Bright-Blood T2-Weighted MRI Has High Diagnostic Accuracy for Myocardial Hemorrhage in Myocardial Infarction
A Preclinical Validation Study in Swine

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Background—Myocardial hemorrhage after myocardial infarction (MI) usually goes undetected. We investigated the diagnostic accuracy of bright-blood T2-weighted cardiac MRI for myocardial hemorrhage in experimental MI.

Methods and Results—MI was created in swine by occluding the left anterior descending (n=1100) or circumflex (n=5) coronary arteries for 90 minutes followed by reperfusion for ≤3 days (n=2), 10 days (n=7), or 60 days (n=6). MRI was performed at 1.5 T, using bright-blood T2-prepared steady-state free-precession, T2* and early (1 minute) and late (10–15 minutes) gadolinium enhancement (EGE, LGE, respectively) MRI. Left ventricular sections and histology were assessed for hemorrhage by an experienced cardiac pathologist blinded to the MRI data. Hypointense regions on T2-weighted and contrast-enhanced MRI were independently determined by 3 cardiologists experienced in MRI who were also blinded to the pathology results. Eighty ventricular pathological sections were matched with MRI (n=68 for EGE MRI). All sections with evidence of MI (n=63, 79%) also exhibited hyperintense zones consistent with edema on T2-weighted MRI and infarct on LGE MRI. Myocardial hemorrhage occurred in 49 left ventricular sections (61%) and corresponded with signal voids on 48 T2-weighted (98%) and 26 LGE-MRI (53%). Alternatively, signal voids occurred in the absence of hemorrhage in 3 T2-weighted (90% specificity) and 5 LGE MRI (84% specificity). On EGE MRI, 27 of 43 cases of early microvascular obstruction corresponded with hemorrhage (63% sensitivity), whereas 5 of 25 defects occurred in the absence of hemorrhage (80% specificity). The positive and negative predictive values for pathological evidence of hemorrhage were 94% and 96% for T2-weighted, 84% and 55% for LGE MRI, and 85% and 56% for EGE MRI.

Conclusions—Bright-blood T2-weighted MRI has high diagnostic accuracy for myocardial hemorrhage. (Circ Cardiovasc Imaging. 2011;4:738-745.)

Key Words: myocardial infarction • MRI • hemorrhage

The extent of myocardial hemorrhage after acute myocardial infarction (MI) is influenced by the duration of ischemia, the severity of MI, and reperfusion.1-3 Due to imaging limitations, myocardial hemorrhage after acute MI usually goes undetected. In the absence of a diagnostic technique for myocardial hemorrhage, its clinical significance, including the influence of hemorrhage, if any, on drug treatment response and prognosis, is uncertain.4

Clinical Perspective on p 745

Ex vivo experimental MRI studies have provided insights into the pathological basis of hemorrhage in MI. For example, in acute MI, myocardial capillary damage leads to hemorrhage, which may be enhanced by coronary reperfusion.1-3 However, in vivo MRI studies have been limited because of artifacts from cardiorespiratory motion and blood flow.5 Whereas advances in MRI now enable detection of hemorrhage in the human heart,6 current dark-blood T2-weighted MRI techniques are limited by surface coil intensity problems and spin-echo artifact,7 which may reduce diagnostic accuracy clinically.7,8 The paramagnetic effects of oxidized iron may result in signal loss on T2*- and T2-weighted MRI.1,2 Because changes in myocardial water content and mobility are an early consequence of ischemia,7 alterations in proton...
transverse relaxation times (T2) enable depiction of myocardial edema and hemorrhage.9

The specific aim of the present study was to validate whether or not myocardial hemorrhage can be reliably detected using bright-blood T2-weighted MRI. We hypothesized that bright-blood T2-weighted MRI would have high diagnostic accuracy for myocardial hemorrhage. To investigate this hypothesis further, we used cardiac MRI and pathological studies to evaluate a preclinical model of reperfused MI.

