Tissue Characterization of the Myocardium

State of the Art Characterization by Magnetic Resonance and Computed Tomography Imaging

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KEYWORDS

• Characterization • Myocardium • Magnetic resonance • Computed tomography • T1 mapping
• Late gadolinium enhancement • Extracellular volume fraction

KEY POINTS

- Late gadolinium enhancement (LGE) is a simple, robust, well-validated method for the assessment of scar in acute and chronic myocardial infarction.
- LGE is useful for distinguishing between ischemic and nonischemic cardiomyopathy. Specific LGE patterns are seen in nonischemic cardiomyopathy.
- Patient studies using T1 mapping have varied in study, design, and acquisition sequences.
- Despite the differences in technique, a clear pattern that has been seen is that in cardiac disease postcontrast T1 times are shorter.
- Extracellular volume fraction measured with cardiac computed tomography represents a new approach to the clinical assessment of diffuse myocardial fibrosis by evaluating the distribution of iodinated contrast.

INTRODUCTION

Fibrosis is a feature of many cardiomyopathies and the failing heart and is a major independent predictor of adverse cardiac outcomes. Replacement fibrosis is typically the result of myocardial infarction (MI). Diffuse interstitial fibrosis results from common cardiovascular risk factors; interstitial fibrosis has been shown to be reversible and treatable with early intervention. Noninvasive imaging methods to detect fibrosis are in development. Recent advances have been made in cardiac magnetic resonance (MR) imaging (CMR), computed tomography (CT), and nuclear medicine. This article focuses on CMR and the techniques of late gadolinium enhancement (LGE) and T1 mapping, which are useful in the detection of myocardial scar and diffuse myocardial fibrosis respectively.

PATHOLOGIC BASIS OF FIBROSIS

The extracellular matrix (ECM) is a dynamic molecular network that is essential in giving strength to the heart and in coordinated signaling between cells in the tissue. It anchors cardiac muscle cells (myocytes), regulates tissue mechanics, and stores growth factors.[1–3] The ECM is composed of collagens and elastic fibers buried in a gel of proteoglycans, polysaccharides, and glycoproteins. Aberrant healing processes result in the common pathologic feature called fibrosis. Fibrosis forms from an increased amount of collagen (fibrosis)

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Radiol Clin N Am 53 (2015) 413–423
http://dx.doi.org/10.1016/j.rcl.2014.11.005
0033-8389/15/$ – see front matter Published by Elsevier Inc.

resulting from altered collagen turnover, in which net collagen deposition exceeds net collagen breakdown. Diffuse myocardial fibrosis is known to increase with age and other cardiovascular risk factors.[4] At a molecular level, matrix metalloproteinases also play a key role in the development of myocardial fibrosis.

Increased myocardial collagen deposition is the common end point for a wide variety of cardiomyopathies. Collagen deposition results in abnormal myocardial stiffness and contractility, which leads to progression of heart failure and disruption of the intercellular signaling. These disruptive processes may lead to malignant arrhythmias and sudden death. Multiple clinical studies have shown fibrosis to be a major independent predictor of adverse cardiac outcomes.[5–8] It is always present in end-stage heart failure.[9] Diastolic function is initially affected and is followed by deterioration of systolic function.[10]

The 2 distinct types of fibrosis in the heart are replacement fibrosis and interstitial fibrosis. Replacement fibrosis is focal development of scar that replaces dead cardiomyocytes from injury and is only seen when the integrity of the cell wall is affected.[11] Depending on the cause, both regional and diffuse patterns can be seen. Scarring from MI is the most common cause of replacement fibrosis. Hypertrophic cardiomyopathy, sarcoidosis, myocarditis, chronic renal insufficiency, and toxic cardiomyopathies are other conditions associated with this type of fibrosis.[12,13]

Interstitial fibrosis is generally a diffuse process. It has 2 subtypes: reactive and infiltrative interstitial. Reactive fibrosis is present in a variety of common conditions, including aging and hypertension. It is caused by an increase in collagen production and deposition by stimulated myofibroblasts. Infiltrative interstitial fibrosis is much rarer and is caused by progressive deposition of insoluble proteins or glycosphingolipids in the interstitium. Examples of infiltrative fibrosis include amyloidosis and Anderson-Fabry disease.[14,15] Both interstitial and infiltrative fibrosis eventually lead to cardiomyocyte apoptosis and replacement fibrosis.[10] Unlike replacement fibrosis, interstitial fibrosis may be reversible and is a target for treatment.[16,17]

The ability to noninvasively image fibrosis could be useful for diagnostic and therapeutic purposes in cardiomyopathy treatment. Tissue biopsy has been the gold standard for fibrosis assessment, but it is invasive and prone to sampling error. The emergence of noninvasive imaging modalities like CMR imaging and CT has led to the development of novel imaging methods for a range of cardiomyopathies.

DETECTION OF FIBROSIS WITH ENDOMYOCARDIAL BIOPSY

The gold standard for the detection of myocardial fibrosis is endomyocardial fibrosis. A small (<1 mm^3) sample is taken, typically from the right ventricular side of the distal myocardial septum. The sample is assessed using Masson trichrome staining. Quantitative absolute assessment of the collagen volume fraction in tissue samples is measured by quantitative morphometry with picrosirius red.

Being an invasive technique, this carries a risk of complications. In cases of localized fibrosis, sampling error restricts the accuracy. It is also not possible to determine fibrotic involvement of the whole left ventricle.

DETECTION OF REPLACEMENT/FOCAL FIBROSIS WITH LATE GADOLINIUM ENHANCEMENT CARDIAC MAGNETIC RESONANCE

CMR provides safe, high-resolution imaging without ionizing radiation. CMR is well established as a standard of reference for the evaluation of myocardial structure and function. Pixel signal intensity of CMR images is based on the magnetic properties of hydrogen nuclei in the magnetic field. The 2 most common parameters from CMR are longitudinal relaxation time (T1), and transverse relaxation time (T2).

A unique clinical role of CMR (compared with echocardiography) is the use of LGE to define the presence of focal fibrosis or myocardial scar. For example, for the evaluation of focal fibrosis from MI, LGE imaging has been a gold standard for visualization and quantification of scar. **Fig. 1** shows scar from an inferior wall MI.

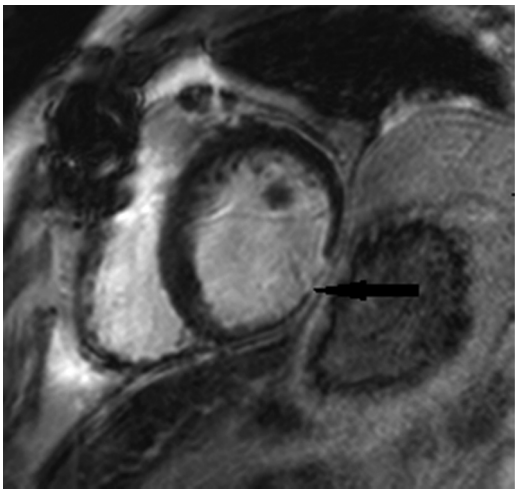

Fig. 1. Inferior wall MI (*black arrow*). Wall thinning and LGE is seen.