Characterizing the Inflammatory Tissue Response to Acute Myocardial Infarction by Clinical Multimodality Noninvasive Imaging

Tim Wollenweber, MD*; Philipp Roentgen, MD*; Andreas Schäfer, MD; Imke Schatka, MD; Caroline Zwadlo, MD; Thomas Brunkhorst, MD; Georg Berding, MD; Johann Bauersachs, MD*; Frank M. Bengel, MD*

**Background**—Myocardial infarction (MI) triggers a systemic inflammatory response which determines subsequent healing. Experimentally, cardiac positron emission tomography and magnetic resonance imaging have been used successfully to obtain mechanistic insights. We explored the translational potential in patients early after MI.

**Methods and Results**—Positron emission tomography/computed tomography and cardiac magnetic resonance were performed in 15 patients <7 days after first MI. Cardiac magnetic resonance showed regional transmural late gadolinium enhancement and edema exceeding the area of late gadolinium enhancement. Using F-18 deoxyglucose with heparin pretreatment, metabolic rate of glucose (MRGlc) was significantly increased in infarct versus remote myocardium (median, 2.0 versus 0.4 mg/min per 100 mL; P=0.0001). MRGlc in infarct correlated with remote myocardium (ρ=0.64; P=0.01), spleen (ρ=0.82; P=0.0002), and bone marrow (ρ=0.57; P=0.03), but not with muscle or liver. Regionally, F-18 deoxyglucose score was highest in segments with late gadolinium enhancement versus edema only and remote (median, 2.0 versus 1.8 versus 0.4; P<0.0001). Patients requiring repeat intervention during preliminary follow-up of 11±5 months tended to have higher early post-MI MRGlc. Five patients with chronic, stable MI served as controls. Opposite to acute MI, MRGlc was lower in infarct (median infarct/remote ratio, 0.6 versus 3.2 for acute MI; P=0.001), and there was no correlation with bone marrow or spleen MRGlc.

**Conclusions**—Increased glucose utilization after heparin-induced suppression of myocyte uptake appears to mostly reflect inflammatory activity in damaged myocardium early after MI. Consistent with prior preclinical observations, and in contrast to chronic MI, this is associated with activity in spleen and bone marrow as sources of inflammatory cells. Positron emission tomography and cardiac magnetic resonance multimodality characterization of the acutely infarcted, inflamed myocardium may provide multiparametric end points for clinical studies aiming at support of infarct healing.  (*Circ Cardiovasc Imaging. 2014;7:811-818.*)

**Key Words:** fluorodeoxyglucose F18 ■ inflammation ■ magnetic resonance imaging ■ myocardial infarction ■ positron-emission tomography

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Recent preclinical studies have shown that postinfarct inflammation is detectable by positron emission tomography (PET) with the glucose analog, 18F-deoxyglucose (FDG), when integrated with the late contrast enhancement signal from the infarct region in concomitant cardiac magnetic resonance (CMR) or computed tomographic (CT) studies. Mechanistic studies have shown that progenitor cells and inflammatory cells are released from the bone marrow, migrate to the myocardium, and transiently accumulate in the spleen, which serves as a cell depot. Also, inflammation is not limited to infarcted myocardium but also affects noninfarcted remote myocardium.
to a lesser degree, providing a rationale for remote remodeling.

But the use of FDG is complicated by the fact that its uptake may also reflect the presence of ischemically compromised, viable myocytes after AMI. To test the feasibility of FDG as an inflammatory marker in patients, we used quantitative FDG PET and CMR to obtain clinical insights into the biology of acutely infarcted, inflamed myocardium. Successful proof of principle may lay the groundwork for subsequent use in therapy monitoring.

Methods

Patients

Fifteen consecutive patients (13 men; 53±12 years) underwent myocardial FDG PET/CT; perfusion imaging, and CMR within 1 week after their first AMI. All patients were treated by percutaneous coronary intervention within 5.3±5.2 hours (range, 2–21) of symptom onset. Ten were stented in the left anterior descending, 1 in the left circumflex, and 4 in the right coronary artery. Peak level of creatine kinase was 3465±2094 U/L (range, 247–6717). Angiographically, 9 had single-vessel, 6 two-vessel, and none triple-vessel disease. The mean time from reperfusion to CMR was 3±1 days (range, 1.2–6.1) and 4±2 days (range, 1.9–7.5) to perfusion/FDG imaging.

