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STATE-OF-THE-ART PAPER

Assessment of Myocardial Fibrosis With Cardiovascular Magnetic Resonance

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Diffuse interstitial or replacement myocardial fibrosis is a common feature of a broad variety of cardiomyopathies. Myocardial fibrosis leads to impaired cardiac diastolic and systolic function and is related to adverse cardiovascular events. Cardiovascular magnetic resonance (CMR) may uniquely characterize the extent of replacement fibrosis and may have prognostic value in various cardiomyopathies. Myocardial longitudinal relaxation time mapping is an emerging technique that could improve CMR's diagnostic accuracy, especially for interstitial diffuse myocardial fibrosis. As such, CMR could be integrated in the monitoring and therapeutic management of a large number of patients. This review summarizes the advantages and limitations of CMR for the assessment of myocardial fibrosis. (J Am Coll Cardiol 2011;57:891–903) © 2011 by the American College of Cardiology Foundation

One of the most common histological features of the failing heart is myocardial fibrosis. Replacement fibrosis, often present in the terminal stages of heart failure, has been reported in histopathological autopsy studies (1,2). The pathophysiological mechanisms that lead to this fibrosis are various, with some being acute, as in myocardial infarction (3), and others being progressive and potentially reversible, as in hypertensive cardiomyopathy (4). Myocardial fibrosis in animal and patient studies is associated with worsening ventricular systolic function, abnormal cardiac remodeling, and increased ventricular stiffness (5–7). In recent clinical studies, fibrosis has also been shown to be a major independent predictive factor of adverse cardiac outcome (8–12).

In therapeutic guidelines for heart failure due to various cardiomyopathies, there are no specific therapeutic strategies based on the tissue composition of the myocardial wall, either in the early or more advanced stages of disease. This lack of specific treatment might result in inappropriate therapies, which can lead to increased morbidity and additional financial burden to health care services (13). Lack of personalized treatment is also secondary to the absence of accurate clinical tools to precisely phenotype patients with heart disease.

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Recent reports have demonstrated the advantages of using cardiovascular magnetic resonance (CMR) for the noninvasive imaging of heart failure patients (14,15). CMR has been established as the reference imaging method for the assessment of cardiac anatomy and function by providing highly accurate and reproducible measures of both the left and right ventricles and also for the assessment of myocardial viability (16–18). The field of CMR is rapidly evolving with continuing technological progress and the recent development of applications that have further enhanced its capacity to characterize myocardial tissue. In this review, we focus on CMR characterization of the different types of myocardial fibrosis and its etiology through late gadolinium enhancement and myocardial longitudinal relaxation time (T_1) mapping.

Myocardial Fibrosis: Pathogenesis and Consequences

Fibrosis pathophysiology. In physiological conditions, the fibrillar collagen network is in intimate contact with all the different cell types of the myocardium and plays a critical role in the maintenance of ventricular shape, size, and function (Fig. 1).

Myocardial fibrosis, defined by a significant increase in the collagen volume fraction of myocardial tissue, is always present in end-stage heart failure (19). The distribution of myocardial fibrosis, however, varies according to the underlying pathology and accounts for discrepancies among different pathological reports in which only qualitative as opposed to quantitative measurements were made (19–22). The progressive accumulation of collagen accounts for a spectrum of ventricular dysfunctional processes that com-

Abbreviations and Acronyms

CMR = cardiovascular magnetic resonance

LGE = late gadolinium enhancement

LV = left ventricle

MOLLI = Modified Look-Locker Inversion Recovery

monly affect diastole first and subsequently involve systolic performance (5).

Subtypes of myocardial fibrosis. Different types of myocardial fibrosis have been reported according to the cardiomyopathic process (Fig. 1).

REACTIVE INTERSTITIAL FIBROSIS. The first type of fibrosis is interstitial reactive fibrosis with a diffuse distribution within the interstitium, but it can also be more specifically perivascular (23). This type of fibrosis has a progressive onset and follows the increase in collagen synthesis by myofibroblasts under the influence of different stimuli. It has mostly been described in hypertension and diabetes mellitus, where the activation of the renin-angiotensin aldosterone system, beta-adrenergic system, the excess of reactive oxygen species, and metabolic disturbances induced by hyperglycemia are major contributors (23–28) (Fig. 2). But this type of fibrosis is also present in the aging heart, in idiopathic dilated cardiomyopathy (2,21), and in left ventricular (LV) pressure-overload and volume-overload states induced by chronic aortic valve regurgitation and stenosis (29,30). It has