Methods

MI Model

A swine model was adopted because the hearts of swine and humans are similar. Swine were pretreated with antiplatelet drug therapies to mimic clinical practice. Yorkshire swine were pretreated with aspirin 81 mg daily, atenolol 50 mg twice daily, and amiodarone 400 mg twice daily for 5 days. Three hundred milligrams of clopidogrel was given the day before induction of MI. Swine were anesthetized with isofluorane (1.5–3%) and ventilated. Eighteen swine were anesthetized. Three of the first 4 swine had acute intractable ventricular fibrillation during coronary balloon inflation and died (mortality rate 17%). Fifteen swine (weight, 43±9.5 kg) survived occlusion of the left anterior descending coronary artery (n=10) or circumflex (n=5) coronary arteries for 90 minutes followed by reperfusion for ≤3 days (n=2), 10 days (n=7), or 60 days (n=6).

Cardiac MRI

Serial cardiac MRI was performed at 1.5-T MAGNETOM Avanto (Siemens Healthcare, Erlangen, Germany) with 12 surface-coil elements. MRI was performed immediately before euthanasia on days 0 (2 hours post), 3, 10, and 60 after MI. Myocardial water was imaged by bright-blood T2-prepared steady-state free-precession (T2p-SSFP) coupled with automated proton density surface coil intensity correction. T2-infarct imaging was followed by gadolinium (Gd)-DTPA contrast-enhanced MRI. The MRI protocol included segmented ECG-gated SSFP (TrueFISP) cine MRI, T2-prepared SSFP (T2p-SSFP) edema MRI, multi-echo gradient echo (GRE) T2*-weighted, early gadolinium enhancement (EGE, 1 minute after contrast administration), and late gadolinium enhancement (LGE, 10–15 minutes after contrast administration) phase sensitive inversion recovery (PSIR) MRI sequences. Sample images are shown in Figures 1 and 2.

We used bright-blood T2-weighted MRI to avoid bright rim artifacts associated with dark-blood T2-STIR MRI.8 A T2p-prepared single-shot SSFP sequence with parallel techniques to reduce imaging duration was used to repetitively acquire an interleaved T2-weighted image and a proton density weighted reference mid-diastolic image every 2 R-R intervals, using prospective ECG gating. The proton density-weighted image was used for surface coil correction. The typical imaging parameters for this method are listed in Table 1. The T2 preparation time (TE) was 60 ms. Parallel imaging (rate 2) was used and 8 respiratory motion corrected images were obtained per acquisition. The T2* method used a multi-echo GRE sequence that provided T2* contrast and permitted T2* estimates through off-line fitting (Table 1).
Microvascular obstruction (MVO) was defined as a dark area on contrast-enhanced MRI 1, 3, 5, and 7 minutes after contrast injection and within an area of LGE. Early and late MVO were determined on PSIR-FLASH scans obtained 1 and 10–15 minutes after contrast administration. MI was imaged using segmented PSIR turbo fast low-angle shot (Table 1), starting about 9 minutes after intravenous injection of 0.15 mmol/kg of gadolinium diethyltriaminepenta-acetic acid (Gd-DTPA, Magnevist, Berlex). The inversion time to achieve myocardial nulling was typically 250–300 ms.

MRI Analyses
All MRIs were analyzed on a Siemens Leonardo workstation (Siemens Healthcare, Erlangen) by cardiologists with at least 3 years of MRI experience. All of the cardiologists were experienced in reviewing images from patients with acute MI.

Definition and Detection of Hemorrhage on T2-Weighted MRI
Myocardial hemorrhage revealed by either T2- or T2*-weighted MRI was defined as an area with a mean signal intensity <2 SD of the mean signal intensity of the surrounding affected brighter area. T2- and T2*-weighted and contrast enhanced MRI were independently determined by 3 cardiologists blinded to the pathology results. Images were deidentified and analyzed in random order. At the end of the assessment, disagreement was resolved by consensus.

Infarct Size
Infarct size was assessed on contrast-enhanced images, using validated software and expressed as a percentage of left ventricular mass.

