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Extent of RV Dysfunction and Myocardial Infarction Assessed by CMR Are Independent Outcome Predictors Early After STEMI Treated With Primary Angioplasty

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OBJECTIVES The aim of this study was to assess the prognostic value of right ventricular (RV) involvement diagnosed by cardiac magnetic resonance (CMR) early after ST-elevation myocardial infarction (STEMI).

BACKGROUND CMR allows accurate and reproducible RV assessment. However, there is a paucity of data regarding the prognostic value of RV involvement detected by CMR early after STEMI.

METHODS Ninety-nine patients (77 men, mean age 57 ± 11 years) who underwent CMR 3 to 5 days after STEMI treated with primary angioplasty were followed for 1,150 ± 337 days for cardiac events (cardiac death, nonfatal myocardial infarction [MI], and hospitalizations due to decompensated heart failure). Cox proportional hazards model was applied in stepwise forward fashion to identify outcome predictors. Event-free survival was estimated by Kaplan-Meier method and compared between groups by the log-rank test.

RESULTS Cardiac events occurred in 34 patients (7 cardiac deaths, 8 MIs, 26 hospitalizations). By multivariable analysis, the independent outcome predictors were left ventricular (LV) MI transmurality index (hazard ratio: 1.03 per 1%; 95% confidence interval: 1.01 to 1.04; $p = 0.001$), RV ejection fraction (RVEF) (hazard ratio: 1.46 per 10% decrease; 95% confidence interval: 1.05 to 2.02; $p = 0.03$), and RVMI extent (hazard ratio: 1.50 per each infarcted RV segment; 95% confidence interval: 1.11 to 2.01; $p = 0.007$). Compared with clinical data (global chi-square = 5.2), LV ejection fraction [LVEF] (global chi-square = 11.1), RVEF (global chi-square = 17.1), LVMI transmural extent (global chi-square = 26.0), and RVMI extent (global chi-square = 34.9) improved outcome prediction in sequential Cox model analysis ($p < 0.05$ for all steps). RVEF stratified risk in patients with LVEF <40% in whom the 4-year event-free survival was 66.7% for RVEF ≥40% and 40.0% for RVEF <40% ($p < 0.05$).

CONCLUSIONS The extent of RVMI and RV dysfunction assessed early after STEMI are independent outcome predictors, which provide incremental prognostic value to clinical data, LV systolic function, and infarct burden. Measurement of RVEF may be particularly useful to stratify risk in patients with depressed LV function after STEMI. (J Am Coll Cardiol Img 2010;3:1237–46) © 2010 by the American College of Cardiology Foundation

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Right ventricular (RV) dysfunction and RV myocardial infarction (MI) are frequent factors complicating acute MI. RVMI occurs in approximately 50% of patients with inferior MI and 10% of patients with anterior MI (1,2). Although RV involvement is usually not the focus of patient care during acute MI, because this complication only becomes evident during hemodynamic compromise, it still plays an important prognostic role. Several studies using different diagnostic approaches including electrocardiography, echocardiography, and radionuclide techniques evaluated the issue (1,3–5). Most of them assessed the prognostic value of RV involvement during acute MI in patients who underwent thrombolytic or no reperfusion therapy. Currently, at skilled centers brisk (Thrombolysis In Myocardial Infarction >2) epicardial coronary flow is restored in most patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary angioplasty (6). Bowers et al. (7) showed that in patients with RVMI, complete reperfusion promptly normalizes RVEF and is associated with improved in-hospital mortality. However, the long-term prognostic value of RV involvement in those patients was not studied. Moreover, most studies evaluated the prognostic value of RVMI in inferior STEMI, and there are limited data regarding the prognostic value of RVMI in an unselected series of patients with STEMI.

Despite the fact that cardiac magnetic resonance (CMR) is the most accurate and reproducible noninvasive diagnostic tool for RV evaluation, there is paucity of data regarding the prognostic value of RV involvement assessed by CMR early after acute MI. Therefore, we decided to test our hypothesis that CMR evaluation of RVMI early after anterior or inferior STEMI treated with primary angioplasty provides prognostic information.

ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CMR = cardiac magnetic resonance

LGE = late gadolinium enhancement

LV = left ventricular

LVEF = left ventricular ejection fraction

LVMI = left ventricular myocardial infarction

MI = myocardial infarction

RV = right ventricular

RVEF = right ventricular ejection fraction

RVMI = right ventricular myocardial infarction

STEMI = ST-segment elevation myocardial infarction

METHODS

Study population. The study was approved by local ethics committee and complied with 1975 Declaration of Helsinki. Informed consent was obtained from each patient. Consecutive survivors of first anterior or inferior STEMI who were treated with primary angioplasty with bare metal stent, were enrolled in the study. STEMI was defined according to European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Foundation criteria including clinical symptoms, myocardial necrosis markers, and typical electrocardiographic changes (8). Exclusion criteria were: 1) contraindication to CMR including magnetic resonance–incompatible implants and electric devices, renal insufficiency (creatinine clearance <30 ml/kg/min), inability to sufficiently hold one's breath, claustrophobia; 2) any known clinical condition that might affect RV function independently of MI, including severe chronic obstructive pulmonary disease, interstitial lung disease, pulmonary embolism, primary pulmonary hypertension, congenital heart disease or known significant valvular disease; and 3) previous percutaneous coronary intervention and/or coronary artery bypass graft.

