Right Ventricular Injury in ST-Elevation Myocardial Infarction
Risk Stratification by Visualization of Wall Motion, Edema, and Delayed-Enhancement Cardiac Magnetic Resonance

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Background—Patients with right ventricular injury (RVI) complicating ST-elevation myocardial infarction (STEMI) have impaired prognosis, but it is unclear which patients are at risk of developing RVI. Cardiac magnetic resonance can identify these patients and might add important information on risk stratification, prognosis, and treatment. Aims were to determine the predictors and the prognostic significance of RVI assessed by wall motion abnormalities, edema, myocardial salvage index, and delayed enhancement in acute reperfused STEMI.

Methods and Results—We studied 450 patients 1–4 days after primary angioplasty in STEMI. T2-weighted and delayed-enhancement cardiac magnetic resonance was used for visualizing edema and scar to calculate myocardial salvage index. Cine-imaging was performed to assess wall motion abnormalities, which, in combination with edema, were considered diagnostic for RVI. Patients with RVI were compared with matched patients with isolated left ventricular infarction. The primary end point was the occurrence of a major adverse cardiac event: a composite of death, reinfarction, and congestive heart failure after a median follow-up period of 20.9 months. RVI was present in 69 patients, and 41 of 69 showed myocardial necrosis. In a multivariable stepwise forward logistic regression analysis, a high RV myocardial mass (odds ratio, 2.06; 95% confidence interval, 1.18–3.58; \( P = 0.012 \)) and a low Thrombolysis In Myocardial Infarction flow before angioplasty (odds ratio, 0.50; 95% confidence interval, 0.32–0.76; \( P = 0.011 \)) were associated with RVI. Cox regression analysis revealed RVI as the most statistically significant predictor of time to major adverse cardiac events (hazard-ratio, 3.36; 95% confidence interval, 1.99–5.66; \( P < 0.001 \)).

Conclusions—RVI detected by cardiac magnetic resonance is a strong and independent predictor of clinical outcome after acute reperfused STEMI.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01359306.

Key Words: acute myocardial infarction • cardiac MRI • right ventricle infarction • myocardial salvage • prognosis

Right ventricular injury (RVI) in ST-elevation myocardial infarction (STEMI) can cause severe hemodynamic derangements and is associated with increased mortality and morbidity.\(^1\) Owing to the RV volume pump characteristics, RVI with hemodynamic compromise requires a specific treatment.\(^2\) Hence, for optimizing therapeutic strategies, an early and accurate diagnosis is mandatory.

In necropsy studies, RVI can be found in up to 50% of patients with inferior STEMI.\(^3\) In clinical routine, however, RVI is diagnosed by echocardiography, electrocardiography, and clinical findings, and detection rates show a wide range, depending on the population and diagnostic criteria used.\(^3\)

Cardiac magnetic resonance (CMR) emerged as a powerful tool in visualizing myocardial injury after left ventricular (LV) STEMI. High signal intensity in T2-weighted imaging visualizes myocardial edema representing myocardium at risk,\(^4\) and delayed enhancement (DE) indicates myocardial necrosis.\(^5\) Comparing the extent of reversible to irreversible injured myocardium allows for calculation of myocardial...
salvage or myocardial salvage index (MSI), which to max-
imize is the goal of reperfusion because of its prognostic
impact.6

Recently, CMR has been also introduced for detection and
visualization of RVI. Previous studies demonstrated that early
postinfarction RVI is common and is characterized by the
presence of myocardial edema, DE, and functional abnormal-
ities.7 However, to date, there is no systematic evaluation of
the clinical prognostic value of RVI assessed by CMR in a
large STEMI population.

The aim of this study was to investigate the predictors for
RVI development and its prognostic impact after reperfused
STEMI. A secondary objective was to evaluate the utility and
clinical value of RV MSI assessment in a large STEMI
cohort.

