Prediction of Reverse Remodeling at Cardiac MR Imaging Soon after First ST-Segment–Elevation Myocardial Infarction: Results of a Large Prospective Registry[1]

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Purpose: To assess predictors of reverse remodeling by using cardiac magnetic resonance (MR) imaging soon after ST-segment–elevation myocardial infarction (STEMI).

Materials and Methods: Written informed consent was obtained from all patients, and the study protocol was approved by the institutional committee on human research, ensuring that it conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Five hundred seven patients (mean age, 58 years; age range, 24–89 years) with a first STEMI were prospectively studied. Infarct size and microvascular obstruction (MVO) were quantified at late gadolinium-enhanced imaging. Reverse remodeling was defined as a decrease in left ventricular (LV) end-systolic volume index (LVESVI) of more than 10% from 1 week to 6 months after STEMI. For statistical analysis, a simple (from a clinical perspective) multiple regression model preanalyzing infarct size and MVO were applied via univariate receiver operating characteristic techniques.

Results: Patients with reverse remodeling (n = 211, 42%) had a lesser extent (percentage of LV mass) of 1-week infarct size (mean ± standard deviation: 18% ± 13 vs 23% ± 14) and MVO (median, 0% vs 0%; interquartile range, 0%–1% vs 0%–4%) than those without reverse remodeling (n = 296, 58%) ($P < .001$ in pairwise comparisons). The independent predictors of reverse remodeling were infarct size (odds ratio, 0.98; 95% confidence interval [CI]: 0.97, 0.99; P = .04) and MVO (odds ratio, 0.92; 95% CI: 0.86, 0.99; P = .03). Once infarct size and MVO were dichotomized by using univariate receiver operating characteristic techniques, the only independent predictor of reverse remodeling was the presence of simultaneous nonextensive infarct-size MVO (infarct size < 30% of LV mass and MVO < 2.5% of LV mass) (odds ratio, 3.2; 95% CI: 1.8, 5.7; $P < .001$).

Conclusion: Assessment of infarct size and MVO with cardiac MR imaging soon after STEMI enables one to make a decision in the prediction of reverse remodeling.

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Left ventricular (LV) remodeling can occur in a wide variety of abnormal conditions associated with heart failure, and the course and clinical implications of this process have been extensively analyzed (1,2). The term LV reverse remodeling (hereafter referred to as reverse remodeling) refers to the concept that the failing heart is capable of undergoing favorable changes in LV volume and mass as a consequence of medical, device-based, and surgical interventions and reassuming a more normal and energetically favorable elliptical shape (1,3–5). Interestingly, most of these clinical studies have reported that reverse remodeling is associated with an improvement in patient outcome (5–8).

ST-segment–elevation myocardial infarction (STEMI) has become one of the main causes of heart failure (9). Cardiac magnetic resonance (MR) imaging, including parameters that were recently shown to be crucial to patient outcome—namely, infarct size and microvascular obstruction (MVO) —has become the reference standard noninvasive imaging technique for comprehensive assessment of patients with STEMI, (10,11). So far, no study specifically designed to address reverse remodeling after STEMI at cardiac MR imaging has been reported. Our hypothesis was that a simultaneous assessment of infarct size and MVO as derived from cardiac MR imaging can help predict reverse remodeling after STEMI. In this study, we aimed to assess predictors of reverse remodeling by performing cardiac MR imaging soon after STEMI.

Advance in Knowledge

- This large prospective registry of patients with a first ST-segment–elevation myocardial infarction (STEMI) treated with percutaneous coronary intervention shows that the detection of simultaneous nonextensive infarct size and microvascular obstruction at cardiac MR imaging performed 1 week after infarction is decisive in predicting reverse remodeling during the following 6 months.

Materials and Methods

Patients

This study stems from an ongoing prospective registry carried out in a university hospital (12,13). Patients were considered for inclusion in the study group if they were admitted for a first STEMI that was defined according to current definitions, treated with PCI within 12 hours of chest pain onset, and underwent cardiac MR imaging 1 week and 6 months after STEMI (14). We discarded the presence of a prior myocardial infarction on the basis of the absence of any previous admissions due to cardiovascular diseases and by the absence of electrocardiographic abnormalities, which suggest prior myocardial infarction. Exclusion criteria were death, reinfarction, or clinical instability at cardiac MR imaging performed 1 week or 6 months after STEMI, as well as incomplete cardiac MR imaging studies, insufficient image quality, and contraindications to cardiac MR imaging. From January 2008 to December 2010, 507 patients were prospectively included (Fig 1).

