Contrast-Enhanced Magnetic Resonance and Thallium Scintigraphy in the Detection of Myocardial Viability

A Prospective Comparative Study

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SUMMARY

The aim of the present study was to prospectively compare contrast-enhanced magnetic resonance imaging (CE-MRI) with single-photon emission tomography using ²⁰¹Thallium chloride (SPECT Tl) in the detection of myocardial viability. Patients with chronic coronary artery disease and systolic dysfunction defined by an ejection fraction (EF) ≤ 45% were included. CE-MRI was performed 10-15 minutes after the administration of a gadolinium-based contrast agent using an Inversion Recovery Turbo FLASH (fast low-angle shot) sequence. A 4-hour rest redistribution protocol was used for SPECT Tl. Radionuclide ventriculography was used for the assessment of EF. Forty patients with an EF of 33.1 ± 7.7% were included. Thirty-two underwent a follow-up examination after revascularization. Comparison of viability assessment was performed in 1360 segments. Agreement was noted in 1065 (78.3%) segments, resulting in a kappa value of 0.336. Discrepancies were observed in 96 SPECT Tl viable segments that were described as nonviable according to CE-MRI and in 199 SPECT Tl nonviable segments that were viable in the CE-MRI study.

In patients undergoing the follow-up examination, EF increased by 5.5 ± 7.3% (33.6 ± 8.6% to 39.2 ± 9.7%), but the relation between the amount of dysfunctional viable myocardium defined by both methods studied and the change in EF after revascularization was very weak and not statistically significant.

Moderate agreement in the myocardial viability assessment between CE-MRI and SPECT Tl was observed. CE-MRI seems to be more accurate in identifying myocardial viability in inferior and inferolateral segments. We were unable to verify if either of the methods studied is useful for the prediction of EF improvement after revascularization.

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Key words: Magnetic resonance imaging, Myocardial viability, SPECT Thallium scintigraphy, Coronary artery disease, Left ventricular systolic dysfunction

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Reduced ejection fraction (EF) is a strong predictor of poor prognosis in patients with coronary artery disease (CAD). Impaired left ventricular systolic function does not necessarily represent irreversible injury.\textsuperscript{1) Assessment of the extent of viable and nonviable myocardium in clinical decision-making is especially important in cases where the surgical revascularization of the myocardium is considered due to the increased perioperative mortality and morbidity in these patients. It has been shown that patients with a significant amount of dysfunctional but viable myocardium benefit the most from the revascularization.\textsuperscript{2,3) On the contrary, the low amount of viable tissue may lead to an increased number of perioperative complications without a long-term benefit.

Magnetic resonance is a newer imaging technique used for the clinical evaluation of patients with CAD. The administration of a gadolinium-based contrast agent enables direct visualization of myocardial perfusion.\textsuperscript{4) Delayed scans display the extent of irreversible injury as the contrast agent increasingly accumulates in the areas of acute necrosis and subsequent scar tissue.\textsuperscript{5) Contrast-enhanced magnetic resonance imaging (CE-MRI) thus has become a novel technique in the assessment of myocardial viability. In comparison to other techniques, it is characterized by more detailed visualization of irreversible myocardial damage.\textsuperscript{6,7) The aim of this study was to compare CE-MRI with single photon emission tomography using Thallium-201 chloride (SPECT Tl), which is one of the most common diagnostic techniques used in diagnosing myocardial viability. These methods were compared with respect to both the viability assessment and in predicting an improvement in global systolic function after revascularization.

\textbf{METHODS}

1. Study population: Patients with left ventricular systolic dysfunction and coronary artery disease who were indicated for coronary artery by-pass surgery were enrolled. Systolic dysfunction was defined by EF $\leq 45\%$ determined by radionuclide ventriculography (RNV) or dynamic magnetic resonance imaging (cine-MRI).

Patients with the following conditions were excluded from the study: significant valvular heart disease, acute coronary syndrome in the past 4 months prior to entering the study and during the follow-up, cardiomyopathy with a suspected nonischemic origin and contraindication to magnetic resonance or SPECT Tl imaging. The local ethics committee approved the study and the patients provided informed, written consent before entering the study.