Methods

Patient Population and Study Design

Primary angioplasty was performed in 524 consecutive patients with
STEMI at our tertiary care institution. Of these, 450 patients were
referred to CMR 24–96 hours after the index event. Eligibility
criteria were the onset of symptoms <12 hours before angioplasty
and ST-segment elevation of >0.1 mV in ≥2 extremity leads or
>0.2 mV in ≥2 precordial leads. Exclusion criteria were usual CMR
contraindications such as implanted defibrillators/pacemakers and
ferromagnetic intracranial metallic implants.

After physical examination and assessment of medical history, the
Thrombolysis In Myocardial Infarction (TIMI) risk score was
calculated for each patient.8 We conducted follow-up by a standard-
ized telephone questionnaire after a median follow-up period of 20.9
months (range, 4.7–39.0 months). The interviewers were blinded to
the CMR results. Reported adverse events were verified by hospital
or outpatient documentation.

Some of the patients included in this prospective analysis have
been included in randomized trials published previously.3,5,9,10 The
study was approved by the local ethics committee and complies with
the Declaration of Helsinki. All patients gave written informed
consent.

Primary Angioplasty, Angiographic Analysis, and
Subsequent Treatment

Intravenous application of 500 mg aspirin and 60 IU/kg body wt
heparin was performed in all patients before angioplasty. Clopi-
dogrel with a 600-mg loading dose was given orally at the earliest
time point followed by daily administration of 75 mg for 12 months
plus 100 mg aspirin indefinitely. According to current guidelines,
glycoprotein IIb/IIIa inhibitors, angiotensin-converting enzyme
inhibitors, β-blockers, and statins were administered.11 Primary angio-
plasty was performed according to standard clinical practice. In the
case of a high thrombus burden, additional thrombectomy was
conducted. Before and after angioplasty, coronary angiography was
performed with the same projections. Post–TIMI flow was catego-
rized as TIMI flow III: reperfusion success, and TIMI flow 0–II: no
reperfusion success. Angiographic visual analysis was performed
offline by 2 blinded observers.

ST-Segment Resolution and Enzymatic Infarct
Size Analysis

Early ST-segment resolution was evaluated by measuring the sum of
ST-segment elevation before and approximately 90 minutes after
angioplasty in a standard 12-lead ECG and expressed as percentage.
Data were also categorized as complete (≥70%), partial (<70% to
30%), and no ST-segment resolution (<30%). The number of leads
with ST-segment elevation was obtained. Plasma creatine kinase and
creatine kinase–myocardial band were assessed on admission and
subsequently every 8 hours for 2 days.

Cardiac MRI

All CMR examinations were performed on a 1.5-T scanner (Intra
CV, Philips Medical Systems, Best, The Netherlands). The scan
protocol and technical parameters have been described in detail
previously.6 In brief, cine steady-state free precession sequences in
short-axis and horizontal and vertical long-axis orientation were
acquired for volumetric and functional imaging. Visualization of
myocardial edema was performed using a black-blood T2-weighted,
short inversion time, turbo spin-echo sequence in short-axis orien-
tation. DE images, also covering both ventricles in short-axis orien-
tation, were acquired for quantification of necrosis and micro-
vascular obstruction (MO) 10–15 minutes after application of
0.15 mmol/kg/body wt gadobutrol (Gadovist, BayerSchering,
Berlin, Germany), using a 3D, T1-weighted, inversion recovery
turbo gradient echo sequence. Inversion time for optimal nulling of
RV and LV myocardium was individually optimized within a
range of 200–300 ms.

CMR image analysis was performed by fully blinded observers on
an independent work station in the CMR core laboratory, which has
proven low intraobserver and interobserver variability as well as
reproducibility for assessment of infarct size, MSI, and MO.9

Biventricular volumes and function were determined by manually
tracing endocardial and epicardial borders in end-systole and end-
diastole. Biventricular myocardial masses were calculated on cine
images in end-diastole. In T2-weighted images and in the corre-
sponding DE images, the area of high signal intensity was manually
delineated in each short-axis slice. For RV edema assessment, signal
intensity of LV edema was taken as reference, and slices were
compared with short-axis cine images as described previously.7 MO
was included into infarct size and additionally assessed in a separate
fashion. Patients with nondiagnostic image quality of the RV
myocardium were excluded from further analysis. RV regional wall
motion abnormalities were assessed qualitatively and classified as
dyskinesia, akiniesia, or hypokinesia. Wall motion impairment in com-
bination with edema was considered as being diagnostic for RVI.

