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iREVIEW

STATE-OF-THE-ART PAPER

Left Atrial Reverse Remodeling

Mechanisms, Evaluation, and Clinical Significance

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CME Objective for This Article: After reading this article the reader should be able to: 1) evaluate LA remodeling and reverse remodeling of the left atrium using structural (volume) and functional metrics in the context of clinical scenarios; 2) compare the various noninvasive imaging modalities—echocardiography, cardiac CT and MR—in the evaluation of left atrial remodeling; and 3) understand the potential for cardiac imaging to evaluate atrial fibrosis.

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ABSTRACT

The left atrium is considered a biomarker for adverse cardiovascular outcomes, particularly in patients with left ventricular diastolic dysfunction and atrial fibrillation in whom left atrial (LA) enlargement is of prognostic importance. LA enlargement with a consequent decrease in LA function represents maladaptive structural and functional "remodeling" that in turn promotes electrical remodeling and a milieu conducive for incident atrial fibrillation. Medical and nonmedical interventions may arrest this pathophysiologic process to the extent that subsequent reverse remodeling results in a reduction in LA size and improvement in LA function. This review examines cellular and basic mechanisms involved in LA remodeling, evaluates the noninvasive techniques that can assess these changes, and examines potential mechanisms that may initiate reverse remodeling. (J Am Coll Cardiol Img 2017;10:65–77) © 2017 by the American College of Cardiology Foundation.

Evaluation of the left atrium as a cardiovascular biomarker (**Central Illustration**) has become increasingly important, particularly in 2 common clinical scenarios; namely, left ventricular (LV) diastolic dysfunction (1) and atrial fibrillation (AF) (2), both associated with left atrial (LA) enlargement. LV diastolic dysfunction is acknowledged to be the predominant pathophysiological mechanism in patients with heart failure with preserved ejection fraction and in hypertrophic and infiltrative cardiomyopathies. AF is the most common clinical arrhythmia, with evidence from the Framingham study to suggest there is a lifetime risk of 25% for the development of AF in individuals >40 years of age (3). Additionally, chronic cardiovascular conditions including systemic hypertension, ischemic heart disease, and heart failure cause LA enlargement and increase the risk of developing AF (4). Mitral valve disease, although less common, causes LA remodeling from pressure or volume overload (5). Timely intervention for patients with these conditions may arrest and perhaps reverse LA remodeling with a consequent reduction in LA size with improved function. This review examines cellular and basic mechanisms that are involved in LA remodeling, evaluates the noninvasive techniques that can assess these changes, and examines potential mechanisms that may initiate reverse remodeling.

LA REMODELING: ETIOLOGY AND MECHANISMS

Atrial remodeling is a time-dependent response of cardiac myocytes to varying "stressors" including electrical, mechanical, and metabolic stressors (6). Remodeling is a complex process that is poorly understood, but it is defined as a persistent change in LA size or function (2,7). In a broad clinical context, atrial remodeling is largely due to the development of rapid atrial tachyarrhythmias or consequent to alteration in atrial structure secondary to pressure or volume overload. Pressure and/or volume overload may result from a variety of causes including cardiomyopathies with consequent diastolic dysfunction, heart failure, or valvular heart disease. The magnitude of LA structural or functional alteration varies and is dependent on the type, severity, and duration of exposure to the varying external stressors. Additionally, some components of the LA alterations are reversible (adaptive) whereas others are permanent (maladaptive).

The process of atrial remodeling has been attributed to a variety of pathophysiologic processes (8). Interestingly, it appears that LA remodeling results in metabolic changes with a shift in energy source to fetal glycolysis via beta oxidation of fatty acids (9) with a consequent reduction in energy production. At a neurohormonal level, increases in atrial and brain natriuretic peptides (10,11), angiotensin II (Ang II) (12), transforming growth factor beta (13), and aldosterone (14) have been described. Additionally, Ang II, aldosterone, transforming growth factor beta, and platelet-derived growth factor (15) all promote atrial fibrosis. Systemic inflammation, mediated by C-reactive protein, interleukins, and cytokines may additionally contribute to the remodeling process (16,17).

Acute atrial remodeling that occurs within 1 week of exposure to stressors is often reversible (18,19).