Myocardial Tissue Characterization of Left Ventricular Reverse Remodeling in Ischemic Cardiomyopathy

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Pathological left ventricular (LV) remodeling, defined as maladaptive LV cavity enlargement and structural change, occurs after myocardial damage, which is characterized by the combination of myocyte hypertrophy, apoptosis and interstitial fibrosis.¹ Pathological LV remodeling leads to the deterioration of LV ejection fraction (LVEF) and the development of functional mitral regurgitation, contributing to further remodeling and worse prognosis in patients with heart failure (HF).¹ Reduction of LV chamber volumes with an improvement in LVEF due to optimized treatment is termed “reverse remodeling”,² which can be achieved by coronary intervention, medical treatment including angiotensin-converting enzyme inhibitors and β -blockers, cardiac resynchronization therapy and pressure unloading with LV assist device.³⁻⁵ Reverse remodeling has been also observed in a wide variety of clinical settings including viral myocarditis, postpartum cardiomyopathy, or after removal of a cytotoxic agent (Figure).⁶ At the molecular level, reverse remodeling can be in part explained by the calcium handling alteration, decrease in apoptosis,⁷ improvement of mitochondrial function,⁸ and reduction of the extracellular matrix remodeling promoted by matrix metalloproteinases.⁹

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Although reverse remodeling has been associated with favorable prognosis in HF, not all patients experience this process.¹⁰ Furthermore, the predictors of reverse remodeling have not been fully clarified, which may be due to lack of information on myocardial tissue characteristics during reverse remodeling. From this point of view, cardiac magnetic resonance imaging (CMR) has the high spatial and temporal resolution and the high contrast with late gadolinium enhancement (LGE) to assess the pathological changes of myocardium in HF patients. Intriguingly, there is some evidence that CMR could be used to predict the occurrence of reverse remodeling in HF:^{10,11} the degree of myocardial fibrosis estimated on LGE-CMR could better predict reverse remodeling compared with that on endomyocardial biopsy in non-ischemic HF.¹¹

In this issue of the Journal, Park et al present additional evidence for myocardial tissue characterization during reverse LV remodeling based on their single-center retrospective study in Korea.¹² The authors carried out detailed investigation of CMR parameters after surgical coronary revascularization in

26 ischemic cardiomyopathy patients with severe LV systolic dysfunction (LVEF <35%). Reverse LV remodeling was observed in 20 (77%) of the 26 patients 21 $\pm$ 14 months after coronary revascularization. As expected, absolute infarct mass did not change during the follow-up period in the reverse remodeling group, but relative infarct mass was significantly increased, due to reduction of myocardial mass in the segments with non-transmural infarction.

Figure. Reverse remodeling can be achieved by optimized treatment including angiotensin-converting enzyme inhibitors, β -blockers, coronary interventions, cardiac resynchronization therapy and pressure unloading with left ventricular (LV) assist device (LVAD). Reverse remodeling can be also observed in a wide variety of clinical settings such as viral myocarditis, postpartum cardiomyopathy and after removal of a cytotoxic agent. (Reprinted with permission from Mann D, et al.⁶) ALM, acute lymphocytic myocarditis; AVR, aortic valve replacement; CPAP, continuous positive airway pressure; CRT, cardiac resynchronization therapy; CSD, cardiac support device; MVR, mitral valve replacement; RAAS, renin-angiotensin-aldosterone system.

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Their main findings, unchanged infarct mass and reduction of myocardial mass during reverse remodeling, may not be surprising to cardiologists because this phenomenon has been well documented in previous pathological and echocardiographic studies.² Nevertheless, this study is important because myocardial tissue characterization during reverse remodeling was beautifully visualized in a non-invasive manner, which may help cardiologists more deeply understand this dynamic process. Also, this study clearly demonstrated CMR-defined viable and non-viable myocardium. Regional reverse remodeling after revascularization was observed if regional transmural extent of LGE was $\leq 75\%$. Although this small retrospective study did not provide predictive values for reverse LV remodeling, the cut-off for transmural LGE extent $\leq 75\%$ may be used to predict the occurrence of reverse remodeling, which should be tested in a large prospective study in the future.

This study raises questions regarding the mechanism of reverse remodeling. Interstitial fibrosis plays a critical role in the development of pathological LV remodeling,¹³ although Park et al did not show whether the extent of interstitial fibrosis was reduced during reverse remodeling. This is because conventional LGE techniques are limited in the detection of diffuse interstitial fibrosis.¹⁴ The use of T1-mapping¹⁵ might be effective for investigating correlations between interstitial fibrosis and reverse remodeling. Further development in imaging technology, including in CMR to assess failed myocardium, may provide new insights into the mechanism of reverse remodeling and thus into treatment strategies for HF in the future.

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Conflict of Interest

None.

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