The following parameters were calculated for both the RV and LV:
end-diastolic, end-systolic, stroke volume index, and myocardial
mass index (related to body surface area)

ejection fraction

% area at risk=volume edema/ventricular mass

% infarct size=volume infarct/ventricular mass

MO=volume MO/ventricular mass

MSI=area at risk minus infarct size/area at risk

For comparison, every patient with RVI was matched without
replacement to a patient with isolated LV infarction with the same
vessel (right coronary artery, left anterior descending, or left circum-
flex), and, where possible, with the same vessel segment (proximal,
mid, distal). Furthermore, age (±3 years) and sex were matched.
Isolated LV infarction was defined by CMR absence of RVI (Table 1).

End Points

The primary end point of this study was the occurrence of major
adverse cardiac events (MACE), a composite of death, reinfarction,
and new congestive heart failure. Secondary end points were the
individual components of the primary end point.

At index hospitalization, reinfarction was diagnosed on the basis
of clinical symptoms, new ST-segment changes, and an increase in
the creatine kinase–myocardial band levels, as previously de-
scribed.12 During follow-up, any new ischemic symptoms leading to
hospital admission in combination with troponin elevation were
defined as recurrent infarction. Congestive heart failure was diag-
nosed in the case of rales and dyspnea (New York Heart Association
class III–IV) occurring >24 hours after the index and requiring
medical attention. In the case of more than 1 event, the first event
was chosen for the combined clinical end point. When ≥2 events
occurred simultaneously, the most severe event was chosen
(death>myocardial reinfarction>congestive heart failure).

Statistical Analysis

Categorical variables are expressed as number and percentage.
Normally distributed variables are presented as mean±SD; nonnor-

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mally distributed variables are given as median [25, 75 percentiles]. Differences between groups were assessed by the Student t test for continuous data with normal distribution and homogeneity of variance. The Wilcoxon rank-sum test was used for continuous nonnormally distributed data or for continuous data without homogeneity of variance. Differences between categorical variables were assessed either by the χ² or Fisher exact test. Differences between related continuous variables were tested using the paired t test or the Wilcoxon signed rank, depending on their distribution.

Univariate and multivariable conditional binary logistic regression analyses were performed to find factors associated with RVI. This method accounts for the matched-pair nature of the sample. Categorical variables included Killip class on admission, categorized TIMI flow after angioplasty, and categorized ST-segment resolution. Continuous variables included pain-to-balloon time, biventricular myocardial mass index, LV area at risk, LV infarct size, LV MSI, peak creatine kinase, peak creatine kinase–myocardial band, number of leads with ST-segment elevation, sum of ST-segment elevation, mean blood pressure, heart rate, and TIMI risk score as quasi-continuous. A stepwise forward regression procedure was performed to select variables into multivariable models.