An additional group of 5 consecutive patients with chronic, stable MI (4 men; 72±9 years) underwent PET and CMR at 6.5±3.3 years after MI. All showed stable symptoms of heart failure (2 New York Heart Association class), new cardiovascular events (infarct or stroke), or additional in-hospital or after-discharge events (11 patients, 3 New York Heart Association class), angina pectoris (Canadian Cardiovascular Society class), and myocardial ischemia on exercise stress testing. Exclusion criteria were a history of prior acute coronary syndrome, new cardiovascular events (infarct or stroke), or additional in-hospital or after-discharge events (11 patients, 3 New York Heart Association class), new cardiovascular events (infarct or stroke), or additional in-hospital or after-discharge events (11 patients, 3 New York Heart Association class), angina pectoris (Canadian Cardiovascular Society class), and myocardial ischemia on exercise stress testing.

Noninvasive Imaging

Cardiac Magnetic Resonance

All examinations were performed on a 1.5-T scanner (Magnetom Avanto, Siemens). Cine images of left ventricular (LV) function were obtained after their first AMI. All patients were treated by percutaneous coronary intervention within 5.3±5.2 hours (range, 2–21) of symptom onset. Ten were stented in the left anterior descending, 1 in the left circumflex, and 4 in the right coronary artery. Peak level of creatine kinase was 3465±2094 U/L (range, 247–6717). Angiographically, 9 had single-vessel, 6 two-vessel, and none triple-vessel disease. The mean time from reperfusion to CMR was 3±1 days (range, 1.2–6.1) and 4±2 days (range, 1.9–7.5) to perfusion/FDG imaging. An additional group of 5 consecutive patients with chronic, stable MI (4 men; 72±9 years) underwent PET and CMR at 6.5±3.3 years after MI. All showed stable symptoms of heart failure (2 New York Heart Association class), new cardiovascular events (infarct or stroke), or additional in-hospital or after-discharge events (11 patients, 3 New York Heart Association class), angina pectoris (Canadian Cardiovascular Society class), and myocardial ischemia on exercise stress testing. Exclusion criteria were a history of prior acute coronary syndrome, new cardiovascular events (infarct or stroke), or additional in-hospital or after-discharge events (11 patients, 3 New York Heart Association class), new cardiovascular events (infarct or stroke), or additional in-hospital or after-discharge events (11 patients, 3 New York Heart Association class), angina pectoris (Canadian Cardiovascular Society class), and myocardial ischemia on exercise stress testing.

Noninvasive Imaging

Cardiac Magnetic Resonance

All examinations were performed on a 1.5-T scanner (Magnetom Avanto, Siemens). Cine images of left ventricular (LV) function were obtained using steady-state free precession sequences. Extent and severity of myocardial edema were determined by T2-weighted triple inversion recovery sequences in corresponding slices. Then, late contrast enhancement (LE) was imaged by phase-sensitive inversion recovery sequences 10 to 15 minutes after bolus injection of 0.15 mmol/kg gadolinium-diethylene triamine pentaacetic acid (Gadobutrol, Bayer Healthcare).

F-18 Deoxyglucose Positron Emission Tomography/Computed Tomography

For improved detection of infarct-induced presence of inflammatory cells, myocyte glucose metabolism was suppressed according to previously established protocols for detection of cardiac sarcoidosis. After an extended fasting period of >12 hours, 50 IU/kg of nonfractionated heparin was injected intravenously to increase plasma free fatty acid levels. Two patients with chronic MI did not receive heparin because of ongoing coumadin therapy. Fifteen minutes later, 360±44 MBq of FDG was injected and list-mode PET was obtained for 60 minutes using a Siemens Biograph Duo scanner. A low-dose CT was obtained for attenuation correction. List-mode data were resampled to attenuation corrected, iteratively reconstructed, static (30–60 minutes), and dynamic images (22 frames: 12x10, 3x30, 3x300, 4x600 seconds).

