The development of molecular therapies aiming at supporting a balanced inflammatory response after AMI has, therefore, been a focus of recent research. A growing spectrum of agents interfering, for example, with chemokine, interleukin, or growth factor pathways, are under investigation on the preclinical and early clinical level. But because of the complex, variable, and transient nature of post-infarct inflammation, timing and appropriate candidate selection may be critical for such therapies. This is where targeted noninvasive imaging for guidance of novel inflammation-targeted therapy to optimal candidates at the appropriate time after AMI. This approach could facilitate a personalized approach toward prevention of adverse ventricular remodeling.

Besides its well-recognized value as a tumor imaging agent, the glucose-analogue F-18 deoxyglucose (FDG) has been increasingly used for imaging of inflammation because it avidly accumulates in macrophages and other metabolically active inflammatory cells. FDG has emerged as a marker of atherosclerotic activity, and it is penetrating the clinical arena for the detection of myocardial sarcoidosis. More recently, several groups have also used FDG as a marker of post-infarct myocardial inflammation. Initial validation has been obtained in mice, but other reports also provided proof of feasibility in large animals and humans. Importantly, FDG not only gives quantitative information about the localization and severity of inflammation in the myocardium but also provides insights on systemic activation of hematopoietic organs, such as spleen and bone marrow.

A consequential next step after initial proof of principle is to demonstrate that the FDG-derived inflammation signal early after AMI has predictive value for the occurrence of subsequent adverse remodeling and that this novel diagnostic approach provides information beyond current standard diagnostic parameters, such as infarct size, left ventricular geometry and function, and blood markers of myocardial damage or systemic inflammation. Only the proof of such an incremental value will support the clinical usefulness of inflammation-targeted imaging for guidance of novel inflammation-targeted therapy and for use as an early end point to monitor effectiveness. In this issue of Circulation: Cardiovascular Imaging, the article by Rischpler et al provides important first clinical evidence. In a group of 49 patients who had undergone coronary interventions for their first ST-segment–elevation MI, hybrid positron emission tomography (PET)/magnetic resonance imaging (MRI) was performed after a median of 5 days, using FDG under conditions to suppress myocyte uptake. The FDG-derived extent and intensity of post-infarct inflammation were correlated with infarct size and systemic inflammatory markers. Cardiac MRI was again performed in a subgroup of 29 patients ≈6 to 9 months later. At the time of follow-up, detrimental changes in left ventricular ejection fraction and volumes were associated with infarct size and, importantly, with the extent of FDG uptake at early PET/MR. Using multivariable analysis, FDG uptake remained independently associated, suggesting that the extent of early myocardial inflammation is a predictor of subsequent functional outcome after AMI.

The work has several additional strengths: it uses high-end PET/MR hybrid imaging methodology, which facilitates integration of PET-derived inflammation markers with MRI-derived markers of infarct size and left ventricular geometry. Also, it provides a sophisticated correlation of FDG imaging findings with systemic, flow cytometry–derived counts of
leukocyte subpopulations, showing an association between FDG signal and proinflammatory rather than reparative monocytes. It integrates PET-MR findings with single photon emission computed tomography-derived measures of the area at risk before intervention, showing that FDG uptake exceeds the MRI-derived infarct area and correlates with the risk area.

Some limitations, however, should also be considered: first, the sample size of patients with a complete follow-up is limited because, in part, of a relatively high dropout rate, which may introduce bias. The results will require confirmation in larger registries. Second, it is noteworthy that the intensity of FDG uptake was not a determinant of adverse functional outcome—only the extent of elevated FDG uptake was. This emphasizes the need for standardized approaches for image analysis. Finally, FDG is a complicated marker because the signal may not only reflect inflammatory cells. It is well known that ischemically damaged but viable myocytes also show elevated FDG uptake and that such damaged but viable myocytes will also contribute to functional recovery after reperfusion. The used protocols for suppression of myocardial FDG uptake may not work equally well for healthy or jeopardized myocardium. Integration of FDG PET with MRI-derived measures of nonviable infarct and scar, at best within the same imaging session, may help in distinguishing between inflamed tissue and compromised but viable myocardium as the source of elevated FDG uptake. Also, FDG as an approved agent is more easily implemented into the clinics. Nevertheless, other more specific markers of inflammatory cells with limited or no uptake in viable myocytes may be desirable.

By the demonstration of an independent association of a molecular imaging marker of early inflammation with later development of adverse remodeling, an important next step has been made toward clinical implication. Further steps may include the evaluation of tracers other than FDG, such as the amino acid methionine or the chemokine-targeted agent pentixafor. In parallel, early inflammation-targeted molecular imaging may not work equally well for healthy myocardium after reperfusion. The used protocols for suppression of bone marrow progenitor cell recruitment to the neovasculature and reduces mortality after myocardial infarction. Proc Natl Acad Sci U S A. 2010;107:11008–11103. doi:10.1073/pnas.0914284107.


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