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Entire Patient Group (n=421)</th>
<th>RVI Group (n=69)</th>
<th>Non-RVI Group (n=69)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>66±12</td>
<td>65±13</td>
<td>65±11</td>
<td>0.81</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>321 (76)</td>
<td>55 (80)</td>
<td>55 (80)</td>
<td></td>
</tr>
<tr>
<td>Killip class on admission, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>I</td>
<td>304 (72)</td>
<td>53 (77)</td>
<td>56 (82)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>92 (22)</td>
<td>12 (17)</td>
<td>11 (16)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>19 (5)</td>
<td>3 (5)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>6 (1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>TIMI risk score</td>
<td>3 [2, 4]</td>
<td>2 [1, 3]</td>
<td>1 [0, 2]</td>
<td>0.14</td>
</tr>
<tr>
<td>Pain-to-balloon time, min</td>
<td>211 [140, 352]</td>
<td>240 [157, 431]</td>
<td>179 [129, 324]</td>
<td>0.04</td>
</tr>
<tr>
<td>RV injury, n</td>
<td>69</td>
<td>69</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>TIMI flow after angioplasty, n</td>
<td></td>
<td></td>
<td></td>
<td>0.81</td>
</tr>
<tr>
<td>0-II</td>
<td>53</td>
<td>9</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>368</td>
<td>60</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>ST-segment resolution, %</td>
<td>73 [49, 95]</td>
<td>61 [37, 91]</td>
<td>91 [66, 100]</td>
<td>0.004</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>49±12</td>
<td>48±9</td>
<td>50±10</td>
<td>0.29</td>
</tr>
<tr>
<td>RV ejection fraction, %</td>
<td>50±9</td>
<td>43±10</td>
<td>54±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV end-diastolic volume index, mL/m²</td>
<td>77±17</td>
<td>78±18</td>
<td>73±14</td>
<td>0.10</td>
</tr>
<tr>
<td>RV end-diastolic volume index, mL/m²</td>
<td>77±19</td>
<td>79±19</td>
<td>75±20</td>
<td>0.27</td>
</tr>
<tr>
<td>LV myocardial mass index, g/m²</td>
<td>66±15</td>
<td>65±15</td>
<td>60±14</td>
<td>0.045</td>
</tr>
<tr>
<td>RV myocardial mass index, g/m²</td>
<td>25±5</td>
<td>23±4</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Infarct size, % LV</td>
<td>21±12</td>
<td>17±14</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Infarct size, % RV</td>
<td>5±6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV myocardial salvage index</td>
<td>0.57±0.25</td>
<td>0.47±0.2</td>
<td>0.59±0.26</td>
<td>0.006</td>
</tr>
<tr>
<td>RV myocardial salvage index</td>
<td>0.80±0.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microvascular obstruction, % LV</td>
<td>1.47±4.46</td>
<td>1.12±1.80</td>
<td>0.79±1.26</td>
<td>0.19</td>
</tr>
<tr>
<td>Localization of culprit lesion, n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD (proximal/mid/distal)</td>
<td>185 (74/104/7)</td>
<td>11 (5/5/1)</td>
<td>11 (4/6/1)</td>
<td></td>
</tr>
<tr>
<td>RCA (proximal/mid/distal)</td>
<td>182 (89/51/42)</td>
<td>53 (23/21/9)</td>
<td>53 (26/15/12)</td>
<td></td>
</tr>
<tr>
<td>LCX (proximal/distal)</td>
<td>54 (46/8)</td>
<td>5 (5/0)</td>
<td>5 (5/0)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular risk factors, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>111 (26)</td>
<td>15 (22)</td>
<td>14 (20)</td>
<td>0.83</td>
</tr>
<tr>
<td>Hypertension</td>
<td>292 (69)</td>
<td>46 (67)</td>
<td>46 (67)</td>
<td>1.00</td>
</tr>
<tr>
<td>Smoking</td>
<td>175 (42)</td>
<td>33 (48)</td>
<td>27 (39)</td>
<td>0.30</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>142 (34)</td>
<td>21 (30)</td>
<td>24 (35)</td>
<td>0.59</td>
</tr>
<tr>
<td>Family history of coronary artery disease</td>
<td>128 (30)</td>
<td>17 (25)</td>
<td>20 (29)</td>
<td>0.56</td>
</tr>
<tr>
<td>Heart rate, beats per minute</td>
<td>80±17</td>
<td>77±17</td>
<td>78±14</td>
<td>0.58</td>
</tr>
<tr>
<td>Mean blood pressure, mm Hg</td>
<td>95±17</td>
<td>93±16</td>
<td>94±14</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Continuous data are presented as mean±SD or median (interquartile range). Categorical variables are given as frequency and percentage.