2. Study protocol: Myocardial viability and left ventricular systolic function were assessed before revascularization. Patients who had no signs of myocardial
viability (according to both SPECT Tl and CE-MRI) in the myocardium supplied by the coronary artery designated for revascularization, and those who were without limiting symptoms of angina pectoris were excluded from the study for ethical reasons.

The follow-up examination included left ventricular systolic function assessment performed at least 4 months after the revascularization procedure.

For the purpose of myocardial viability and regional systolic function assessment, the myocardium of the left ventricle was depicted in corresponding short and long axis views. The short axis views were acquired at 1 cm increments from 1 cm below the insertion of the mitral valve to the apex. The 2 distal short axis slices from the apical portion of the ventricle were divided into 4 segments of 90 degrees. The rest of the short axis views were divided into 6 segments of 60 degrees. The segments were aligned using landmarks provided by the insertion of the right ventricle into the septum. The apex was evaluated separately from horizontal and vertical long axis views. Myocardial viability was evaluated both by SPECT Tl and CE-MRI. RNV and cine-MRI were used for the assessment of left ventricular systolic function.

3. Myocardial viability assessment:

3-1. Thallium scintigraphy.

A dual-head, digital, rotating gamma camera (VariCam (Elscint) with infrared body contouring and general all-purpose collimators was used. A 10% window was centred at photo peaks of 70 keV and 167 keV. Gated SPECT (60 projections each for 30 seconds, a circular 180° orbit, matrix 64 × 64, zoom 1.27) of the myocardium was performed 4 hours after intravenous administration of 80 - 120 MBq of Thallium-201 chloride (Tl). The dose of Tl was adjusted according to the body weight of the patient. Data acquisition was performed in both the supine and prone positions with the left arm raised. Cardiac slicing in the long and short views of the left ventricle was performed using a conventional software processing system (Xpert-Pro), with no correction for scatter or attenuation. The myocardial viability in each segment was assessed semiquantitatively by the consensus of 2 nuclear medicine specialists. The segments were scored 1 - 0.66 - 0.33 - 0. A score of 1 was used for normal Tl uptake with activity of > 80% of the maximum in the myocardium evaluated. Scores of 0.66 and 0.33 represented mild and moderate defects in Tl uptake and a score of 0 described Tl activity of < 50% and these segments were considered to be nonviable.8)

3-2. Contrast-enhanced magnetic resonance imaging.

A high-field 1.0 Tesla MR system Magnetom Expert (Siemens) was used for contrast-enhanced magnetic resonance imaging. The viability study was performed 12-25 minutes after the administration of 0.15 mmol/kg of gadolinium-based contrast agent using an Inversion Recovery Turbo FLASH (fast low-angle
shot) sequence with a slice thickness of 10 mm, in plane resolution 1.5 mm × 1.8 mm. Inversion times were adjusted individually in each patient to attenuate the signal from normal myocardium.

The myocardial viability in each segment was assessed according to the relative amount of contrast-enhanced tissue within the segmental area. The segments were scored visually semiquantitatively by the consensus of 2 experienced observers using a 5-point scale. A score of 1 represented segments with no contrast enhancement. A score of 0.75 indicated segmental area hyperenhancement of 1 to 25 percent, a score of 0.5 hyperenhancement of 26 to 50 percent, and a score of 0.25 hyperenhancement of 51 to 75 percent. A score of 0 was used for segments with hyperenhancement exceeding 76 percent of the segmental area.

We assumed that the visual assessment was an accurate method with which to quantify the extent of scar tissue, as was recently reported by Schuijf, et al.9)

In order to permit a binary distinction of CE-MRI between viable and non-viable myocardium, the segments with ≤ 50% scar were designated as viable and those with > 50% scar as nonviable.10)

4. Left ventricular systolic function assessment:

4-1. Global systolic function.

Global systolic function of the left ventricle was evaluated by equilibrium, ECG gated isotope ventriculography using autologous erythrocytes labeled in vivo by Technetium -99m pertechnate. A digital rotating gamma camera (Elscint) with an Xpert-Pro computer system (Elscint) was used. The images were taken in left anterior oblique projections. Global systolic function was assessed using a conventional software system (Elscint). Manual tracking of the borders of the left ventricle, when necessary, was performed by the consensus of 2 specialists. Special attention was given to the fact that both examinations included in the study protocol were performed in the same projection. Based on these data, end-diastolic and end-systolic volumes were calculated.