Pathology
Spatially matched left ventricular sections were visually inspected, photographed, and processed for histology with stains that included hematoxylin and eosin and Perls stain. Gross images and histology were scored for myocardial hemorrhage by an experienced cardiac pathologist blinded to all other data. The main histopathologic feature of hemorrhage was extravasated red blood cells within the interstitium between cardiac myocytes.

Statistics
The frequencies of categorical data were analyzed with a χ2 test. Inter-rater agreement was determined with the κ-statistic. The sensitivity, specificity, positive predictive value, and negative predictive values of low signal areas judged by rater consensus were determined for myocardial hemorrhage on bright-blood T2-weighted MRI and T2*-weighted MRI and MVO on EGE and LGE MRI, respectively. To allow for possible correlation between images obtained from the same subject (ie, clustered binary data), sensitivity and specificity were estimated and adjusted using the method of McCarthy and Guo.
A significance level of 5% was used in all tests. No adjustment was made to probability values to account for multiple testing. All statistical analyses were performed using STATA version 7 (Statacorp, College Station, TX).

Results

Eighteen swine were anesthetized and subjected to coronary balloon inflation for 90 minutes to induce reperfused MI, and 15 (83%) swine survived (Table 2). Eighty ventricular slices of pathology from these 15 swine were matched with MRI (n/H11005 68 for EGE MRI, n/H11005 55 for T2* MRI, Table 2). The frequency of myocardial hemorrhage is described in Tables 2 and 3. Examples of axial left ventricular MRI scans and matched pathological sections obtained from 1 pig with anterior MI and 1 pig with infero-posterior MI are shown in Figures 1 through 3.

Table 1. Cardiac MRI Scan Parameters

<table>
<thead>
<tr>
<th></th>
<th>Echo Time (TE), ms</th>
<th>Repetition Time (TR), ms</th>
<th>Flip Angle, Degree</th>
<th>Band Width, Hz/Pixel</th>
<th>Field of View, mm</th>
<th>Spatial Resolution, mm²</th>
<th>Slice Thickness, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cine MRI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>True FISP (SSFP)</td>
<td>1.6</td>
<td>25</td>
<td>80</td>
<td>930</td>
<td>300×300</td>
<td>156×192</td>
<td>1.9×1.6</td>
</tr>
<tr>
<td>T2-weighted MRI</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>T2p-SSFP</td>
<td>1.6</td>
<td>3.2</td>
<td>60–90</td>
<td>977</td>
<td>245×327</td>
<td>145×256</td>
<td>1.7×1.3</td>
</tr>
<tr>
<td>T2*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2*</td>
<td>†</td>
<td>154</td>
<td>20</td>
<td>977</td>
<td>245×327</td>
<td>128×256</td>
<td>1.9×1.3</td>
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<td>EGE MRI</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSIR-FISP</td>
<td>1.1</td>
<td>557</td>
<td>50</td>
<td>1000</td>
<td>300×400</td>
<td>108×192</td>
<td>2.8×2.1</td>
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<tr>
<td>LGE MRI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSIR turbo FLASH</td>
<td>2.53</td>
<td>403</td>
<td>25</td>
<td>201</td>
<td>215×300</td>
<td>119×256</td>
<td>1.8×1.2</td>
</tr>
</tbody>
</table>

EGE indicates early gadolinium-enhanced MRI; FISP, fast imaging in steady-state precession; LGE, late gadolinium-enhanced MRI; MVO, microvascular obstruction; SSFP, steady-state free precession; PSIR, segmented phase-sensitive inversion recovery; and turbo FLASH, fast low-angle shot.

The T2 preparation time (TE) was 60 ms. Parallel imaging (rate 2) was used, and 8 respiratory motion–corrected images were obtained per acquisition.

†The T2* protocol acquired 16 echoes with echo spacing of 2.32 ms, with a minimum echo time of 1.58 ms and a maximum echo time of 36.38 ms (4 phase encodes were acquired per R-R, with 154 ms imaging duration). The PSIR FLASH had 25 views per segment.