Perfusion Imaging

Patients abstained from caffeinated drinks and food ≥12 hours before stress examination. Rest perfusion studies were obtained by 99mTc-Sestamibi-single photon emission computed tomography/CT (329±25 MBq; n=7 patients with AMI and all patients with chronic MI). Additionally, pharmacological stress perfusion studies were obtained after regadenoson-induced vasodilatation in 6 of 8 PET/CT sessions (422±83 MBq 99mTc-Sestamibi) and in 6 of 7 AMI single photon emission computed tomography/CT sessions (654±260 MBq 99mTc-Sestamibi). Low-dose CT scans were obtained for attenuation correction of all studies. Twenty-minute list-mode PET data were resampled to attenuation corrected, iteratively reconstructed, static (10–20 minutes) and dynamic images (21 frames: 12x10, 6x30, 3x300 seconds). Single photon emission computed tomography images were acquired for 25 minutes and 45 minutes after injection and reconstructed iteratively with attenuation correction.

Data Analysis

Cardiac Magnetic Resonance

Images were analyzed using CMR42 (Circle Imaging, Calgary, Canada). LV function was assessed by modified Simpson’s method. Volumes, ejection fraction (EF), and LV mass were obtained by delineation of inner and outer LV contours in end-diastolic and end-systolic frames. Additionally, using the American Heart Association 17-segment model, regional edema, LE and microvascular obstruction (MVO) were graded based on the average transmurality of the signal, and regional wall motion was graded visually (Table). Mean scores per segment were calculated, and individual segmental scores were summed up to generate global scores. Assessment was done on agreement by 2 experienced observers blinded to all other study parameters.

Table. Scoring Template for Regional Analysis According to American Heart Association 17-Segment Model

<table>
<thead>
<tr>
<th>Radiotracer Imaging</th>
<th>CMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG (Relative to Bloodpool)</td>
<td>Perfusion (Relative to LV Max)</td>
</tr>
<tr>
<td>Score</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Below/equal</td>
</tr>
<tr>
<td>1</td>
<td>Mild elevation</td>
</tr>
<tr>
<td>2</td>
<td>Moderate elevation</td>
</tr>
<tr>
<td>3</td>
<td>Strong elevation</td>
</tr>
<tr>
<td>4</td>
<td>Very strong elevation</td>
</tr>
</tbody>
</table>

CMR indicates cardiac magnetic resonance imaging; FDG, 18F-deoxyglucose; LE, late contrast enhancement; LV, left ventricle; and MVO, microvascular obstruction.
Segmental Perfusion and FDG Uptake

Static FDG-PET images were visually analyzed by 2 independent observers, based on a scoring system using the American Heart Association 17-segment model. Each segment was given a score from 0 to 4 for the magnitude of FDG uptake relative to blood pool (Table). For perfusion studies, defect severity was scored, according to the standard summed score approach. Discrepancies between observers were resolved by consensus.

Quantitative Perfusion Analysis

For perfusion defect size quantification, polar maps of the LV were generated and normalized to their maximum using Munich Heart software. For both $^{13}$N-ammonia and $^{99m}$Tc-stestamibi, a threshold of 60% relative to the maximum was chosen to define defect. Also, dynamic $^{13}$N-ammonia PET rest and stress images were quantitatively analyzed by generating myocardium and blood time-activity curves and applying a validated 3-compartment model to determine myocardial blood flow (MBF) at stress and rest, as previously described.22

Quantitative Metabolic Analysis

Metabolic rates of glucose (MRGlc) were determined for infarcted and remote myocardium, bone marrow of vertebral bodies, spleen, liver, and paraverterbral skeletal muscle by using PMOD software and Patlak graphical analysis of dynamic FDG PET images. Spherical volumes of interest (2.5 mm diameter) were placed in left atrium to determine arterial input function in infarcted myocardium (hottest region) and 3-fold in remote myocardium. Guided by CT and fusion images (Figure 1), further volumes of interest were placed in bone marrow of 3 vertebral bodies and paraverterbral skeletal muscle in the field of view and a large volume of interest (8 mm) was placed in the spleen and liver. Using time-activity curves from volumes of interest, MRGlc was estimated by assuming a standard lumped constant of 0.67.