RVI indicates right ventricular injury; TIMI, Thrombolysis In Myocardial Infarction; LV, left ventricular; LAD, left anterior descending coronary artery; RCA, right coronary artery; and LCX, left circumflex coronary artery.
The Kaplan-Meier method was applied for the combined clinical end point and death; differences were assessed by the log-rank test. To identify possible predictors of MACE, univariate Cox regression analyses were performed, using CMR parameters and traditional prognostic factors. A multivariable stepwise forward Cox regression analysis took only 3 of the significant variables into the model. Including matched pairs as strata accounted for the paired structure of the data. The tests were performed as 2-sided, at a significance level of $0.05$. For statistical analyses, SPSS software, version 16.0 (SPSS Inc, Chicago, IL) was used.

Results
Of 524 STEMI patients undergoing primary angioplasty, 450 were referred to CMR 24–96 hours after reperfusion. Reasons for not undergoing CMR are listed in Figure 1. Image quality for RV edema quantification was inappropriate in 29 (6.4%) patients; 7 patients were lost to follow-up. In 414 patients, clinical outcome data were available.

Right Ventricular Injury
RVI as defined by a combination of myocardial edema (Figure 2) and local wall motion impairment occurred in 69 of 421 patients (16.4%). Of these 69 patients, 54 (78%) presented with hypokinesia and 15 (22%) with akinesia. None of the patients showed RV edema without local wall motion abnormalities in the same region. In 41 of these patients (59.4%), RV myocardial necrosis was detected in DE imaging. RV MO was present in only 1 patient (Figure 3). Distribution of the culprit lesion is shown in Table 1. Patients with a lesion in the left circumflex had a left dominant coronary circulation and a lateral to inferior injury of the left ventricular myocardium, extending to the inferior wall of the RV. Baseline characteristics of the entire patient cohort, RVI patients, and the matched control group are presented in Table 1. RVI patients had a significantly higher RV myocardial mass index compared with the non-RVI group. These patients also presented with a significantly longer pain-to-balloon time and a lower LV MSI. Within the RVI group, the number of patients with 100% myocardial salvage (RV MSI $= 1$) was high (28/69; 40.6%), resulting in significantly higher mean RV MSI ($0.80 \pm 0.2$) as compared with the mean LV MSI ($0.47 \pm 0.2$; $P<0.01$). Furthermore, patients with RVI showed a significantly lower ST-segment resolution and a lower RV ejection fraction (Table 1).
Predictors of RVI
In a multivariable stepwise forward regression model adjusted for significant variables in univariate regression analysis, using RVI as the dependent variable, a low TIMI flow before angioplasty was a predictor of RVI (Table 2). Also, RV myocardial mass index was related to RVI. Pain-to-balloon time was associated with RVI in the univariate analysis but failed to predict RVI in the multivariable model. The sum of ST-segment elevation and the number of leads with ST-segment elevation were not related to RVI.

Prognostic Impact of RVI
MACE occurred in 73 of 421 patients (17.3%). Most MACE, with 22 of 69 (31.9%), occurred in patients with RVI compared with 5 of 69 (7.3%) in the matched non-RVI group. There were 8 deaths, 6 nonfatal reinfarctions, and 8 cases of new congestive heart failure in patients with RVI as opposed to 3 deaths and 2 nonfatal reinfarctions in the matched non-RVI patients.

Within the RVI group, patients with MACE demonstrated greater RV area at risk (23.2% [15.3, 34.7] versus 18.2% [10.0, 27.9]; P = 0.047), a greater RV infarct size (8.7% [5.2, 11.7] versus 0% [0.0, 3.9]; P < 0.001), and a lower RV MSI (0.61 [0.57, 0.75] versus 1.00 [0.81, 1.00]; P < 0.001), compared with RVI patients without MACE.

Kaplan-Meier estimates illustrated reduced periods of MACE-free survival and higher mortality in patients with RVI compared with the matched non-RVI group (Figure 4A).
These results were confirmed when the analysis was repeated with LV ejection fraction categorized for the presence or absence of severe LV dysfunction (LV ejection fraction ≤40%) used as stratum. Log-rank tests pooled over these strata were both significant (MACE: \( P<0.001 \), mortality: \( P=0.036 \)) demonstrating the prognostic value of RVI independent of LV dysfunction. Within the RVI group, patients with RV MSI=1 had a better prognosis than patients with MSI<1 (Figure 5 A and 5B). Furthermore, prognosis of patients with RV MSI=1 was not different from patients with isolated LV infarction (\( P=0.70 \)).