A significance level of 5% was used in all tests. No adjustment was made to probability values to account for multiple testing. All statistical analyses were performed using STATA version 7 (Statacorp, College Station, TX).

Results

Eighteen swine were anesthetized and subjected to coronary balloon inflation for 90 minutes to induce reperfused MI, and 15 (83%) swine survived (Table 2). Eighty ventricular slices of pathology from these 15 swine were matched with MRI (n/H11005 68 for EGE MRI, n/H11005 55 for T2* MRI, Table 2). The frequency of myocardial hemorrhage is described in Tables 2 and 3. Examples of axial left ventricular MRI scans and matched pathological sections obtained from 1 pig with anterior MI and 1 pig with infero-posterior MI are shown in Figures 1 through 3.

Sixty-three (79%) sections had pathological evidence of infarction, and all of the pathological sections with evidence of MI also exhibited hyperintense zones consistent with edema on bright-blood T2-weighted MRI and infarct on LGE-MRI. Thirty two (51%) of the images with LGE had

Table 2. List of Subjects (n=15), Timing of MRI Scans After MI, and Availability of Scan Data Matched With Pathology

<table>
<thead>
<tr>
<th>Days After MI</th>
<th>Animal</th>
<th>Mean Infarct Size, % of LV*</th>
<th>Images Matched With Pathology per Subject, n=80, 100%</th>
<th>Images With Pathological Evidence of Hemorrhage, n=49, 61%</th>
<th>EGE MRI Scan Images, n=68, 85%</th>
<th>T2* Scan Images, n=55, 69%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>1296</td>
<td>13.7</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Day 3</td>
<td>1227</td>
<td>16.5</td>
<td>10</td>
<td>5</td>
<td>7</td>
<td>10</td>
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<tr>
<td>Day 10</td>
<td>399</td>
<td>21.9</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Day 10</td>
<td>1222</td>
<td>13.1</td>
<td>8</td>
<td>6</td>
<td>6</td>
<td>8</td>
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<tr>
<td>Day 10</td>
<td>1223</td>
<td>9.6</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>6</td>
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<tr>
<td>Day 10</td>
<td>1224</td>
<td>4.8</td>
<td>7</td>
<td>4</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Day 10</td>
<td>1225</td>
<td>12.7</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Day 10</td>
<td>1226</td>
<td>20.9</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Day 10</td>
<td>1229</td>
<td>13.9</td>
<td>6</td>
<td>5</td>
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<td>5</td>
</tr>
<tr>
<td>Day 60</td>
<td>397</td>
<td>11.3</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Day 60</td>
<td>400</td>
<td>9.2</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Day 60</td>
<td>511</td>
<td>1.0</td>
<td>5</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Day 60</td>
<td>512</td>
<td>5.7</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Day 60</td>
<td>754</td>
<td>15.5</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Day 60</td>
<td>758</td>
<td>2.4</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction; LV, left ventricle; and EGE, early gadolinium-enhancement MRI.

*Mean±SD infarct size was 11.5±6.2% of left ventricular mass.
evidence of MVO on EGE MRI. The frequency of inter-rater agreements for areas of low signal intensity within the infarct zone are described in Table 4.

The sensitivity, specificity, positive predictive values, and negative predictive values for detection of myocardial hemorrhage with bright-blood T2-weighted MRI, MVO on LGE-MRI, MVO on EGE MRI, and signal voids on T2*-weighted MRI are shown in Tables 5, 6, 7, and 8, respectively. Myocardial hemorrhage revealed by pathological assessment occurred in 49 left ventricular sections (61%) and corresponded with signal voids on 48 T2-weighted MRI (98%; Table 5) and 26 LGE-MRI (53%; Table 6) images. Alternatively, signal voids occurred in the absence of hemorrhage in 3 T2-weighted MRI (90% specificity) and 5 LGE-MRI (84% specificity). On EGE (1 minute) MRI (Table 7), 27 of 43 cases of early MVO corresponded with hemorrhage (63% sensitivity), whereas 5 of 25 defects occurred in the absence of hemorrhage (80% specificity). On T2*-weighted MRI, 35 of 37 low signal intensity areas corresponded with hemorrhage (95% sensitivity), whereas 1 of 17 low signal intensity areas occurred in the absence of hemorrhage (Table 8).