Electrocardiography. Twelve-lead standard electrocardiography and V_{4r} right precordial lead were recorded on admission and interpreted by an experienced, independent observer blinded to other results. STEMI was diagnosed by ≥1 mm ST-segment elevation in ≥2 contiguous leads: V_1 to V_4 for anterior MI and II, III, and aVF for inferior MI. RVMI was considered present when V_{4r} demonstrated ST-segment elevation ≥0.1 mm.

Coronary angiography. Coronary angiograms were evaluated by an experienced observer blinded to other data. The culprit lesion was defined as the most severe and/or the lesion with local dissection or thrombus. Antegrade epicardial coronary blood flow in the infarct vessel before and after primary angioplasty was evaluated using Thrombolysis In Myocardial Infarction criteria (9). Collateral flow from patent vessels to the infarct-related artery was graded using the Rentrop scale (10).

CMR: imaging protocol. Breath-hold electrocardiography-gated imaging was performed using a cardiac phased-array coil on a 1.5-T whole-body scanner (Magnetom Sonata Maestro Class, Siemens, Erlangen, Germany) in left ventricular (LV) and RV short-axis and axial views 3 to 5 days after primary angioplasty. After scout imaging, cine imaging (steady-state free precision gradient echo technique; 8-mm slice thickness, no gap, 256 × 192 matrix, 1.3 × 1.3-mm^2 in-plane resolution) was acquired. 10 min after infusion of 0.15 mmol/kg body weight gadobutrol (Gadovist, Bayer Schering Pharma, Berlin, Germany) late gadolinium-enhanced (LGE) imaging (T1-weighted segmented inversion-recovery pulse sequence; 8-mm slice thickness, no gap, 256 × 192 matrix, 1.3 × 1.3-mm^2 in-plane resolution) was performed with inversion time set to null normal myocardium.

CMR: image analysis. Cine and LGE images were assessed offline (MASS Medis, Leiden, the Netherlands) using 17 LV and 9 RV segment models by independent experienced observers blinded to other data. In the presence of discrepancy in qualitative assessment, the consensus was reached.

Cine images. Endocardial and epicardial borders were outlined on short-axis images as previously described (11) (Fig. 1). If the basal slice contained both ventricular and atrial myocardium, contours were drawn up to their junction and joined by a straight line through the blood pool. In the basal slice, if pulmonary valve was visible, only the portion of volume surrounded by trabeculated myocardium below the pulmonary valve level was included. For RV inflow, the portion blood volume was excluded from the RV volume if the surrounding wall was thin and not trabeculated because it was considered to be in the right atrium. LV and RV end-diastolic volume, end-systolic volume, myocardial mass, and ejection fraction were computed. End-diastolic volume, end-systolic volume, and myocardial mass were indexed to body surface area.

LGE images. LV infarct size was assessed manually with planimetry on short-axis slices, delineating hyperenhanced areas, including surrounded by them hypoenhancement regions, considered as microvascular obstruction. LV infarct and microvascular obstruction size were expressed as a percentage of LV myocardial volume. The LVMI transmurality index was calculated as total hyperenhanced area divided by total area of infarcted segments. RVMI was defined as the presence of LGE in any segment of RV free wall, and RVMI extent was assessed as the number of RV segments with LGE (12) (Fig. 2).

Follow-up. Clinical follow-up was prospectively performed every year after CMR. Clinical information regarding cardiac death, MI, hospitalizations due to decompensated heart failure, and coronary revascularizations was obtained by telephone interviews with patients, contact with patients' physicians as well as hospital and administrative records by individuals blinded to other data. Adverse cardiac events were defined as cardiac death (i.e., death of any cardiac cause, including MI, arrhythmia, and heart failure), nonfatal MI (according to European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Foundation criteria), and hospitalizations due to decompensated heart failure (admission to any health care facility due to new or worsening heart failure requiring intravenous treatment with inotropic, diuretic, or vasodilator therapy) (8). When a patient experienced >1 cardiac event, the first event was chosen. In the case of ≥2 simultaneous cardiac events, the worst event was chosen (cardiac death > nonfatal MI > hospitalization).

Statistical analysis. There were no sample size calculations. Categorical data are presented as numbers or percentages and continuous data as mean ± SD or median with interquartile range, where appropriate. The normal distribution was verified