Analysis of the entire patient group showed that RVI remained associated with MACE in the univariate Cox regression analysis, but other established markers of increased patient risk also demonstrated significant associations with MACE (Table 3). However, in a multivariable Cox regression, RVI together with LV ejection fraction and TIMI risk score remained the only independent predictors for occurrence of MACE. In the subgroup of patients with RVI plus matched non-RVI patients (n=138), RVI showed association with the combined end point in univariate (hazard ratio [HR], 6.74; 95% confidence interval [CI], [2.32–19.59]) and multivariable (HR, 5.5; 95% CI, [1.71–14.94]) Cox regression analysis.

Table 3. Predictors of MACE in the Univariate and Stepwise Forward Multivariable Cox Regression Analysis of the Entire Patient Group (n=421)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter name</td>
<td>( P ) Value</td>
<td>Hazard Ratio [CI]</td>
</tr>
<tr>
<td>RV injury</td>
<td>&lt;0.001</td>
<td>2.66 [1.61–4.11]</td>
</tr>
<tr>
<td>RV ejection fraction</td>
<td>0.02</td>
<td>0.97 [0.94–0.99]</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>&lt;0.001</td>
<td>0.93 [0.94–0.97]</td>
</tr>
<tr>
<td>LV-MSI</td>
<td>&lt;0.001</td>
<td>0.12 [0.04–0.36]</td>
</tr>
<tr>
<td>LV % infarct size</td>
<td>&lt;0.001</td>
<td>1.04 [1.02–1.05]</td>
</tr>
<tr>
<td>TIMI flow after angioplasty, 0–II</td>
<td>0.002</td>
<td>2.41 [1.38–4.21]</td>
</tr>
<tr>
<td>Microvascular obstruction, % LV</td>
<td>0.001</td>
<td>1.04 [1.02–1.07]</td>
</tr>
<tr>
<td>TIMI risk score</td>
<td>&lt;0.001</td>
<td>1.25 [1.13–1.38]</td>
</tr>
<tr>
<td>ST-segment resolution, %</td>
<td>0.03</td>
<td>0.99 [0.99–1.00]</td>
</tr>
</tbody>
</table>

MACE indicates major adverse cardiac events; CI, confidence interval; RV, right ventricular; LV, left ventricular; MSI, myocardial salvage index; and TIMI, Thrombolysis In Myocardial Infarction.

Discussion

To the best of our knowledge, this is the first CMR study to evaluate the prognostic impact of RV area at risk as measured with edema-sensitive, T2-weighted images and infarct size by using DE in a large group of reperfused STEMI patients. The results might be summarized as follows: (1) RVI with DE is a strong independent prognostic marker of long-term prognosis after STEMI; (2) similar to isolated LV infarction, RV area at risk, infarct size, and MO can also be calculated; (3) RVI is associated with a low LV MSI, an impaired ST-segment resolution, and a high RV mass index; (4) RVI defined by regional RV edema and wall motion impairment or right-sided infarction can be found in approximately 17% of STEMI patients after mechanical reperfusion.