All patients gave written informed consent. The study protocol was approved by the institutional committee on human research in our institution and conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

In all patients, clinical and angiographic characteristics were registered upon admission. Patients were managed by a specific STEMI unit both in the hospital and after discharge, and current recommendations were strictly followed (15,16). Baseline characteristics of the entire study group and of patients both with and without reverse remodeling are shown in Table E1 (online).

Implications for Patient Care

- The information derived from cardiac MR imaging performed 1 week after a first STEMI relates to the occurrence of reverse remodeling during the following 6 months.
- Reverse remodeling of the left ventricle (LV) can be predicted by using the presence of simultaneous nonextensive infarct size (<30% of LV mass) and nonextensive microvascular obstruction (<2.5% of LV mass) at late gadolinium-enhanced imaging performed 1 week after infarction; this result was derived from a multiple logistic regression model in which the two independent variables were dichotomized by preanalyzing the data with univariate receiver operating characteristic techniques.

Cardiac MR Imaging

All patients were examined with a 1.5-T MR imaging system (Sonata Magnetom; Siemens, Erlangen, Germany) according to our study protocol. Images were acquired with the use of a phased-array body surface coil, breath holding, and

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Abbreviations:
LV = left ventricle
LVEDVI = LV end-diastolic volume index
LVEF = LV ejection fraction
LVESVI = LV end-systolic volume index
MACE = major adverse cardiac events
MVO = microvascular obstruction
PCI = percutaneous coronary intervention
ROC = receiver operating charactistics curve
STEMI = ST-segment–elevation myocardial infarction

Author contributions:
Guarantor of integrity of entire study, V.B.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, V.B., J.V.M., J.T.O.P., M.P.L.L., O.H., G.M., C.G., J.N., M.J.F., A.H., E.d.D., D.M., X.B., F.J.C.; clinical studies, V.B., M.P.L.L., C.B., J.N., X.B., F.J.C.; statistical analysis, V.B., J.V.M., J.T.O.P., O.H., M.J.F., D.M.; and manuscript editing, V.B., E.d.D., F.J.C.

Conflicts of interest are listed at the end of this article.

Figure 1

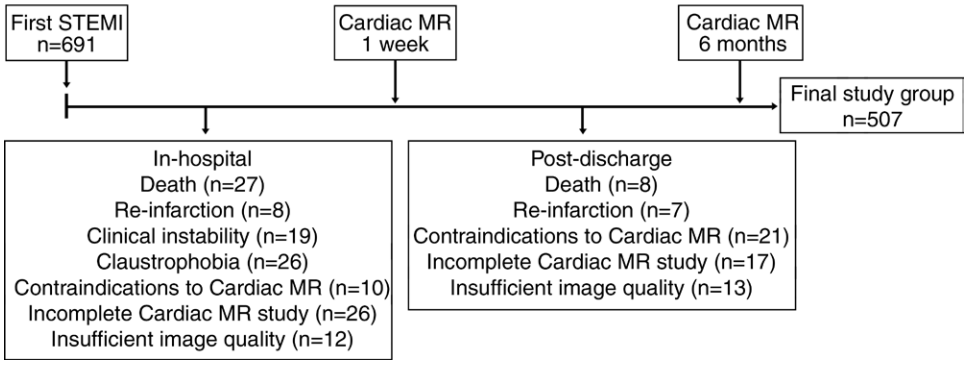


Figure 1: Flowchart shows the reasons patients were excluded from the study.

electrocardiographic triggering. In all studies, images were acquired by two cardiologists (M.P.L.L. and J.V.M., both with 15 years of experience) who specialized in cardiac MR imaging. Then, studies were quantified offline by a third operator (F.C., with 8 years of experience), who was blinded to all patient data, by using customized software (QMASS MR 6.1.5; Medis, Leiden, the Netherlands). Inter- and intraobserver variability for calculating all cardiac MR imaging indexes used in the present study are reported in Table E2 (online). Cardiac MR imaging data were prospectively and immediately included in the registry database.