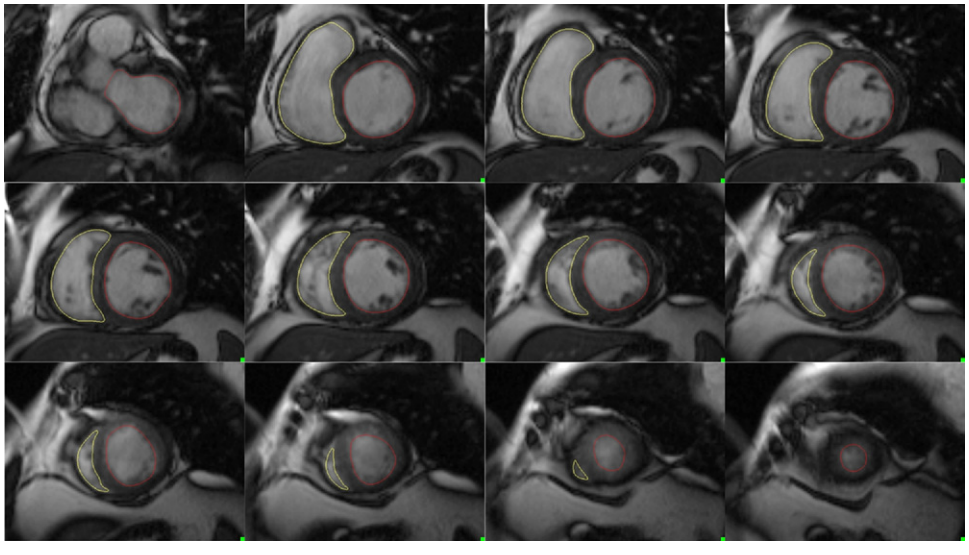

Figure 1. Example of Volumetric Cardiac Magnetic Resonance Measurements Performed for the Right Ventricle and Left Ventricle

The endocardial borders of the right ventricle **(yellow outline)** and left ventricle **(red outline)** were manually delineated at each short-axis view from the atrioventricular valves to the apex to determine cavity areas at end-diastole (shown here) and end-systole.

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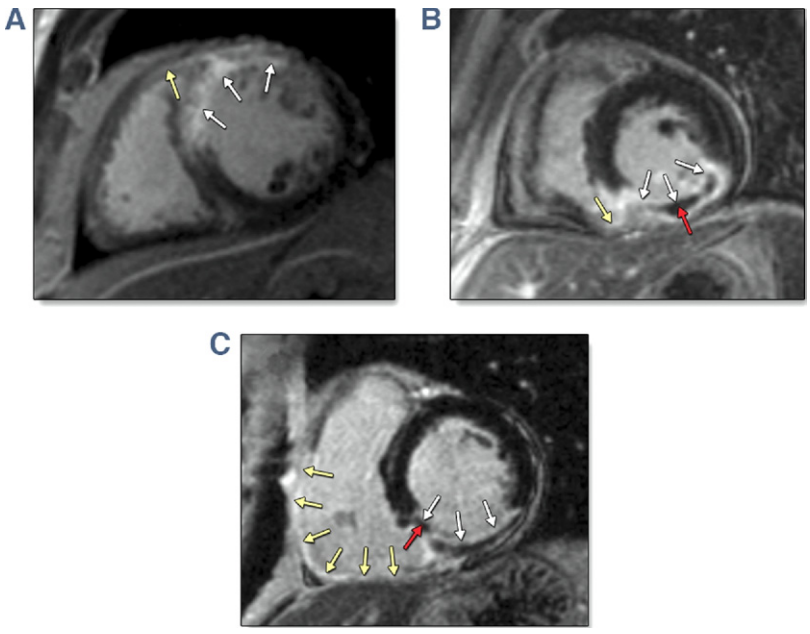

Figure 2. Short-Axis LGE Images Showing Contrast Enhancement and Microvascular Obstruction Areas

In a patient with anterior ST-segment elevation myocardial infarction (STEMI), late gadolinium enhancement (LGE) is present in the anterior part of the right ventricular (RV) free wall **(A)**, whereas in patients with inferior STEMI, LGE areas encompass the inferior **(B)** or both the inferior and the mid-part of RV free wall. **Yellow arrows** indicate LGE in RV free wall, **white arrows** indicate LGE in left ventricular wall, and **red arrows** indicate microvascular obstruction.

using the Shapiro-Wilk test. Categorical variables were compared by the Fisher exact test or chi-square test and continuous variables by an unpaired Student *t* test or Wilcoxon rank-sum test. Cox proportional hazards analysis was performed to determine the association between variables and composite outcomes defined as cardiac death/nonfatal MI/hospitalization due to decompensated heart failure. Patients who underwent revascularization during follow-up were not censored. A hazard ratio with a 95% confidence interval (CI) was calculated for each variable. For analysis, we selected clinical and CMR-derived parameters that might be associated with outcomes from a pathophysiologic standpoint. Univariable analysis of selected variables was performed to identify potential predictors. Finally, multivariable models were created to assess the independent predictive value of RV parameters corrected for individual LV parameters demonstrating $p < 0.05$ on univariable analysis. To identify independent predictors in each model, a forward stepwise multivariable analysis was performed. Multivariable models were limited to 3 variables to avoid model overfitting. To determine the incremental prognostic benefit of CMR-derived parameters over clinical data, a sequential Cox model analysis was performed. Entry and retention was set at $p < 0.05$. The incremental prognostic value was defined by a significant increase in global chi-square. To test proportional hazards assumptions, a linear regression of partial residuals against survival was performed. Absence of significant correlation ($p \geq 0.05$) was taken to signify that proportional hazards assumptions were not violated. Cumulative event rates as a function over time was estimated by the Kaplan-Meier method and compared among groups by log-rank test. The reproducibility for RVEF and RVMI extent assessment was determined as mean absolute difference (bias) and 95% CI of the mean difference (limits of agreement) according to the Bland-Altman method. To assess it, CMR images were evaluated by the same observer unaware of previous results and by the second observer blinded to the results obtained by the first one. Statistical analyses were performed using SPSS software (version 12.0, SPSS Inc., Chicago, Illinois). Differences were considered statistically significant at $p < 0.05$.