Assessment of RV Area at Risk, Infarct Size, and MO

The concept of myocardial salvage calculated by the area at risk in T2-weighted images and the infarct size in DE images is increasingly used for the assessment of reperfusion therapy in LV infarction.\(^6,13\) Whereas a few studies showed the applicability for DE of the RV,\(^7,14\) only limited studies evaluated the RV area at risk.\(^3\)
Our study clearly demonstrates that RV area at risk, visualized by T2-weighted imaging, can be quantified in the majority of patients with RVI. Consequently, RV MSI can be calculated with significantly higher MSI values compared with the LV.\textsuperscript{13} As shown by our data, a substantial number of patients reach major or even complete salvage of the RV area at risk. Such a high incidence of aborted RV infarctions is in line with a recent publication\textsuperscript{7} and may be explained by the lower oxygen demand and the dual anatomic supply system of the RV myocardium, making it less vulnerable to ischemia. Our findings in part underline a previous thesis assuming that acute right ischemic dysfunction represents viable myocardium.\textsuperscript{16} Nevertheless, ischemic scarring also exists in the RV myocardium, probably too small to cause sustained impairment of global RV function in the majority of cases. According to the lower degree of RV scarring, right-sided MO is a very rare finding after acute reperfused STEMI and was found in only 1 of 421 patients. Further studies with large patient cohorts might be necessary to assess the incidence and potentially the prognostic impact of RV MO.

**Predictors of RVI**

RVI typically occurs with infarction of the LV inferior wall. In the present study population, the culprit lesion was located in most patients (84%) in the right coronary artery, mainly in the proximal and mid segments. Additionally, we were able to identify a low TIMI flow before angioplasty as a further parameter associated with RVI. Patients with RVI also demonstrated with an increased RV myocardial mass index.

Only 1 patient in the RVI group had severe pulmonary hypertension as a cause of RV hypertrophy. Two more patients in this group demonstrated with mild pulmonary hypertension and an RV myocardial mass within the upper normal range. An increased oxygen demand in high RV mass might result in injury of the RV myocardium, which would confirm the results of nonimaging studies.\textsuperscript{17–19} These studies in part also report necropsy data of chronic RV infarctions in which edema can be excluded. On the other hand, there are studies reporting an increase of LV myocardial mass caused by edema,\textsuperscript{20} and swelling of the thin, compacted layer of RV myocytes might also result in an increase of measured RV myocardial mass. Actually, we assessed RV myocardial mass after infarction and certainly included a substantial amount of RV edema in the calculation of myocardial mass. Thus, it is most likely that increased RV mass is the result rather than the cause of RVI.

**Comparison With Recent Studies**

Compared with other studies assessing RVI in STEMI, the percentage of RVI was lower in our larger consecutive patient group (approximately 17%). Kumar et al found RV DE in 57% of patients with inferior infarction and a mean pain-to-balloon time of 8.8±5.4 hours.\textsuperscript{21} This difference might be explained by the shorter pain-to-balloon time in our patient group, with a median of only 211 minutes. Masci et al also presented a higher percentage of RV edema (51%) and RV DE (31%),\textsuperscript{2} but again in this study, the pain-to-balloon-time was longer (252±134 minutes for RVI patients, 270±166 minutes for non-RVI patients) compared with the current cohort. One discrepancy in the assessment of RV edema was the use of the integrated body coil in the current approach, whereas Masci et al used surface coils with a correction algorithm to homogenize signal. However, it is unlikely that this accounts for the significant difference in the occurrence of RV edema. Other parameters were comparable between Masci et al and the present study: In both, the RCA was identified as the infarct-related artery in 43%, and the distribution of the affected RCA segments was similar.

In a recent study, Francione et al reported on the influence of time to reperfusion on myocardial injury assessed by CMR after STEMI with primary angioplasty.\textsuperscript{22} The authors found that the extent of myocardial edema did not change significantly as pain-to-balloon time progressed. This is in contradiction to our results, which show an association of pain-to-balloon time to the occurrence of RVI defined by edema. However, Francione et al report on LVs and our findings relate to RVs. Owing to the better collateralization of the RV, the oxygen supply of the myocardium might be initially sufficient for not developing edema.

**Prognostic Impact of RVI**

Our study clearly demonstrates the prognostic impact of RVI in a large group of reperfused STEMI patients when no complete myocardial salvage can be achieved. This is in line with 2 recent studies, which found RV edema being a prognostic factor for RV function recovery at follow-up.\textsuperscript{7,23} However, in one of these studies, no clinical follow-up data were reported\textsuperscript{7} and the other study included only “soft” clinical end points such as recurrent angina and repeated revascularization. A recent study demonstrated a strong predictive value of RV infarction assessed by CMR.\textsuperscript{24} The authors also defined RV ejection fraction as an important prognostic marker. However, this study did not measure RV edema and RV myocardial salvage. Moreover, our study did not find such a strong relationship between RV ejection fraction and clinical outcome. In contrast, we could demonstrate that the prognosis of patients with RVI mainly depends on RV MSI rather than RV ejection fraction.