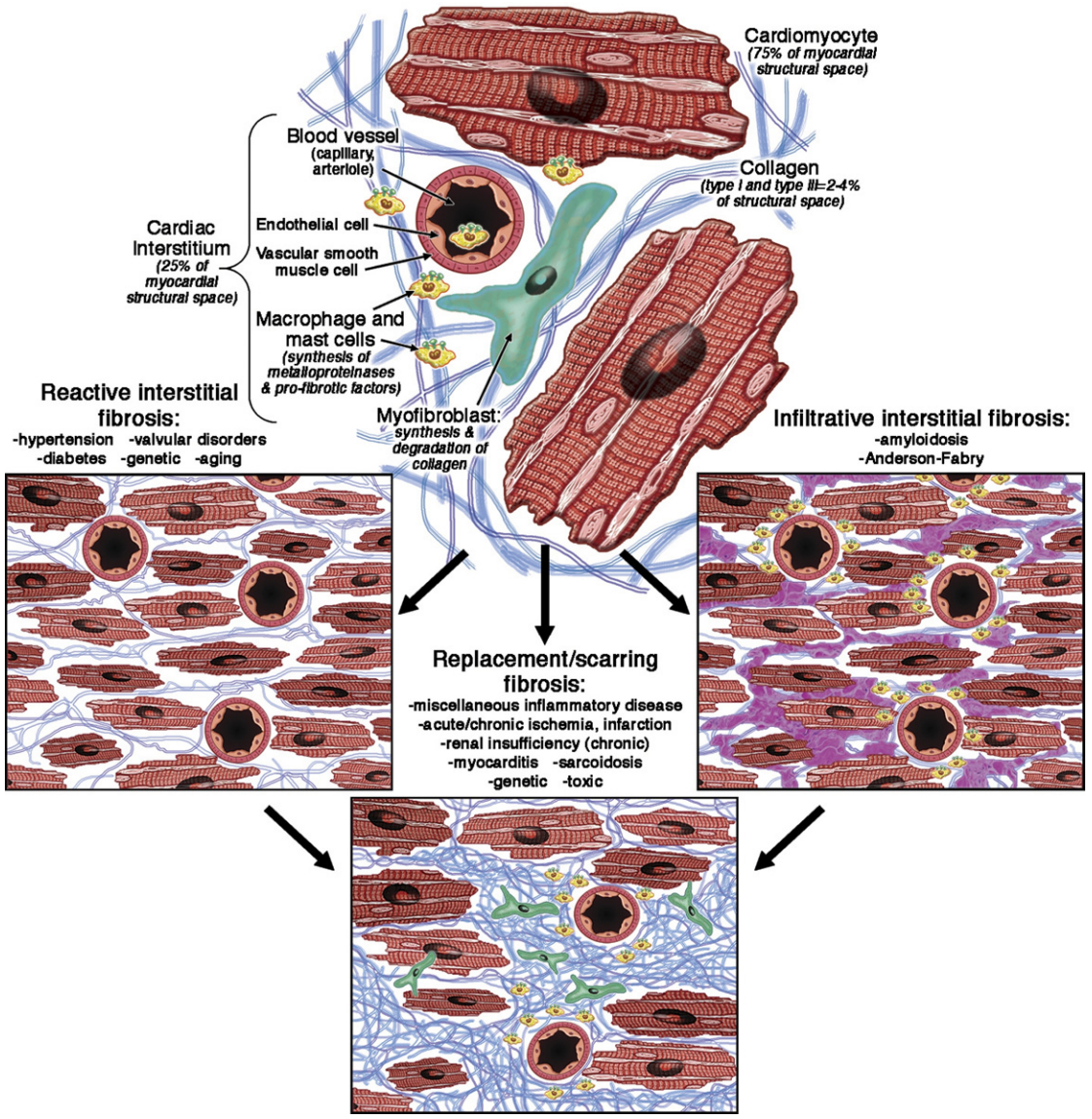

Figure 1 Etiophysiopathology of Myocardial Fibrosis

Myocardial fibrosis is a complex process that involves each cellular component of the myocardial tissue. The myocardial fibroblast has a central position in this process by increasing the production of collagen and other extracellular matrix components under the influence of various factors (renin-angiotensin system, myocyte apoptosis, pro-inflammatory cytokines, reactive oxygen species).