Statistical Analysis

Statistical analysis was performed with MedCalc v12.7.0.0 (Ostend, Belgium). Because of small sample sizes, data are expressed as median and (25th–75th quartile) ranges. Spearman correlation was performed to describe the relationship between continuous variables. Interobserver reproducibility of ordinal segmental scores was assessed by k-statistics with 95% confidence intervals. Comparisons between groups of continuous variables were performed using Wilcoxon signed-rank and Mann–Whitney U test, as appropriate. The Bonferroni procedure was used in the case of multiple hypothesis tests. P<0.05 was considered as statistically significant. Analyses on the segmental level were based on the assumption of independence of segments within the same patient, as specified previously.23

Results

Perfusion and CMR Tissue Characterization

In patients with AMI, LVEF was 46% (44%–50%) and resting perfusion defect size was 33% (15.0%–42.0%) of LV. Stress perfusion imaging did not reveal significant ischemia in remote territories. CMR showed transmural LE in the infarct region in 12 of 15 patients, with a summed LE score of 22 (16–28). Edema was present and tended to exceed the infarct area, with a summed score of 28 (20–36) (P=0.05 versus LE score). MVO was observed in 10 of 15 patients, comprising a median of 4.0 (0.0–5.0) segments.

In patients with chronic MI, LVEF was 30% (28%–41%), and resting perfusion defect size was 47% (42%–55%) of LV. CMR showed transmural LE in the infarct region in 3 of 5 patients, with a summed LE score of 15 (12–24). No edema or MVO was identified.

Regional Glucose Utilization

In the AMI group, diet and heparin pretreatment resulted in good suppression of FDG uptake in remote myocardium, whereas regionally increased FDG uptake was detected in the hypoperfused infarct region in 12 of 15 patients (Figure 2). Summed FDG score was 19 (12–25) and correlated significantly with the global scores for LE (ρ=0.54; P=0.04; Figure 3A) and edema (ρ=0.76; P=0.002; Figure 3B). Consistently, the mean FDG score was significantly elevated in segments with LE compared with those without (2.0 [1.5–2.3] versus 0.6 [0.3–0.7]; P=0.0001). There was no significant difference in FDG score between LE segments with or without
MVO (2.1 [1.3–2.8] versus 1.8 [1.0–3.0]; P=0.54; Figure 3C). Also, there was significantly increased FDG score in segments with edema compared with regions without, whereas there was no significant difference among edema segments with or without LE (2.0 [1.5–2.6] versus 1.8 [1.4–2.0] versus 0.4 [0.0–0.5] for edema with LE versus edema without LE versus remote; P=0.26 for edema with LE versus edema without LE; P<0.0001 for edema with or without LE versus remote; Figure 3D). Finally, FDG score tended to correlate with wall motion score (r=0.42; P=0.12). It was significantly elevated in segments with impaired wall motion (1.8 [1.4–2.5] versus 0.5 [0.4–0.8]; P=0.0008).

In patients with chronic MI, a reverse pattern was observed. Fasting and heparin yielded suppression of myocardial uptake, and if at all detectable, FDG uptake in the infarct region was lower than in remote myocardium (Figure 4). FDG scores in segments without LE were consistently higher than in those with LE, resulting in a ratio of 1.2 (1.1–1.5), which was opposite to AMI (ratio of FDG scores in segments without relative to with LE: 0.3 [0.1–0.4]; P=0.001). Unlike in AMI, summed segmental FDG score did not correlate with global LE score (r=0.1; P=0.93). Of note, interobserver reproducibility for segmental analysis was in good agreement for FDG PET (κ=0.93 [0.86–1.00]) and CMR (LE: κ=0.72 [0.51–0.94]; edema: κ=0.88 [0.74 to 1.00]; MVO: κ=0.77 [0.50–1.00]).