RESULTS

Baseline characteristics. Of a total of 105 consecutive patients enrolled in the study, 3 patients had unsuccessful CMR: 2 due to respiratory problems and

1 due to cardiac arrhythmia. Of the remaining 102 patients, follow-up was complete for 99 patients (77 men, mean age 57 ± 11 years), who formed the study group. Among the 3 patients lost to follow-up, no deaths were identified through the Polish Death Registry. Patients' clinical characteristics are shown in Table 1.

CMR. CMR characteristics are summarized in Tables 2 and 3. Fifty patients had an LV ejection fraction (LVEF) <40% and 23 an RVEF <40%. RVMI was found in 26 patients including 10 (15%) with anterior MI and 16 (47%) with inferior MI (p = 0.001 for MI location). In patients with RVMI, LGE was detected in 2.0 (interquartile range: 1.0 to 2.3) RV segments. Comparing patients with and without angiographically visualized collateral flow from patent vessels to infarct-related artery, the former less frequently had an RVEF <40% (2 [7%] vs. 21 [29%], p = 0.03). No significant difference between these groups was found with respect to the prevalence of RVMI (4 [15%] vs. 22 [31%], p = 0.13). Intra- and interobserver variability for RVEF was −0.5% (95% CI: −3.9 to 2.9) and 1.1% (95% CI: −2.7 to 4.9), whereas for RVMI extent analysis −0.1 RV segment (95% CI: −0.6 to 0.4) and −0.1 RV segment (95% CI: −0.7 to 0.5), respectively.

Follow-up. During 1,150 ± 337 days of follow-up, cardiac events occurred in 34 patients: 7 cardiac deaths, 8 nonfatal MIs, and 26 hospitalizations due to decompensated heart failure. Eleven patients were revascularized: 10 percutaneous coronary intervention and 1 coronary artery bypass graft. Tables 4 and 5 demonstrate the univariable and multivariable predictors of follow-up events. Compared with clinical data, LVEF, RVEF, LVMI transmural extent, and RVMI extent improved prediction of adverse cardiac events (p < 0.05 for all sequential steps) (Fig. 3). The 4-year event-free survival in patients with an LVEF ≥40%

Table 1. Clinical Characteristics

		Event		RVMI	
	All Patients (n = 99)	Yes / No (n = 34) / (n = 65)	p Value	Present / Absent (n = 26) / (n = 73)	p Value
Female/male	22/77	8/26 / 14/51	0.98	8/18 / 14/59	0.34
Age, yrs	57 ± 11	59 ± 10 / 56 ± 12	0.20	57 ± 9 / 57 ± 12	0.98
Current tobacco use, %	32	32 / 32	0.82	42 / 29	0.31
Hypercholesterolemia, %	92	94 / 91	0.71	88 / 93	0.43
Hypertension, %	72	79 / 68	0.32	81 / 68	0.31
Diabetes mellitus, %	20	26 / 17	0.39	35 / 15	0.18
Family history of CAD, %	36	38 / 35	0.95	42 / 34	0.05
Body mass index, kg/m^2	27.8 ± 3.7	27.2 ± 3.3 / 28.1 ± 3.9	0.29	27.4 ± 3.5 / 27.9 ± 3.8	0.60
Pre-infarction angina, %	30	35 / 28	0.58	27 / 32	0.85
Worst Killip-Kimball class: 1/2/3/4	80/17/2/0	24/8/2/0 / 56/9/0/0	0.06	21/3/2/0 / 59/14/0/0	0.04
Time: chest pain onset to balloon, h	4.8 ± 3.1	4.9 ± 3.2 / 4.8 ± 3.0	0.92	4.9 ± 3.9 / 4.8 ± 3.3	0.83
Time: door to balloon, min	34 ± 31	38 ± 37 / 32 ± 27	0.34	33 ± 31 / 34 ± 31	0.82
Nonsinus rhythm, %	6	6 / 6	1.0	8 / 5	0.65
Heart rate, beats/min	83 ± 17	82 ± 17 / 83 ± 17	0.93	80 ± 14 / 83 ± 18	0.50
Heart rate >100 beats/min, %	15	21 / 12	0.43	8 / 18	0.34
Anterior/inferior STEMI	65/34	24/10 / 41/24	0.60	10/16 / 55/18	0.30
V_{4r}: ST-segment elevation ≥0.1 mm, %	30	41 / 25	0.14	58 / 21	0.31
CPK_{max}, U/l	5,097 ± 4,131	5,527 ± 4,203 / 4,872 ± 4,107	0.46	6,588 ± 4,510 / 4,566 ± 3,882	0.03
$CPK\text{-}MB_{max}$, U/l	560 ± 401	620 ± 432 / 529 ± 383	0.29	677 ± 384 / 519 ± 401	0.08
TnI_{max}, μg/l	74 ± 59	77 ± 57 / 73 ± 61	0.77	90 ± 66 / 69 ± 56	0.12
Culprit lesion: LAD/RCA/LCX	65/32/2	24/10/0 / 41/22/2	0.50	10/16/0 / 55/16/2	0.0009
TIMI before PCI: 0/1/2/3	81/14/2/2	27/7/0/0 / 54/7/2/2	0.30	24/2/0/0 / 57/12/2/2	0.10
TIMI after PCI: 0/1/2/3	0/0/17/82	0/0/8/26 / 0/0/9/56	0.35	0/0/7/19 / 0/0/10/63	0.22
Rentrop scale: 0/1/2/3	72/20/6/1	25/8/1/0 / 47/12/5/1	0.65	22/3/1/0 / 50/17/5/1	0.45
Single/multivessel disease	53/46	16/18 / 37/28	0.47	15/11 / 38/35	0.79
Angiotensin-converting enzyme inhibitors, %	92	88 / 94	0.44	88 / 93	0.43
Beta-blockers, %	95	91 / 97	0.34	92 / 95	0.60
Statins, %	91	88 / 92	0.49	88 / 92	0.69

