Combined Positron Emission Tomography and Magnetic Resonance as Translational Tool in Cardiology

Markus Schwaiger, MD

In this issue of Circulation: Cardiovascular Imaging, Bulluck et al. introduce simultaneous positron emission tomography and magnetic resonance (PET-MR) imaging as a sophisticated research tool to correlate cardiac function, area of risk, metabolism, and infarct size in patients with acute myocardial infarction. Imaging is increasingly applied for the noninvasive characterization of acute and chronic ischemic injury. Impaired perfusion and wall motion are considered to be diagnostic hallmarks of ischemic injury. Therefore, myocardial perfusion imaging and echocardiography are commonly used to identify location, extent, and severity of ischemic injury. With the advent of cross-sectional imaging, such as single photon emission tomography (SPECT), PET, and MR, more sophisticated means have become available for tomographic visualization of myocardial ischemia and its consequences. At the same time, new tracer techniques have been introduced to provide molecular signals beyond myocardial perfusion. Thallium-201 imaging was the first technology to be applied for the differentiation between reversible perfusion abnormalities as a marker of viable myocardium and persistent defects associated with scar formation, but this imaging approach is only rarely used anymore because of high radiation exposure. With the introduction of PET in the 1980s, metabolic characterization of regional ischemic injury became possible. Using tracers such as C-11 palmitate, C-11 acetate, and FDG, acute metabolic effects of ischemia have been documented.

See Article by Bulluck et al

On the basis of these first metabolic imaging studies, the clinical application of 18F-fluorodeoxyglucose (FDG) emerged as a sensitive marker of tissue viability. Multiple studies in patients with chronic coronary artery disease and impaired ventricular function established the role of PET/FDG as a prognostic marker for functional recovery after revascularization. The observation of reversible dysfunction after revascularization provoked several experimental and clinical studies to elucidate the mechanism of hibernating or stunned myocardium as the pathophysiological explanation for reduced left ventricular function in the presence of viable myocardium. With the clinical acceptance of reversible dysfunction as a therapeutic target in patients with heart failure, several imaging methods competed for clinical application, from which FDG-PET and cardiac MR imaging with late gadolinium enhancement (LGE) emerged as “gold standards” for tissue viability and scar formation, respectively. However, the lower risk of revascularization either by percutaneous techniques or by surgery has reduced the clinical imperative for viability studies in recent years. In addition, a large prospective trial (Surgical Treatment to Ischemic Heart Failure [STICH] trial) suggested that the delineation of myocardial viability did not significantly affect clinical outcome of patients considered for revascularization. However, limitations in study design of this trial remain, questioning the validity of the conclusions, and further studies are needed to refine the clinical role of viability testing in chronic ischemic heart failure.

In contrast to studies in patients with chronic ischemic ventricular dysfunction, the application of imaging studies in patients with acute myocardial infarction are reserved primarily to research questions. With cross-sectional imaging modalities, it is now possible to assess many parameters in vivo, which were in the past only obtainable in experimental settings. Today, parameters such as area of risk can be assessed by SPECT and MR imaging during and after acute myocardial injury. In addition, the extent of acute myocardial necrosis can be accurately quantified by the gadolinium kinetics. Evaluation of LGE by MR imaging has been found to correlate closely with extent of acute necrosis, as shown by triphenyltetrazolium staining. With the recent introduction of PET/MR, simultaneous and coregistered acquisition of established PET and MR signals can be performed in patients with acute myocardial infarction. In the article by Bulluck et al., interesting first results of the application of this new and unique multimodal technology in patients with acute myocardial infarction are presented. PET/MR after glucose insulin load was performed in 21 patients early after acute myocardial infarction. PET and MR parameters were compared and correlated with a follow-up PET/MR study 12 months later. The main finding of this study is that there is good agreement of FDG/PET as well as cardiac MR late in the follow-up study, confirming the validity of both methods to estimate infarct size several months after infarction. During the acute phase, however, the relative FDG defect in the infarct territory seemed to be larger when compared with LGE as a marker of necrosis. In addition, the area of reduced FDG uptake correlated closely with T2 mapping as a marker of area of risk. These results suggest that in reversibly injured myocardium...
FDG uptake is reduced and recovers over time, as shown in a subset of patients with follow-up PET/MR study. To interpret this unexpected finding of reduced FDG uptake in viable but injured myocardium, one has to consider various methodological aspects of PET. As stated above, the FDG uptake reflects cardiac metabolism depending on the overall metabolic state. During glucose and insulin loading, FDG uptake in normal myocardium is maximized. Therefore, the relative uptake of FDG within an ischemic injury highly depends on thresholds applied to define abnormal FDG. As shown in figure 6 of the article by Bulluck et al., the correlation of FDG uptake with extent of LGE strongly depends on threshold values, and as indicated in the article, the best agreement with T2 MR signal as a marker of area of risk was observed with a threshold of 50%. However, a threshold of 45% best predicted functional extent of LGE. This is in agreement with the article quoted above. Hence, quantitative measurements of FDG uptake have to be interpreted appropriately.

Recent studies have shown that quantitative measurements of FDG uptake are associated with functional outcome, suggesting that exaggerated inflammatory responses are detrimental for healing process. Therefore, even in the presence of acute inflammation, PET studies after glucose load or insulin exposure show relatively reduced FDG uptake in the ischämically injured area. For this reason, the interpretation of relative FDG uptake in ischämically injured myocardium has to be evaluated in the context of the overall metabolic milieu and absolute quantification of FDG uptake may support an improved interpretation of the results.

The PET/MR study by Bulluck et al. indicates that multimodality imaging provides many important parameters, which can be related to extent, severity and outcome of an ischemic injury. PET/MR performed 5 days after myocardial infarction can accurately predict outcome of an ischemic injury. This may be most appropriate in intervention studies evaluating new drug regimens to modify myocardial salvage or remodeling. In addition, combination of MR with other PET tracers addressing specific molecular targets may be helpful in the setting of acute myocardial infarction. With the advent of multimodality imaging, various physiological and molecular parameters can be simultaneously studied and represent a major step in translating experimental knowledge into clinical imaging protocols.

Myocardial performance can be modified by therapeutic interventions and evaluated how these interventions relate to clinical outcome of patients with acute myocardial infarction.

Disclosures

A research grant has been received from Siemens Medical Research. The research leading to these results has received funding from the European Union Seventh Framework Program (FP7) under Grant Agreement No. 294582 ERC Grant MUMI and DZHK (German Centre for Cardiovascular Research).

References


Combined Positron Emission Tomography and Magnetic Resonance as Translational Tool in Cardiology
Markus Schwaiger

Circ Cardiovasc Imaging. 2016;9:e004549
doi: 10.1161/CIRCIMAGING.116.004549
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2016 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/9/3/e004549

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Imaging can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Imaging is online at:
http://circimaging.ahajournals.org/subscriptions/