Cine images were acquired in two-, three-, and four-chamber and short-axis views by using a steady-state free precession sequence (repetition time msec/echo time msec, 25/1.6; flip angle, 61°; matrix, 256 × 256, field of view, 320 × 270 mm, section thickness, 7 mm). Late gadolinium contrast material–enhanced imaging was performed 10–15 minutes after administering 0.1 mmol/kg of gadolinium diethylenetriamine pentaacetic acid (Magnograf; Juste S.A.Q.F., Madrid, Spain) in the same locations as in cine imaging by using a segmented inversion recovery steady-state free precession sequence (750/1.26; flip angle, 45°; matrix, 256 × 184; field of view, 340 × 235 mm, section thickness, 7 mm). Inversion time was adjusted to nullify healthy myocardium.

Black-blood, T2-weighted, and short TI inversion recovery sequences were performed in mid diastole in the same short-axis view as the cine sequences. A half-Fourier acquisition single-shot turbo spin-echo multisection sequence was used (recovery time, 2 R-R intervals; echo time, 33 msec, inversion time, 170 msec; section thickness, 8 mm; section interval, 2 mm; flip angle, 160°; matrix, 256 × 151; bandwidth, 781 Hz/pixel). Additionally, a segmented turbo spin-echo sequence was performed with one section per breath hold (recovery time, 2 R-R intervals; echo time, 100 msec; inversion time, 170 msec; section thickness, 8 mm; section interval, 2 mm; flip angle, 180°; matrix, 256 × 146; bandwidth, 235 Hz/pixel). LV ejection fraction (LVEF), LV end-diastolic volume index (LVEDVI), LV end-systolic volume index (LVESVI), and LV mass were calculated with manual planimetry of endocardial and epicardial borders on short-axis cine images.

On the basis of recent literature, reverse remodeling was defined as a decrease in LVESVI of more than 10% on cardiac MR images obtained 1 week and 6 months after STEMI (3,17,18). This cut-off value was more than twice the mean intraobserver variability (3%) that we detected for LVESVI in the reproducibility test (Table E2 [online]).

Initially, late gadolinium enhancement was regarded as signal intensity higher than 5 standard deviations above that of a remote noninfarcted area in the same section. Subsequently, areas with late gadolinium enhancement were visually revised and quantified with manual planimetry. Infarct size was assessed as the percentage of LV mass with late gadolinium enhancement. MVO was quantified with manual planimetry and defined as the percentage of LV mass with a lack of contrast material uptake in the core of tissue with late gadolinium enhancement (11–13).

Myocardial edema was regarded as areas of high signal intensity on T2-weighted images. A core of low signal intensity surrounded by an area with high signal intensity was considered to indicate myocardial hemorrhage. In each study, for quantification of all sections, only one of the two T2-weighted sequences performed (that with the highest image quality) was used to analyze edema and hemorrhage. All short-axis sections were separately analyzed, and the presence of signal intensity higher than 2 standard deviations above that of a remote noninfarcted area in the same section was considered to indicate edema. Then, myocardial edema and myocardial hemorrhage were manually revised and expressed as percentage of LV mass. The myocardial salvage index was calculated by subtracting the mass of infarcted myocardium from myocardium showing edema and expressed as percentage of LV mass with myocardial edema (10,11).

End Points and Follow-up

The end points of the present study were to analyze the incidence of reverse remodeling and its predictors at cardiac MR imaging performed 1 week after STEMI in a prospective series of patients with a first STEMI. We explored the association between the occurrence of reverse remodeling and major adverse cardiac events (MACE), a composite of cardiac death, nonfatal myocardial infarction, and readmission for heart failure (whichever occurred first), according to current recommendations (14,19). To adjudicate an event, consensus between two cardiologists was required.

Statistical Analysis

Data were tested for normal distribution by using the Kolmogorov-Smirnov test. Continuous normally distributed data were expressed as the mean plus or minus the standard deviation of the mean and compared by using the unpaired or paired samples Student *t* test where appropriate. The analysis of variance test (*P* for the trend) was used to compare more than two groups. Nonparametric data were expressed as the median with the interquartile range and compared by using the Mann-Whitney *U* test. Group percentages were compared by using the χ^2 test or Fisher exact test where appropriate. *P* for the trend was used to compare more than two percentages.