CAD = coronary artery disease; CPK_{max} = maximum creatine phosphokinase; $CPK\text{-}MB_{max}$ = maximum creatine phosphokinase-myocardial bound; LAD = left anterior artery; LCX = left circumflex artery; RCA = right coronary artery; RVMI = right ventricular myocardial infarction; STEMI = ST-segment elevation myocardial infarction; TnI_{max} = maximum troponin I.

Table 2. Cardiac Magnetic Resonance Characteristics With Regard to Right Ventricular Myocardial Infarction and Adverse Cardiac Events

		Event		RVMI	
	All Patients (n = 99)	Yes / No (n = 34) / (n = 65)	p Value	Present / Absent (n = 26) / (n =73)	p Value
LVEF, %	39 ± 11	34 ± 12 / 41 ± 10	0.002	32 ± 11 / 41 ± 11	0.001
LVEF <40%, %	50	65 / 43	0.07	65 / 45	0.12
LVEDV index, ml/m^2	75 ± 18	77 ± 18 / 73 ± 18	0.41	81 ± 16 / 72 ± 18	0.04
LVESV index, ml/m^2	47 ± 17	52 ± 18 / 44 ± 16	0.04	55 ± 17 / 44 ± 17	0.003
LV mass index, g/m^2	78 ± 21	79 ± 17 / 78 ± 23	0.87	87 ± 25 / 75 ± 19	0.01
LVSV index, ml/m^2	28 ± 8	25 ± 8 / 29 ± 8	0.008	25 ± 8 / 29 ± 8	0.08
RVEF, %	51 ± 13	47 ± 12 / 54 ± 13	0.009	44 ± 12 / 54 ± 13	0.001
RVEF <40%, %	23	38 / 15	0.02	38 / 18	0.06
RVEDV index, ml/m^2	55 ± 15	57 ± 16 / 53 ± 14	0.23	60 ± 15 / 53 ± 14	0.047
RVESV index, ml/m^2	27 ± 12	31 ± 12 / 25 ± 12	0.04	33 ± 13 / 25 ± 11	0.002
LVLGE index, %	22 ± 15	28 ± 16 / 18 ± 13	0.001	25 ± 13 / 21 ± 16	0.24
LVMO present, %	63	82 / 54	0.01	85 / 56	0.01
LVMO index, %	2.7 (IQR: 0.0–4.9)	3.7 (2.5–6.6) / 1.4 (0.0–4.2)	0.002	4.0 (2.9–7.4) / 1.6 (0.0–4.3)	0.002
LVMI transmurality index, %	59 ± 27	72 ± 23 / 52 ± 27	<0.001	62 ± 27 / 58 ± 27	0.51
RVMI present, %	26	44 / 17	0.007	100 / 0	<0.001
RVMI extent: 0/1/2/3/4/5 segments	73/11/8/3/3/1	19/5/6/2/1/1 / 54/6/2/1/2/0	0.04	0/11/8/3/3/1 / 73/0/0/0/0/0	<0.001

IQR = interquartile range; LV = left ventricular; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVLGE = left ventricular late gadolinium enhancement; LVMI = left ventricular myocardial infarction; LVMO = left ventricular microvascular obstruction; LVSV = left ventricular stroke volume; RVEDV = right ventricular end-diastolic volume; RVEF = right ventricular ejection fraction; RVESV = right ventricular end-systolic volume; RVMI = right ventricular myocardial infarction.

or an LVEF<40% was 74% and 51%, respectively ($p < 0.05$), whereas that in patients with an RVEF ≥40% or an RVEF <40% was 70% and 42%, respectively ($p < 0.01$). RVEF stratified risk in patients with LVEF <40% in whom the 4-year event-free survival was 66.7% for RVEF ≥40% and 40.0% for RVEF <40% ($p < 0.05$) (Fig. 4).

DISCUSSION

This is the first study to demonstrate that RV dysfunction and RVMI extent detected by CMR early after STEMI treated with primary angioplasty with stent implantation are independent prognosticators of adverse clinical events. The assess-

Table 3. Cardiac Magnetic Resonance Characteristics With Regard to STEMI Location