Discussion

We have used an in vivo large animal model of reperfused MI which closely represents human MI to validate bright-blood T2-weighted MRI for the detection of myocardial hemorrhage.

Our results indicate that bright-blood T2-prepared SSFP MRI has high diagnostic accuracy for myocardial hemorrhage. The heterogeneity of signal intensity associated with acute MI on T2-weighted MRI is partially due to intramyocardial hemorrhage. Our results are relevant to clinical practice since recent cohort studies have shown that myocardial hemorrhage is an independent predictor of left ventricular remodeling after MI\(^6,17\) and is associated with adverse clinical outcomes.\(^18\)

Early and late contrast enhancement MRI scan parameters are physiologically different from hemorrhage because the contrast-enhanced MRI images are influenced by both infarction and altered perfusion. Therefore, even though early and late MVO on gadolinium-enhanced MRI colocalize with the hemorrhage, infarct and MVO are not as closely linked physiologically or diagnostically as T2 and T2* are with hemorrhage. Our observations indicate that hemorrhage was spatially coincident with early MVO but do not prove a causal relationship. Consequently, our observation that the presence of signal voids on T2-weighted MRI has higher specificity than MVO on EGE and LGE MRI (Table 6) for myocardial hemorrhage indicates that only the availability of bright-blood T2-weighted MRI enables a diagnosis of myocardial hemorrhage, when present, to characterize infarct pathology and MVO noninvasively. The reduced specificity of MVO for hemorrhage may be because, among other reasons, MVO can be caused by capillary obstruction.

Iron accumulation results in signal loss in affected tissues because the paramagnetic effects of iron induce local irregularities in the magnetic field, which in turn cause water protons to lose phase coherence.\(^19,20\) This effect is concentration dependent.\(^21\) T2* is related to T2 by summation of transverse relaxation (T2) and magnetic inhomogeneity.
T2* should be the superior approach to detecting iron changes for detecting myocardial hemorrhage. Theoretically, observations are consistent with those of Reeder et al,22 which problems related to shimming and susceptibility artifacts. Our unreliable in these areas.23 Therefore, because the left ventricular septum is more remote from these areas, myocardial T2* measurements have mainly been restricted to the left ventricular septum.25 In fact, myocardial T2* measurements have mainly been restricted to the left ventricular septum in clinical practice. T2 is influenced by energy exchange with neighboring magnetic moments and is also reduced by oxidized iron deposits but not by extrinsic magnetic field inhomogeneities. Recently, a new T2 method has been developed as an alternative to T2* MRI.23 In patients with thalassemia, the breath-hold, black-blood spin-echo method with a nonselective refocusing train developed by He et al24 confers good reproducibility for myocardial T2 measurement, albeit restricted to the left ventricular septum.23 In fact, myocardial T2 and T2* values have a strong linear correlation in patients with iron overload (R²=0.89) indicating that iron accumulation has comparable effects on the relaxation values of these parameters.

Both T2- and T2*-weighted MRI have potential applications for detecting myocardial hemorrhage. Theoretically, T2* should be the superior approach to detecting iron changes associated with hemorrhage. In our experience, T2-prepared SSFP has enough sensitivity to pick up on most of these hemorrhages, and, whereas T2* measurements are restricted to the left ventricular septum, this is not the case for T2*, making this approach potentially more applicable for use in patients with a history of MI. Only recently have technical advances overcome previous problems such that T2-weighted cardiac MRI is now possible in acute MI patients.7,8

Table 5. Detection of Myocardial Hemorrhage Using Bright-Blood T2*-Weighted MRI in 80 Images Matched With Pathology