In patients in whom it was not possible to perform RNV, the EF was calculated from cine-MRI data obtained from short axis views using standard segmentation software provided by the manufacturer (Argus).

4-2. Regional systolic function assessment.

Gradient echo sequences - segmented FLASH were used for the acquisition of cine-MRI images. Regional myocardial wall systolic function was assessed visually and scored semiquantitatively by the consensus of 2 experienced observers: 3 - normal, 2 - mild hypokinesis, 1 - severe hypokinesis, and 0 - akinesis/dyskinesis. Segments with a score of less than 3 were considered dysfunctional.

5. Data acquisition and statistical analysis: Data collection for viability studies and systolic function assessment was performed independently. Both methods were compared with regard to the myocardial viability assessment and improve-
ment in global left ventricular systolic function.

The change in EF was related to the mass of dysfunctional viable myocardium (DVM), which was defined by the number of dysfunctional viable segments divided by the total number of segments in the myocardium evaluated. The EF was considered improved if it increased ≥5% after revascularization.11,12)

The t-test and Fischer exact test were used to compare the differences between the 2 groups. The level of agreement in the distinction between viable and nonviable myocardium was calculated using the kappa statistic. The linear regression model characterized the association between the EF change and myocardial viability defined both by SPECT TI and CE-MRI.

RESULTS
1. Study population: A total of 40 patients were included in the study. Two patients did not undergo the planned myocardial revascularization. Both had a history of anterior myocardial infarction and were indicated for revascularization of the left anterior descending coronary artery (LAD). CE-MRI and SPECT TI viability studies revealed a large extent of irreversible myocardial damage in the myocardium supplied by the LAD. Thirty-eight patients underwent myocardial revascularization. Surgical revascularization was performed in 37 of the patients and percutaneous coronary intervention was chosen for one patient who refused the planned coronary surgery. Two patients died of complications shortly after the operation. Two patients refused to undergo follow-up examinations and one was

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<th>Table I. Characteristics of Study Population</th>
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<tr>
<td>Number of patients (women)</td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>History</td>
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<tr>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
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<tr>
<td>Arterial hypertension</td>
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<tr>
<td>Hyperlipidemia</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Ejection fraction before revascularization (%)</td>
</tr>
<tr>
<td>Extent of coronary artery disease</td>
</tr>
<tr>
<td>Three vessel disease</td>
</tr>
<tr>
<td>Two vessel disease</td>
</tr>
<tr>
<td>One vessel disease</td>
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<tr>
<td>Number of vessels revascularized *</td>
</tr>
<tr>
<td>Time from revascularization to follow-up exam (days) *</td>
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Values are expressed as the number of patients (%) or mean (± standard deviation). * signifies the subset of study population (32 patients) who underwent a follow-up examination at least 4 months after the revascularization.
lost to follow-up. The follow-up examination was performed in 33 patients. One patient was excluded from the final analysis because of signs of constrictive pericarditis that were apparent in a follow-up cine-MRI study. No patient was excluded from the study because of myocardial infarction or worsening of the cardiac symptoms during the period of follow-up. The principal characteristics of the study population are given in Table I.

2. Myocardial viability assessment: Myocardial viability was assessed in all patients entering the study. A total of 1360 segments were evaluated. The detailed results of head to head comparison of segmental myocardial viability scores are shown in Table II.

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<tr>
<th>Table II. Comparison of Myocardial Viability Assessment Using CE-MRI and SPECT Tl</th>
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<tbody>
<tr>
<td>SPECT Tl (n)</td>
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<tr>
<td>Score number</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>0.75</td>
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<td>0.5</td>
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<td>0.25</td>
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CE-MRI indicates contrast enhanced magnetic resonance imaging; n, number of segments; and SPECT Tl, single photon emission tomography using Thallium-201 chloride.