	STEMI		Anterior STEMI		Inferior STEMI	
	Anterior / Inferior (n = 65) / (n = 34)	p Value	Yes / No (n = 24) / (n = 41)	p Value	Yes / No (n = 10) / (n = 24)	p Value
LVEF, %	37 ± 11 / 41 ± 12	0.11	34 ± 12 / 39 ± 9	0.10	33 ± 11 / 45 ± 10	0.005
LVEF <40%, %	58 / 35	0.20	67 / 54	0.44	60 / 25	0.12
LVEDV index, ml/m^2	75 ± 19 / 74 ± 17	0.93	75 ± 18 / 74 ± 20	0.79	79 ± 9 / 72 ± 16	0.26
LVESV index, ml/m^2	48 ± 18 / 44 ± 16	0.34	51 ± 19 / 46 ± 18	0.37	55 ± 19 / 40 ± 13	0.02
LV mass index, g/m^2	78 ± 20 / 79 ± 23	0.83	75 ± 14 / 80 ± 23	0.34	88 ± 21 / 75 ± 23	0.12
LVSV index, ml/m^2	27 ± 7 / 30 ± 9	0.06	25 ± 8 / 28 ± 6	0.11	25 ± 7 / 32 ± 9	0.04
RVEF, %	52 ± 13 / 51 ± 14	0.62	46 ± 12 / 55 ± 12	0.007	48 ± 11 / 52 ± 15	0.43
RVEF <40%, %	22 / 26	0.76	42 / 10	0.004	30 / 25	1.00
RVEDV index, ml/m^2	52 ± 14 / 59 ± 15	0.04	58 ± 16 / 49 ± 13	0.02	56 ± 15 / 60 ± 15	0.40
RVESV index, ml/m^2	26 ± 12 / 30 ± 13	0.17	32 ± 13 / 23 ± 10	0.003	28 ± 8 / 30 ± 15	0.75
LVLGE index, %	24 ± 16 / 17 ± 13	0.02	28 ± 17 / 22 ± 14	0.14	30 ± 15 / 12 ± 8	<0.001
LVMO present, %	63 / 65	0.95	75 / 56	0.21	100 / 50	0.006
LVMO index, %	2.5 (IQR: 0.0–4.9) / 2.9 (IQR: 0.0–4.5)	0.95	3.5 (IQR: 1.4–6.6) / 1.4 (IQR: 0.0–4.3)	0.08	4.9 (IQR: 3.4–6.4) / 0.7 (IQR: 0.0–3.7)	0.003
LVMI transmurality index, %	62 ± 26 / 52 ± 29	0.07	71 ± 24 / 58 ± 26	0.049	75 ± 22 / 43 ± 26	0.002
RVMI present, %	15 / 47	0.002	21 / 12	0.48	100 / 25	<0.001
RVMI extent: 0/1/2/3/4/5 segments	55/3/5/1/0/1 / 18/8/3/2/3/0	0.39	19/1/3/0/0/1 / 36/2/2/1/0/0	0.45	0/4/3/2/1/0 / 18/4/0/0/2/0	<0.001

STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Tables 1 and 2.

ment of RVEF and RVMI enhances the prognostication of CMR-derived LV parameters and provides incremental prognostic value to clinical data, LV systolic dysfunction, and infarct burden. Moreover, RVEF allows risk stratification of patients after STEMI, especially those with an LVEF <40%.

So far, several trials have showed that after STEMI either RV dysfunction or RVMI are important determinants of short- and long-term prognosis (1,3–5). The present study demonstrates that RV involvement diagnosed early after STEMI is a strong outcome predictor and that both RVEF and RVMI have an important prognostic impact irrespective of LVMI burden. Compared with previous studies, cardiac mortality in the current trial was low, which may have several plausible explanations. First, previous observations were derived predominantly from STEMI patients treated with thrombolysis or no reperfusion therapy, whereas in the present study, the majority of subjects underwent primary angioplasty within 6 h after STEMI symptom onset. Second, in the current trial, primary angioplasty with stent implantation successfully established normal Thrombolysis In Myocardial Infarction grade 3 epicardial flow in most individuals. As previously demonstrated, patients with RVMI who have timely and complete reperfusion of right coronary artery have an excellent short-term prognosis (7). Finally, patients with severe heart/respiratory failure who were unable to undergo CMR early after STEMI, were excluded. To our knowledge, we are the first to show that both RV dysfunction and RVMI extent are independently associated with clinical outcomes. It may be due to the fact that RV involvement was previously diagnosed by electrocardiography, echocardiography, or radionuclide angiography, but not CMR, which, being actually the gold standard for RV assessment, has been performed only in 2 studies evaluating the prognostic value of RV involvement after MI (11,13). In the first study, Larose et al. (11) demonstrated by univariable analysis that both RVMI and RVEF were associated with clinical outcomes. However, by multivariable analysis, only RVEF, but not RVMI, determined prognosis. Moreover, in the second study, the prognostic value of RVMI was not confirmed by Hombach et al. (13), who performed CMR early after acute MI. This discrepancy with our findings may be related to shorter follow-up, lower prevalence of RVMI, and a lower number of observed events in those trials. As previously reported, our data demonstrate that assessment of RV involvement enhances prognostication after acute MI (1,3–5,11). In the current study, both RVEF and RVMI extent improved risk as-