<table>
<thead>
<tr>
<th>Low Signal Intensity Area</th>
<th>No Low Signal Intensity Area</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage, n=49</td>
<td>48</td>
<td>98% (94–100%) Sensitivity</td>
</tr>
<tr>
<td>No hemorrhage, n=31</td>
<td>3</td>
<td>90% (83–98%) Specificity</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive value. Sensitivity and specificity were adjusted for possible correlation between images for clustered binary data.16

known as T2 prime (T2′): 1/T2′ = 1/T2 + 1/T2*. The short echo times used in the multigradient method mean it is less sensitive to motion artifact. However, T2*-weighted MRI has several limitations for assessment of myocardial hemorrhage in routine clinical practice. T2* measurements are affected by problems related to shimming and susceptibility artifacts. Our observations are consistent with those of Reeder et al,22 which indicated that field homogeneities from the anterior and posterior cardiac veins and lungs rendered T2* measurement unreliable in these areas.23 Therefore, because the left ventricular septum is more remote from these areas, myocardial T2* measurements have mainly been restricted to the left ventricular septum in clinical practice.

T2 is influenced by energy exchange with neighboring magnetic moments and is also reduced by oxidized iron deposits but not by extrinsic magnetic field inhomogeneities. Recently, a new T2 method has been developed as an alternative to T2* MRI.23 In patients with thalassemia, the breath-hold, black-blood spin-echo method with a nonselective refocusing train developed by He et al24 confers good reproducibility for myocardial T2 measurement, albeit restricted to the left ventricular septum.23 In fact, myocardial T2 and T2* values have a strong linear correlation in patients with iron overload (R²=0.89) indicating that iron accumulation has comparable effects on the relaxation values of these parameters.

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Our data (Table 3) suggest that hemorrhage may be more frequently observed 10 days after MI than acutely (days 0–3) or in the longer term (day 60). This observation is consistent with the findings of Folz et al26 in a pig model of reperfused MI and also of hemorrhagic transformation after brain infarction.27 The pathological basis of a higher frequency of detectable hemorrhage around days 7–10 could be due to enhanced capillary fragility, red cell lysis, and the development of coagulative necrosis in the infarct healing period. In the longer term, tissue and vascular remodeling may make the chronic appearances of hemorrhage (eg, hemosiderin deposition) less apparent.

Hemoglobin and related degradation products have differing magnetic susceptibilities according to their oxidation status and compartmentalization within intact cells or compartmentalization after cell death and release to the extracellular space. T2 and T2* shortening (ie, relaxation) occur due to the paramagnetic effects of deoxyhemoglobin, which accumulates in coagulative hemorrhagic necrosis. Therefore, T2*-weighted MRI may be less susceptible to detection of fresh hemorrhage in the hours after acute MI compared with a few days later, when deoxyhemoglobin and hemosiderin have accumulated in the infarct zone.

The bright-blood T2*-weighted MRI method that we have used was developed to overcome some of the limitations with dark-blood T2*-weighted MRI, including motion artifact and signal variation with depth of field because of coil sensitivity issues, which may both impair diagnostic accuracy.7,8 T2*-prepared SSFP involves a T2 preparation pulse with a steady-state free precession readout. This method was developed by Kellman et al7 in our laboratory and is available as a

Table 7. Detection of Myocardial Hemorrhage According to MVO on EGE MRI (1 Minute) in 68 Images Matched With Pathology

<table>
<thead>
<tr>
<th>Early MVO</th>
<th>No Early MVO</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage, n=43</td>
<td>27</td>
<td>16</td>
</tr>
<tr>
<td>No hemorrhage, n=25</td>
<td>5</td>
<td>20</td>
</tr>
</tbody>
</table>

PPV indicates microvascular obstruction; EGE, early gadolinium-enhanced MRI; PPV, positive predictive value; and NPV, negative predictive value. EGE MRI scans were not available for 12 tissue sections.