<table>
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<th>Table III. Agreement in Diagnosing Myocardial Viability Between CE-MRI and SPECT Tl</th>
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<tr>
<td>SPECT Tl (n)</td>
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<tr>
<td>--------------</td>
</tr>
<tr>
<td>CE-MRI (n)</td>
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<tr>
<td>Nonviable</td>
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kappa = 0.336.
Myocardial viability was defined as contrast enhancement ≤ 50% of segmental area and Thallium activity ≥ 50% of the maximum in the myocardium evaluated.
CE-MRI indicates contrast enhanced magnetic resonance imaging; n, number of segments; and SPECT Tl, single photon emission tomography using Thallium-201 chloride.
Five hundred and thirteen of 944 (54.3%) segments with normal Tl uptake displayed signs of irreversible injury on CE-MRI study and 44 (13.4%) of 328 SPECT Tl nonviable segments had no signs of contrast enhancement on CE-MRI study.

Table III shows a pairwise comparison of both methods in regard to the binary (yes/no) evaluation of segmental myocardial viability. An agreement in the myocardial viability assessment was achieved in 78% of the segments, which reflects a kappa value of 0.336. The discordant results were observed in 199 SPECT Tl nonviable/CE-MRI viable segments and 96 SPECT Tl viable/CE-MRI nonviable segments.

SPECT Tl nonviable/CE-MRI viable segments were found in 28 patients. In 16 of these 28 patients, their number exceeded 15% of all segments in the myocardium evaluated and in 3 patients their number surpassed 30%. They were localized significantly more often in the inferior and inferolateral wall \( (P < 0.0001) \). CE-MRI viability was observed in 103 (79.2%) of 130 SPECT Tl nonviable segments in the inferior and inferolateral walls as opposed to 96 (48.5%) of 198 segments in the remaining myocardial areas.

On the other hand, SPECT Tl viable/CE-MRI nonviable segments were found in 29 patients. CE-MRI showed signs of contrast enhancement in more than half of the myocardial segments in 28 of these patients. In 4 patients the number of SPECT Tl viable/CE-MRI nonviable segments exceeded 15% of all myocardial segments. Two patients with a significant extent of contrast enhancement and CE-MRI nonviable segments had a completely normal SPECT Tl myocardial scan.

3. Assessment of global systolic function after revascularization: Follow-up examination after revascularization was performed in 32 of 40 patients entering the study. The preferred method used for global systolic function assessment was RNV. However, in 4 patients RNV could not be used due to technical reasons and the EF was measured from cine-MRI data both before and after revascularization.

The mean time from the revascularization to the follow-up study was 168 ± 36 days.

The mean EF increased by 5.5 (± 7.3%) (from 33.6 ± 8.8 to 39.2 ± 9.7) and this increase was statistically significant \( (P < 0.0001) \). An improvement of global systolic function of the left ventricle (defined as EF increase ≥ 5%) was observed in 17 (53.1%) patients. EF in this subgroup increased by 10.6% (from 33.7 (± 8.6) to 44.4 (± 8.3)%).

The relation between DVM and the change in EF after revascularization in the whole group was very weak and not statistically significant (Figure). The trends were similar for both methods studied. Redefining DVM by a lower wall motion score (< 2) and/or different CE-MRI and SPECT Tl viability scores also
did not yield a statistically significant relation.

**DISCUSSION**

The results of the present study demonstrate only moderate agreement between CE-MRI and SPECT Tl. A discrepancy in the viability assessment was observed in 22% of the segments (Table III). Similar results were recently reported by Nelson, *et al.*

Better agreement was observed when assessing the septal and anterolateral segments (kappa, 0.419) in comparison to segments localized in the inferior and
inferolateral wall (kappa, 0.169). The discordant results might be attributed to both imaging artifacts and principal differences in the definition of myocardial viability between the 2 methods studied.

The SPECT TI definition of segmental viability is based on radioisotope activity related to the maximum detected in the myocardium evaluated, whereas CE-MRI defined viability gives information about the relative extent of viable and scar tissue in a given segment not reflecting myocardial thickness or an absolute amount of viable tissue. Limited thinning of the myocardium without irreversible damage might result in a viability defect in a SPECT TI study. On the other hand, the patients with extensive subendocardial scars may thus exhibit high (> 50%) TI activity in segments with a large amount of irreversibly damaged myocardial tissue. In our study, 2 patients with extensive CE-MRI contrast enhancement had completely normal SPECT TI scans.