Table 4. Univariable Predictors of Adverse Cardiac Events

Variable	Univariable Predictors	
	Hazard Ratio (95% CI)	p Value
Male	0.84 (0.38–1.86)	0.67
Age, yrs	1.02 (0.99–1.05)	0.18
Current tobacco use	1.01 (0.49–2.07)	0.98
Hypercholesterolemia	1.41 (0.34–5.89)	0.64
Hypertension	1.7 (0.74–3.91)	0.21
Diabetes mellitus	1.49 (0.69–3.19)	0.31
Family history of CAD	1.08 (0.54–2.16)	0.83
Body mass index, kg/m^2	0.94 (0.85–1.04)	0.20
Pre-infarction angina	1.28 (0.63–2.60)	0.50
Worst Killip-Kimball class	2.26 (1.19–4.32)	0.01
Time: chest pain onset to balloon, h	1.01 (0.91–1.13)	0.87
Time: door to balloon, min	1.01 (1.00–1.02)	0.31
Nonsinus rhythm	1.11 (0.26–4.66)	0.89
Heart rate, beats/min	1.00 (0.98–1.02)	0.92
Heart rate >100 beats/min	1.48 (0.65–3.41)	0.35
Anterior STEMI	1.53 (0.73–3.22)	0.26
Inferior STEMI	0.65 (0.31–1.58)	0.26
V_{4r}: ST-segment elevation ≥0.1 mm	2.00 (1.01–3.97)	0.047
CPK_{max} per 100 U/l	1.00 (0.96–1.05)	0.95
CPK-MB_{max} per 10 U/l	1.01 (0.97–1.05)	0.63
TnI_{max} per 10 μg/l	1.05 (0.79–1.39)	0.74
TIMI 0 before PCI	1.32 (0.58–3.05)	0.51
TIMI 3 after PCI	0.54 (0.24–1.19)	0.12
Rentrop 0	1.04 (0.49–2.23)	0.92
Multivessel disease	1.25 (0.64–2.46)	0.52
Angiotensin-converting-enzyme inhibitors	0.54 (0.19–1.52)	0.24
Beta-blockers	0.36 (0.11–1.17)	0.09
Statins	0.67 (0.24–1.9)	0.45
LVEF <40%	2.17 (1.08–4.38)	0.03
LVEF per 10% decrease	1.56 (1.15–2.11)	0.004
LVEDV index per 1 ml/m^2	1.01 (0.99–1.03)	0.33
LVESV index per 1 ml/m^2	1.02 (1.00–1.04)	0.02
LVSV index per 1 ml/m^2 decrease	1.07 (1.02–1.14)	0.005
LVmass index per 1 g/m^2	1.00 (0.99–1.02)	0.95
RVEF <40%	2.66 (1.33–5.33)	0.006
RVEF per 10% decrease	1.69 (1.27–2.25)	<0.001
RVEDV index per 1 ml/m^2	1.01 (0.99–1.04)	0.23
RVESV index per 1 ml/m^2	1.03 (1.00–1.05)	0.04
LVLGE index, %	1.03 (1.01–1.05)	0.001
LVMI transmurality index, %	1.02 (1.01–1.04)	0.001
LVMO present	3.1 (1.29–7.53)	0.01
LVMO index, %	1.06 (1.01–1.11)	0.02
RVLGE present	2.82 (1.43–5.55)	0.003
RVLGE segment number	1.51 (1.18–1.92)	0.001

CI = confidence interval; LV = left ventricular; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Tables 1, 2, and 3.

Table 5. Multivariable Models for Prediction of Adverse Cardiac Events

		Multivariable Predictors		
Model	**Variables Tested**	**Hazard Ratio (95% CI)**	**p Value**	**Chi-Square**
1	LVEF per 10% decrease			
	RVEF per 10% decrease	1.69 (1.27–2.25)	<0.001	13.9
	RVLGE segment number			
2	LVLGE index, %	1.03 (1.01–1.05)	0.005	
	RVEF per 10% decrease	1.39 (1.00–1.92)	0.049	22.4
	RVLGE segment number	1.36 (1.02–1.80)	0.04	
3	LVMO index, %			
	RVEF per 10% decrease	1.69 (1.27–2.25)	<0.001	13.9
	RVLGE segment number			
4	LVMI transmurality index, %	1.03 (1.01–1.04)	0.001	
	RVEF per 10% decrease	1.46 (1.05–2.02)	0.03	29.8
	RVLGE segment number	1.50 (1.11–2.01)	0.007	

Abbreviations as in Tables 2, 3, and 4.

sessment after STEMI; in particular, RVEF stratified risk in subjects with an LVEF <40%. Interestingly, biventricular dysfunction occurred in 20% of individuals and was associated with the highest annualized event rate, reaching 15%. It emphasizes the need to assess RV function after STEMI, especially in those who have depressed LV function.

The present study confirms previous observations that RV systolic dysfunction is predominantly related to LV systolic dysfunction in anterior STEMI and to RVMI in inferior STEMI (3,14). Our data suggest that in patients with inferior STEMI, adverse cardiac events may be more strongly associated with RVMI than with RVEF, which is in line with early recovery of RV function after successful reperfusion of inferior STEMI (7). Conversely, in patients with anterior STEMI, the outcome was related to depressed RVEF, but not RVMI. This may be explained by the fact that, if present, the area of RV necrosis accompanying anterior STEMI is small. Recently, it was demonstrated that in successfully reperfused anterior STEMI, RVMI