Analysis of the entire patient group showed that RVI was independently related to “hard” outcome parameters. In addition, RVI assessed by CMR was compared with established clinical, angiographic, and CMR parameters.

In clinical routine, RVI is diagnosed by echocardiography and/or ECG, but both modalities have their specific limitations. Wall motion impairment of the inferior RV wall is sometimes difficult to visualize in echocardiography and may lead to false-negative results. ECG changes of RV are transient, frequently vanishing 8–10 hours after symptom onset.\textsuperscript{25} CMR is a promising tool to fill this diagnostic gap and to identify patients with RVI. This might lead to an early adequate therapy before developing severe hemodynamic compromise.

**Limitations**

Assessment of myocardial edema is discussed controversially.\textsuperscript{26} Quantification of RV edema is even more challenging than in the LV. Using a black-blood, T2-weighted, short inversion time, turbo spin-echo sequence with a surface coil...
leads to inhomogeneities of the myocardium that might result in misinterpretation of edema. Therefore, we combined the T2-weighted sequence with the body coil to achieve signal homogeneity in the biventricular myocardium. Nevertheless, signal-to-noise ratio in this sequence is relatively low, and the thin, compacted myocardial layer of the RV makes hyperintense areas less obvious. Additionally slow-flow artifacts in the intertrabecular recesses, which are adjacent to edema, can complicate quantification of the latter.

Also, visualization of DE in the thin RV myocardium is more difficult as compared with the thicker, compacted myocardial layer of the LV wall. We used the same inversion time for both ventricles. Choosing a shorter inversion time for the RV does not improve image quality and reproducibility and may result in dark rim artifacts.27

Owing to these specific challenges, both acquisition and evaluation of CMR in RVI is time-consuming and requires expertise in this field. Therefore, calculation of RV edema and RV MSI might only be accomplished in CMR referral centers.

**Conclusions**

This large, prospective study demonstrates that RVI, defined as edema, wall motion impairment, and DE as assessed by CMR, is a strong predictor for the occurrence of death, reinfarction, and congestive heart failure when no complete myocardial salvage can be achieved. It should therefore be considered for further risk stratification and optimized clinical treatment.

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**Disclosures**

Dr Gutberlet serves as a consultant/advisory board member for Philips iCT Advisory Board.

**References**


**CLINICAL PERSPECTIVE**

Cardiac magnetic resonance (CMR) is a useful tool to evaluate left ventricular myocardial damage after reperfused ST-elevation myocardial infarction. It provides detailed prognostic information by visualizing edema, infarct size, and microvascular obstruction. Recently, CMR has also been introduced for detection of right ventricular injury (RVI); however, the prognostic significance of such findings has not yet been established. RVI is typically detected by echocardiography and/or ECG, but wall motion impairment of the inferior RV wall is difficult to visualize in echocardiography, and ECG changes of RVI may be transient. This work demonstrates the value of CMR value for not only diagnosis but also prognosis in demonstrating and quantifying RVI after ST-elevation myocardial infarction. Similar to the left ventricle, myocardial salvage index can be calculated for the RV. RVI is a strong indicator for major adverse cardiac events when no complete RV myocardial salvage is achieved after angioplasty.
Right Ventricular Injury in ST-Elevation Myocardial Infarction: Risk Stratification by Visualization of Wall Motion, Edema, and Delayed-Enhancement Cardiac Magnetic Resonance

Matthias Grothoff, Christian Elpert, Janine Hoffmann, Johannes Zachrau, Lukas Lehmkuhl, Suzanne de Waha, Steffen Desch, Ingo Eitel, Meinhard Mende, Holger Thiele and Matthias Gutberlet

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