Quantitative MRGlc in Heart and Lymphoid Tissue

In AMI, consistent with visual regional analysis, quantitative MRGlc was significantly elevated in infarct versus remote myocardium (2.0 [1.2–2.8] versus 0.4 [0.2–1.2] mg/min per 100 mL; P=0.0001). Infarct MRGlc was positively correlated with MRGlc in remote myocardium (r=0.64; P=0.01; Figure 5A) and showed a trend to an inverse correlation with time after reperfusion (r=-0.40; P=0.14; Figure 5B). There was no correlation with other parameters of myocardial damage, including
perfusion defect size \( (\rho = 0.28; P = 0.32) \), LVEF \( (\rho = 0.13; P = 0.65) \), peak level of creatine kinase \( (\rho = 0.17; P = 0.54) \), or with markers of systemic inflammation including blood leukocyte count \( (\rho = 0.14; P = 0.61) \) or C-reactive protein \( (\rho = 0.12; P = 0.73) \). Interestingly, however, glucose use in infarcted myocardium showed a significant positive correlation with MRGlc in lymphoid tissue, that is, the spleen \( (\rho = 0.82; P = 0.0002) \) and the vertebral bone marrow \( (\rho = 0.57; P = 0.03) \), whereas it did not correlate with nonlymphatic organs such as skeletal muscle \( (\rho = 0.34; P = 0.21) \) or liver \( (\rho = 0.1; P = 0.73) \).

In contrast to AMI, MRGlc in chronic MI was consistently lower in infarct relative to remote myocardium, with an infarct/remote ratio of 0.6 (0.5–1.1) versus 3.2 (2.4–6.4) for AMI \( (P = 0.001) \). Also, there was no correlation between infarct MRGlc and that of bone marrow or spleen in this group.

**Regional MRGlc and MBF**

In the subgroup of 8 patients with AMI who had \(^{13}\)N-ammonia perfusion PET, MBF data were available and allowed for a preliminary analysis. Of note, rest MBF in remote myocardium tended to correlate with MRGlc \( (\rho = 0.84; P = 0.0002) \), and the vertebral bone marrow \( (\rho = 0.57; P = 0.03) \), whereas it did not correlate with nonlymphatic organs such as skeletal muscle \( (\rho = 0.34; P = 0.21) \) or liver \( (\rho = 0.1; P = 0.73) \).

Follow-Up in Patients With AMI

Two patients were lost to follow-up. Among the remaining 13, no deaths occurred. At the time of the interview, 7 patients were in New York Heart Association class I, 2 in class II, 3 in class III, and 1 in class IV. Canadian Cardiovascular Society class was 0 in 8 patients, I in 2, and IV in 3. Seven patients underwent an additional coronary angiography. Five of these patients underwent percutaneous coronary intervention, whereas 2 had no intervention. One patient had bypass surgery, and only 1 patient had reinfarction.

Patients without angina symptoms (Canadian Cardiovascular Society 0) at follow-up tended to have higher MRGlc in the infarct region \( (2.4 [1.5–3.2] \text{ vs } 1.4 [1.1–1.6] \text{ mg/min per 100 mL; } P = 0.17) \) and bone marrow \( (1.1 [0.9–1.5] \text{ vs } 0.8 [0.6–1.0] \text{ mg/min per 100 mL; } P = 0.106) \) early after the event, compared with patients with angina at follow-up (Canadian Cardiovascular Society I–IV). Also, those requiring additional intervention or bypass surgery \( (n = 6) \) showed a trend toward higher MRGlc in remote myocardium than those without intervention \( (n = 7; 1.2 [0.21–1.37] \text{ vs } 0.3 [0.23–0.47] \text{ mg/min per 100 mL; } P = 0.23) \). Overall, however, there was no significant association between early imaging results and subsequent outcome in this small sample of infarct patients.

**Discussion**

In summary, our study demonstrates a specific pattern of regionally increased glucose uptake in the area of acutely infarcted myocardium, early after reperfusion. Pretreatment with heparin (an approach commonly used for clinical detection of cardiac sarcoid as an inflammatory disease)\(^{26}\) facilitated the identification of this increase, because it efficiently suppressed uptake of FDG in remote myocardium. Also, for the first time, our study demonstrates that the magnitude of increased glucose utilization in the infarct region is associated with activation of lymphoid tissue in humans.