The association of reverse remodeling with time to MACE was assessed with Kaplan-Meier curves and the log-rank test. Patients were censored from the survival analysis at the moment of the first MACE (ie, cardiac death, nonfatal myocardial infarction, or readmission for heart failure), at the moment they were lost to follow-up, or 5 years after the inclusion of the first patient in the study group. Patients were included in the survival analysis until they reached any of the reasons for censorship, at which point they were excluded from this test.

To predict reverse remodeling, forward, backward, and forward-backward stepwise multiple logistic regression procedures were tested and adjusted by baseline, angiographic, and cardiac MR imaging variables, yielding $P < .2$ in univariate analyses. Odds ratios with the respective 95% confidence intervals were computed. Two analyses were used in this article: First, multiple logistic regression was performed, in which all variables were used as predictors and all continuous variables were treated as continuous. Infarct size and MVO (tested as continuous variables) were the independent predictors in the forward, backward, and forward-backward stepwise multiple logistic regression procedures. Then, a simpler (from a clinical perspective) multiple logistic regression model was proposed by dichotomizing infarct size and MVO via univariate receiver operating characteristics curve (ROC) techniques. Once the best cut-off values of infarct size (considered extensive if more than 30% of LV mass) and MVO (considered extensive if more than 2.5% of LV mass) for predicting reverse remodeling were obtained, nonoverlapping patients were categorized as having simultaneous nonextensive infarct size and MVO, extensive MVO and nonextensive infarct size, extensive infarct size and nonextensive MVO, or simultaneous extensive infarct size and MVO. The in-sample predictive value of these categories to predict reverse remodeling in univariate and multiple regression analyses was assessed. The association of these categories with the state of LVEF, LVEDVI, and LV mass at cardiac MR imaging performed 6 months after STEMI was also investigated.

The final forward, backward, and forward-backward multiple regression models yielded the same independent predictors of reverse remodeling both when continuous variables were treated as continuous and when infarct size and MVO were dichotomized. Data shown throughout this article refer to the forward multiple regression models. A two-tailed $P < .05$ was considered to indicate a significant difference. The SPSS statistical package (version 18.0; SPSS, Chicago, Ill) was used.

Results

Of 691 patients with STEMI who were consecutively admitted to our institution between January 2008 and December 2010 and treated with PCI within the first 12 hours after chest pain onset, 184 were excluded due to death, reinfarction, clinical instability, claustrophobia, contraindications to cardiac MR imaging, incomplete cardiac MR imaging studies, or insufficient image quality before cardiac MR imaging performed 1 week or 6 months after STEMI (Fig 1). Thus, the final study group comprised 507 patients who were successfully evaluated with cardiac MR imaging 1 week and 6 months after STEMI (Fig 1). The mean age was 58 years (range, 24–89). Women ($n = 81$; mean age, 64 years; age range, 31–86 years) were significantly older ($P < .001$) than men ($n = 426$; mean age, 57 years; age range, 24–89 years). Baseline and cardiac MR imaging characteristics are shown in Table E1 (online).

Incidence and Structural Consequences of Reverse Remodeling

Reverse remodeling (>10% decrease in LVESVI at 6 months) occurred in 211 patients (42%). Baseline characteristics of patients with and without reverse remodeling are shown in Table E1 (online), and dynamic changes in cardiac MR imaging indexes from 1 week to 6 months in the whole study group are shown in Table E3 (online).

From 1 week to 6 months, a −5% (range, −21% to 11%) reduction in LVESVI occurred in the entire study group. Patients with reverse remodeling showed a decrease in LVESVI of −25% (range, −35% to −18%), whereas the opposite (4%; range, −3% to 20%) was seen in those without reverse remodeling; $P < .001$.

In patients with reverse remodeling, from 1 week to 6 months, LVEDVI and LVESVI diminished, whereas LVEF increased ($P < .001$ for all pairwise comparisons). Conversely, patients without reverse remodeling exhibited substantial dilation of LVEDVI and LVESVI, as

well as deterioration of LVEF ($P <$ .001 for all pairwise comparisons) (Table 1).

