further investigation. However, the myocardial pattern of pathology in AS is variable (often multiple focal or diffuse) in response to pressure overload and can be the result of other coexisting cardiomyopathies, including coronary disease, which exists in 30% to 50% of patients with severe AS; this needs to be accounted for in future studies. Newer classification schemes based on sophisticated imaging have the promise to help in "early detection of subclinical ventricular decompensation" and may ultimately guide decisions regarding the timing of AV replacement; however, these should be introduced thoughtfully and validated robustly, lest we be let down once again, as Thomas Huxley would say, by a beautiful idea slayed by ugly facts.

ADDRESS FOR CORRESPONDENCE: Dr. Y. Chandrashekhar, University of Minnesota/VAMC, Division of Cardiology (Mail Code: 111c), 1 Veterans Drive, Minneapolis, Minnesota 55417. E-mail: shekh003@umn.edu.

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