These observations support the notion that regionally increased FDG uptake in the acutely infarcted myocardium may be, at least in part, a marker of tissue inflammation. Direct proof for this notion by tissue analysis cannot be obtained in a clinical study, but various prior experimental studies have confirmed a link between FDG uptake in the infarct region and inflammation,\(^{25}\) which is known to peak within a few days after the event.\(^{2–4}\) Other results give further support. First, FDG uptake occurred in areas with transmural late
gadolinium enhancement at CMR, suggesting extensive damage of myocytes. Second, there was a trend toward an inverse correlation between infarct FDG signal strength and time after reperfusion. Although this relationship is influenced by multiple factors and probably not linear, the decline with time is consistent with the natural course of inflammation because imaging was likely obtained after the peak inflammatory activity. Third, increased infarct uptake of FDG was associated with increased activity in remote myocardium, consistent with previous experimental observations of infarct and remote inflammation and, more importantly, with activation of bone marrow and spleen as lymphoid organs which are known to play a key role in the systemic immune response to myocardial damage. This relation could not be observed for the liver or the skeletal muscle as organs that are not involved in the inflammatory reaction. And finally, a small control group of patients with chronic MI showed a reverse FDG pattern with lower uptake in the infarct region relative to remote myocardium and no correlation with lymphoid tissue.

An alternative explanation for the regionally increased FDG uptake would be increased glucose utilization by viable myocytes in the infarct region. It needs to be pointed out that myocardial glucose utilization is a complex mechanism which may be stimulated by ischemic compromise, increased catecholamine levels, and other stressors. Prior work has, for example, suggested that increased FDG uptake in the infarct region may represent residual viability, contributing to improved regional wall motion at follow-up. This prior work, however, did not provide information about transmurality of the infarct from CMR, and it did not use heparin-based suppression techniques for reduction of myocyte FDG uptake. In our study, CMR suggests extensive, transmural regional damage. Although late enhancement early after infarction may overestimate irreversible damage to some degree, the mass of residual viable myocardium is likely small and the contribution of viability to the elevated FDG signal may be limited. Likewise, the inflammatory nature of the elevated FDG signal early after AMI has recently been confirmed experimentally in rodents, in which a good correlation with flow cytometry of infarct tissue for inflammatory cells was shown.

Another point of interest was the relationship between MVO and inflammation because MVO is a strong predictor of remodeling and may be a consequence of inflammation. FDG uptake in segments with MVO may be increased because of inflammation, or it may be reduced because of lack of perfusion, high tissue pressure, or hemorrhage—the same factors that result in absence of contrast enhancement at CMR. The lack of difference in FDG uptake between infarct segments with and without MVO suggests that more severe inflammation on the one hand may be counterbalanced by reduced tracer delivery on the other hand.

Further insights into the viable infarct border zone are provided by CMR edema imaging. The edema signal consistently exceeded the area of delayed enhancement in acute but not chronic MI. Interestingly, FDG uptake was increased not only in the infarct region, but also in regions with edema only when compared with remote myocardium. This implies that the viable, but edematous, infarct border zone may be ischemically compromised and involved in the inflammatory response. Consistent with the latter, the infarct border zone commonly shows intense neutrophil margination and infiltration, and preclinical studies observed numerous monocytes/macrophages in the infarct border zone.

Finally, it is of note that increased FDG uptake did not correlate with other measures of myocardial damage such as perfusion defect size, LVEF or peak level of creatine kinase, or systemic markers of inflammation such as C-reactive protein or blood leukocyte count. Severity of functional compromise and cell damage and systemic inflammatory response therefore are not strong determinants of the local tissue inflammatory reaction. This may confirm an independent value of myocardial inflammation imaging after acute infarction. Consistently, it has been assumed that infarct size, ventricular stress, and infarct healing (inflammation) are independent determinants of ventricular remodeling. Also, some studies observed an association between increased leukocyte count or increased CRP and adverse ventricular remodeling, but there are also studies that match our result and likewise found no correlation between infarct size and inflammatory markers or markers of matrix remodeling.