Another possible source of discordant results might be imaging artifacts. A slight overestimation of infarct size by CE-MRI was observed in an experimental model of acute myocardial infarction, but it is not clear whether the same is applicable to chronic fibrous infarction scars. We can also speculate that the voxel size of 1.5 × 1.8 × 10 mm might lead to inaccuracies in the viability assessment in segments with a thinned myocardial wall. Some inaccuracies in segmental comparison may be explained by the marked difference in pixel size between SPECT TI and CE-MRI (6 × 6 mm versus 1.5 × 1.8 mm).

Soft tissue photon attenuation artifacts are often observed in myocardial SPECT imaging. They may mimic myocardial viability defects, especially in the inferior and lateral myocardial wall. We therefore assume that this effect could explain some discrepancies. SPECT nonviable/CE-MRI viable segments were more frequently observed in the inferior and inferolateral wall and a significant portion of SPECT nonviable segments had no signs of irreversible injury on CE-MRI.

From a clinical point of view, it is difficult to interpret the observed discrepancies between the 2 methods studied. Two-thirds of the discordant results were due to SPECT TI nonviable/CMRI viable segments. In 16 (40%) patients their number comprised more than 15% of the segments in the myocardium evaluated and that amount might influence clinical decision making. It is not clear whether it is reasonable to revascularize chronically thinned SPECT TI nonviable segments that fulfill CE-MRI criteria for viability.

SPECT TI viable segments with a marked extent of contrast enhancement on CE-MRI were identified in 29 patients, however, their number surpassed 15% of all segments in the myocardium evaluated in only 4 of the 29 patients. Systolic function in these segments probably does not improve after revascularization, although the remaining viable tissue displayed on SPECT TI may have a prognostic...
The change in global systolic function after revascularization was the only variable that was prospectively evaluated in our study, since the improvement of EF might be one of the determinants of improved prognosis after revascularization. Regional systolic function was not assessed at the follow-up examination. We were not confident when identifying and analyzing the identical segments during follow-up MR imaging due to the possibility of tethering artifacts and changes in left ventricular size after revascularization.

For measuring EF, we chose RNV as an operator independent tool with good reproducibility. In comparison to other reports, we did not demonstrate a significant relation between the change in EF and DVM defined by both imaging techniques studied. This may be due to the facts that an improvement in EF after revascularization was not observed in a large number of patients with a significant amount of DVM and that individuals with a low level of DVM were not enrolled in our study.

Although the mean EF in the whole group increased, the relation between DVM and the change in EF was unsubstantial and statistically insignificant for both methods studied. In fact, the EF increased in only 17 patients. In the rest of the study group there were no significant changes in EF, except for 1 patient in whom EF worsened by 6% in the follow-up period. When a comparison of these 2 subsets of patients was made, no significant differences were identified (Table IV).

The absence of an improvement in EF in a significant part of our study population can be explained by inadequate revascularization, a new silent myocardial infarction, a short period of follow-up, or concomitant nonischemic cardiomyopathy. During the follow-up exam we did not perform coronary angiography to confirm the adequacy of revascularization nor CE-MRI to exclude new myocardial infarctions. However, the clinical status did not worsen in any of the patients in the follow-up.

The absence of functional recovery of the left ventricle may also be due to advanced and irreversible changes from long-term hibernation and cardiac remodeling. Similar results were recently reported by Bax, et al in patients with delayed revascularization and advanced cardiac remodeling. In our study group we were not able to analyze the duration of systolic dysfunction before revascularization.

It is not known whether information about the improvement of global systolic function is essential before a decision concerning myocardial revascularization is made. Patients whose EF improves after revascularization might have a better prognosis in comparison with those in whom it does not, but there are no data available suggesting that the improvement in prognosis after revasculariza-
tion is determined solely by an increase in EF. Samady, et al\textsuperscript{26}) reported that the lack of improvement in global systolic function after revascularization was not related to an unfavorable long-term prognosis.

**CONCLUSION**

A comparison of the 2 methods in the assessment of myocardial viability did not prove there was agreement or that one was clearly superior. We did not find that either method was suitable for predicting global systolic function improvement after revascularization in patients with chronic left ventricular systolic dysfunction.

**REFERENCES**