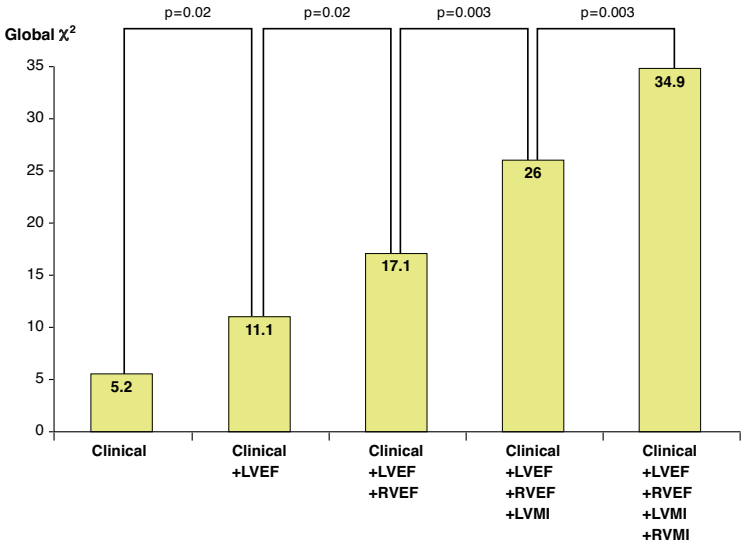

Figure 3. Prognostic Value of Clinical and Cardiac Magnetic Resonance Data in Sequential Cox Model Analysis

Compared with clinical data, left ventricular ejection fraction (LVEF), right ventricular ejection fraction (RVEF), left ventricular myocardial infarction (LVMI) transmural extent and right ventricular myocardial infarction (RVMI) extent improve prediction of adverse cardiac events defined as cardiac death, nonfatal myocardial infarction, and/or hospitalization due to decompensated heart failure.

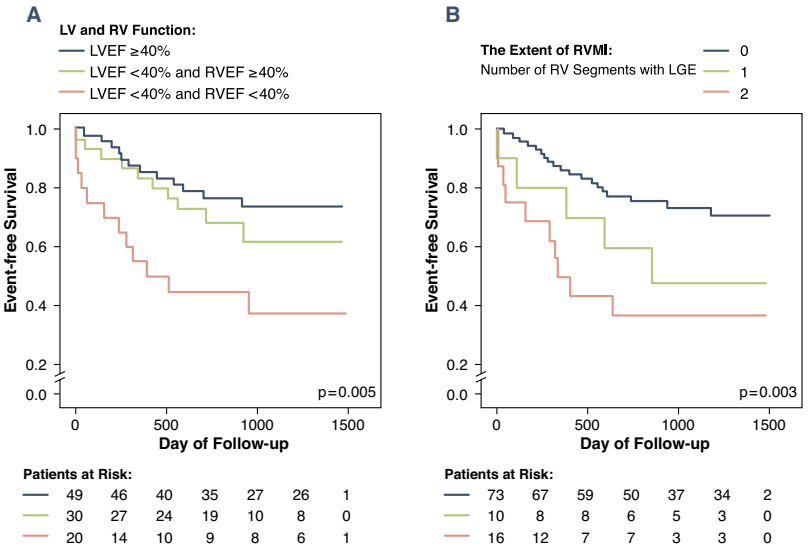

Figure 4. Kaplan-Meier Event-Free Survival Curves With Respect to Systolic Function (A) and the extent of RVMI (B)

Both cardiac magnetic resonance–derived right ventricular ejection fraction (RVEF) and right ventricular myocardial infarction (RVMI) extent stratify risk of adverse cardiac events defined as cardiac death, nonfatal myocardial infarction, and/or hospitalization due to decompensated heart failure. LGE = late gadolinium enhancement; LV = left ventricular; LVEF = left ventricular ejection fraction; RV = right ventricular.

affected only 2% of RV mass despite the large extent of RV myocardium at risk (15). There may be several plausible reasons for the preservation of the RV wall in the settings: its low oxygen demand, its ability to increase oxygen extraction, homogeneous transmural perfusion, extensive collateral system, and complete left anterior descending artery reperfusion (15,16).

Study limitations. First, although CMR may be considered the gold standard for RVEF assessment, there can be difficulties in discriminating the RV from the right atrium wall at the tricuspid valve level in the short-axis view due to through-plane movement of the atrioventricular groove. To better discern it, we carefully observed heart chamber motion and used dedicated software to evaluate cross section lines of short-axis planes in apical 4-chamber and RV cine images. Furthermore, RVEF as assessed by CMR is influenced by loading conditions and may not solely reflect contractility. Unfortunately, echocardiographic assessment of RV function and evaluation of systolic pulmonary pressure were not performed to help clarify the mechanism of RV dysfunction. The relatively low spatial resolution for LGE imaging in the thin RV wall, the difficulty to separate infarcted tissue from surrounding fat, and partial volume effect of fat signal may limit accurate detection of RVMI (12). Moreover, the myocardium at risk for both ventricles was not assessed, not allowing us to determine the myocardial salvage. Finally, due to the inability to perform CMR early after STEMI complicated by severe heart/respiratory failure, the present study may be biased toward a less complicated cohort of patients.

CONCLUSIONS

CMR is an important diagnostic tool for assessing not only LV but also RV involvement early after STEMI. The extent of RVMI and RV dysfunction after primary angioplasty with stent implantation for STEMI are powerful independent predictors of adverse clinical outcomes and provide incremental prognostic information to clinical data, LV systolic dysfunction, and infarct burden. Measurement of RVEF should be considered in all patients with STEMI and may be particularly useful to further stratify risk in those with depressed LV function.

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