Some limitations of the present study need to be recognized. First, the sample size in our study was small so that lack of a significant correlation does not rule out the existence of an association. It just shows that the relative strength of the association is less than that of parameters that correlated significantly. Second, the limitations stemming from complexity of the FDG signal cannot be completely resolved. Besides questions about the partial contribution of elevated FDG uptake from compromised but viable myocytes, we also had to assume the same lumped constant of 0.67 for all tissues, which is not proven to be correct and may partially bias the results. Third, patient follow-up in our study is substantially limited in power because of the small sample size and lack of prospective nature. Confirmation in larger samples is necessary. Also, follow-up did not include repeated measures of ventricular function. But such repeated measures may not necessarily be helpful to resolve the issue of viable myocardium versus inflamed tissue as the origin of the FDG signal in the infarct region. Although viable myocardium would improve in function, this could also be true for ventricles that have an intense but overall more balanced inflammatory response leading to improved healing and less remodeling. And fourth, we included a control group of patients with chronic, stable MI to support our conclusions. But results in this group must be interpreted with caution, too, not only because of the even smaller sample size, but also because glucose utilization in those subjects may be influenced by other pathomechanisms such as remodeling, subclinical ischemia, and heart failure. Nevertheless, the inverse pattern of FDG in infarct versus remote myocardium under heparin suppression in the chronic setting further suggests that elevated infarct activity is a phenomenon of the acute inflammatory phase.

In addition to the aforementioned limitations of FDG as a myocardial inflammation marker and the relatively small sample size, it should be noted that this study was not a prospective project and thereby may have been subject to inherent limitations and bias. It should nevertheless be seen as hypothesis generating for subsequent work, and it may provide a rationale for projects aiming at monitoring of the effect of therapies seeking...
to modulate the inflammatory response to acute infarction to improve myocardial healing. Prior work from our group has, for example, shown that an accelerated but limited inflammatory response by early treatment with eplerenone, a selective aldosterone antagonist, improves early infarct healing in rats.

Furthermore, a recent report has shown some evidence for the anti-inflammatory impact of angiotensin-converting enzyme inhibitors through inhibition of monocyte mobilization from their splenic reservoir. These are examples where the multitarget inflammatory response after MI is already influenced by the current therapy of MI and where molecular imaging of inflammation could provide further insights.

Conclusions

Multimodality imaging using quantitative clinical FDG PET after cardiomyocyte glucose uptake suppression with heparin, combined with multiparametric CMR, confirms prior experimental data and provides noninvasive insights into the acutely infarcted, inflamed myocardium and into the interrelation between myocardium and lymphoid tissue activation. This initial study may serve as a foundation for future work focusing on the early prediction of risk of later remodeling and on the monitoring of new therapies aiming at modulation of the inflammatory response to support myocardial healing.

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Disclosures

None.

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**CLINICAL PERSPECTIVE**

Early treatment by percutaneous coronary intervention is the standard of care in acute myocardial infarction. This is followed by a well-standardized medical treatment. But even optimal therapy cannot prevent that some patients develop heart failure because of cardiac remodeling. It is known that the acute infarct causes an early inflammatory response, which needs to be balanced to ensure optimal wound healing. Because abnormal wound healing may trigger subsequent heart failure development, the early inflammatory phase has emerged as a target for novel therapies. Such novel therapies would benefit from imaging guidance to identify the best time point and best candidates. In this study, an integrative noninvasive imaging approach for characterization of the early inflammatory phase after myocardial infarction is introduced in patients. The approach is based on cardiac magnetic resonance imaging of infarct size and tissue composition, combined with molecular positron emission tomography of glucose utilization, which may be elevated in case of inflammation. If the promising early results presented here are confirmed in larger studies, the technique may be used for the development of novel therapies targeting postinfarct inflammation by providing information about magnitude and quality of the inflammatory reaction in response to the treatment. This may help in the establishment of better care after myocardial infarction, and it may help in tailoring treatment of the individual patient’s biological situation.
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