Cardiac MR Imaging Predictors of Reverse Remodeling

The magnitude of LV dilation and systolic dysfunction soon after infarction was not associated with reverse remodeling; no significant differences in terms of LVEDVI, LVESVI, LV mass, or LVEF were observed between patients with and those without reverse remodeling at 1-week cardiac MR imaging. Nevertheless, compared with patients without reverse remodeling, those with reverse remodeling displayed a much less extensive infarct size and MVO 1 week after infarction ($P <$ .001) (Fig E1 [online]). Less edema and hemorrhage ($P <$ .05) and a trend toward more myocardial salvage index ($P <$ .1) were detected at 1-week cardiac MR imaging in the case of reverse remodeling (Fig E1 [online]).

In the multiple regression analysis, once adjustments for baseline and cardiac MR imaging characteristics showing an association ($P <$ .2) with reverse remodeling in the univariate analysis (ie, age, male sex, diabetes mellitus, anterior infarction, thrombolysis in myocardial infarction flow grade before PCI, edema, hemorrhage, myocardial salvage index, infarct size, and MVO) were made, the only independent predictors of reverse remodeling were infarct size (0.98; range, 0.97–0.99; P = .04) and MVO (0.92; range, 0.86–0.99; P = .03) (Table 2).

Table 1

Evolution of LVEF, Volumes Indexes, and Mass from the First Week to the Sixth Month in Patients with and without Reverse Remodeling

	With Reverse Remodeling (n = 211)			Without Reverse Remodeling (n = 296)		
Characteristic	1 Week	6 Months	*P* Value	1 Week	6 Months	*P* Value
LVEF (%)	51 ± 12	59 ± 11	<.001	50 ± 12	50 ± 13	.9
LVEDVI (mL/m^2)	81 ± 18	71 ± 17	<.001	78 ± 23	88 ± 24	<.001
LVESVI (mL/m^2)	41 ± 17	30 ± 13	<.001	40 ± 20	46 ± 23	<.001
LV mass (g/m^2)	70 ± 15	64 ± 13	<.001	71 ± 18	68 ± 16	.001

Note.—Unless otherwise indicated, data are the means plus or minus standard deviation.

Table 2

Predictors of Reverse Remodeling at Multiple Regression Analyses

Predictor	Odds Ratio	*P* Value
Age (y)	1.01 (0.99, 1.03	.3
Male sex (%)	0.7 (0.40, 1.40)	.3
Diabetes mellitus	0.69 (0.38, 1.27)	.2
Anterior infarction (%)	1.13 (0.68, 1.88)	.6
TIMI flow grade before PCI	1.00 (0.85, 1.18)	.9
Edema (% of LV mass)	1.00 (0.95, 1.05)	.9
Hemorrhage (% of LV mass)	1.00 (0.91, 1.11)	.9
Myocardial salvage index (%)	1.00 (0.98, 1.02)	.8
MVO (% of LV mass)	0.92 (0.86, 0.99)	.03
IS (% of LV mass)	0.98 (0.97, 0.99)	.04
Categories of IS and MVO		
Simultaneous extensive IS and MVO	…	…
Extensive IS and nonextensive MVO	1.65 (0.71, 3.82)	.2
Extensive MVO and nonextensive IS	1.20 (0.54, 2.69)	.6
Simultaneous nonextensive IS and MVO	3.18 (1.77, 5.70)	<.001

Note.—Data in parentheses are 95% confidence intervals. Variables that yielded a *P* value off less than .2 at univariate analyses (age, male sex, diabetes mellitus, anterior infarction, TIMI flow grade before PCI, edema, hemorrhage, myocardial salvage index, MVO, and infarct size) were tested (Table E1 and Fig E1 [online]). All cardiac MR imaging variables (ie, edema, hemorrhage, myocardial salvage index, MVO, and infarct size) were tested as continuous variables. The independent variables (ie, infarct size and MVO) were dichotomized according to their best cut-off values for predicting reverse remodeling on the basis of their respective univariate ROCs (extensive infarct size if > 30% of LV mass and extensive MVO if > 2.5% of LV mass). Simultaneous extensive infarct size and MVO is used as the reference category for comparisons. IS = infarct size, TIMI = thrombolysis in myocardial infarction.