Table 8. Myocardial Hemorrhage According to Low Signal Intensity Regions on T2*-Weighted MRI in 55 Images Matched With Pathology

<table>
<thead>
<tr>
<th>Low Signal Intensity Area</th>
<th>No Low Signal Intensity Area</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage, n=37</td>
<td>35</td>
<td>95% (86–100%) Sensitivity</td>
</tr>
<tr>
<td>No hemorrhage, n=18</td>
<td>1</td>
<td>94% (88–100%) Specificity</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive value. Of 80 T2*-weighted MRI acquisitions, 55 were of diagnostic quality and 35 were affected by posterior field artifacts.
work-in-progress pulse sequence. The $T_2$-prepared SSFP is available as a single-shot method, meaning that it can be used during free breathing. Kellman’s method also involves acquisition of a $B_1$ field map to provide a proton density reference image, which is used to estimate coil sensitivity. Motion correction and averaging are used to enhance signal-to-noise ratio and parallel imaging with phase encode undersampling of the $T_2$-weighted image is used to accelerate imaging.

Our results lend support for research with $T_2$-weighted MRI for the detection of myocardial hemorrhage in patients with a history of acute MI. Recent studies by Ganame et al.\(^{16}\) and Mather et al.,\(^{17}\) using dark-blood STIR-MRI, have found that myocardial hemorrhage is an independent predictor of adverse left ventricular remodeling in patients treated by primary percutaneous coronary intervention for a first ST-elevation–MI. Mather et al.\(^{17}\) also found that hemorrhage was associated with QRS duration on a signal-averaged ECG. In a recent 2-center cohort study involving 346 patients with reperfused ST-elevation–MI, Eitel et al.\(^{18}\) demonstrated that a recent 2-center cohort study involving 346 patients with reperfused ST-elevation–MI. Eitel et al.\(^{18}\) demonstrated that a hypointense infarct core on dark-blood $T_2$-weighted MRI was a univariable predictor of death, reinfarction, and new congestive heart failure after MI. Our results validate bright-blood $T_2$-weighted MRI for detection of myocardial hemorrhage, supporting further studies of the functional and prognostic significance of hemorrhage revealed by this new method in patients with acute MI.

Given that myocardial hemorrhage revealed by $T_2$-weighted MRI is associated with adverse clinical outcomes after MI,\(^{19}\) the question now arises as to what therapeutic strategies might be appropriate to improve outcomes patients with this complication.

Limitations

Our observations were not supported by measurement of myocardial iron concentrations. However, hemorrhage and iron were verified by histology, including with Perls stain.

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Disclosures

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References


CLINICAL PERSPECTIVE

Myocardial hemorrhage after myocardial infarction (MI) usually goes undetected. T2-weighted cardiac MRI has the potential to detect myocardial hemorrhage because of the paramagnetic effects of deoxyhemoglobin. We have used an in vivo large animal model of reperfused MI which closely represents human MI to validate bright blood T2-weighted MRI for the detection of myocardial hemorrhage. MI was created in swine by occluding the left anterior descending coronary artery (n=10) or circumflex (n=5) for 90 minutes followed by reperfusion for ≤3 days (n=2), 10 days (n=7), or 60 days (n=6). MRI was performed at 1.5 T, using bright-blood T2-prepared steady-state free precession, T2*, and gadolinium-enhanced MRI. Left ventricular sections and histology were assessed for hemorrhage by an experienced cardiac pathologist blinded to the MRI data. Hypointense regions on T2*-weighted and contrast-enhanced MRI were independently determined by 3 cardiologists experienced in MRI who were also blinded to the pathology results. In 80 images matched with histology, the positive and negative predictive values for pathological evidence of hemorrhage were 94% and 96% for T2-weighted, 84% and 53% for late gadolinium-enhanced MRI, and 84% and 56% for early gadolinium enhancement. Our results indicate that T2*-weighted MRI has high diagnostic accuracy for myocardial hemorrhage. The heterogeneity of signal intensity associated with acute MI on T2*-weighted MRI is partially due to intramyocardial hemorrhage. Our results are relevant to clinical practice since recent cohort studies have shown that myocardial hemorrhage is an independent predictor of adverse left ventricular remodeling after MI.
Bright-Blood T2-Weighted MRI Has High Diagnostic Accuracy for Myocardial Hemorrhage in Myocardial Infarction: A Preclinical Validation Study in Swine

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