Combined Role of infarct size and MVO at Reverse Remodeling

More extensive infarct size and MVO were independently associated with a lower probability of reverse remodeling. The independent variables (ie, infarct size and MVO) were dichotomized as extensive (infarct size > 30% of LV mass and MVO > 2.5% of LV mass) or nonextensive as derived from the best cut-off values to predict reverse remodeling on the basis of their respective ROCs (infarct size, 0.61; range, 0.56–0.68; MVO, 0.59; range, 0.54–0.64). Simultaneous nonextensive infarct size and MVO occurred in 336 patients (66%), extensive MVO and nonextensive infarct size occurred in 56 (11%), extensive infarct size and nonextensive MVO occurred in 42 (8%), and simultaneous extensive infarct size and MVO occurred in 73 (15%).

From 1 week to 6 months after STEMI, LVESVI diminished in patients with nonextensive infarct size and MVO (35 mL/m^2 ± 15 vs 31 mL/m^2 ± 13; $P <$ .001), did not vary in those with extensive MVO and nonextensive infarct size (42 mL/m^2 ± 11 vs 41 mL/m^2 ± 11, P = .7) or extensive infarct size and nonextensive MVO (54 mL/m^2 ± 26 vs 56 mL/m^2 ± 28; P = .5), and dilated in patients with extensive infarct size and MVO (59 mL/m^2 ± 21 vs 65 mL/m^2 ± 27; P = .004) (Figs 2, 3).

Figure 2

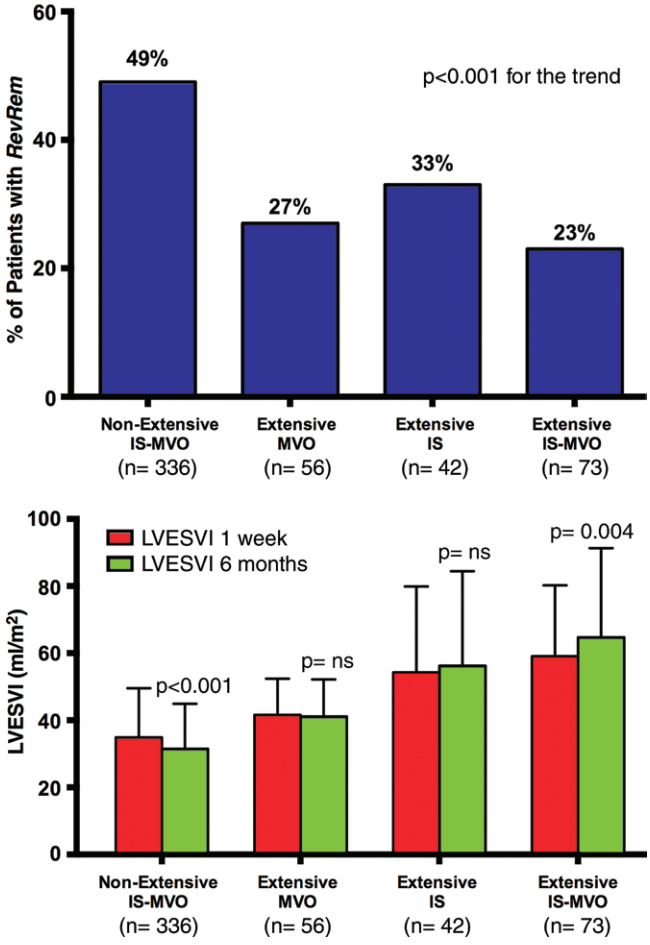


Figure 2: Graphs show the occurrence and course of reverse remodeling *(RevRem)* according to the magnitude of infarct size *(IS)* and MVO at 1-week cardiac MR imaging. The independent variables, infarct size, and MVO were dichotomized as extensive (infarct size > 30% of LV mass and MVO > 2.5% of LV mass) or nonextensive as derived from the best cut-off values to predict reverse remodeling on the basis of their respective univariate ROCs. The occurrence of reverse remodeling was highest in patients with simultaneous nonextensive infarct size and MVO (top). Lower panel: From 1 week to 6 months, LVESVI diminished in patients with simultaneous nonextensive infarct size and MVO, did not vary in those with extensive MVO and nonextensive infarct size or extensive infarct size and nonextensive MVO, and dilated in patients with simultaneous extensive infarct size and MVO (bottom).

Reverse remodeling occurred in 165 of 336 patients (49%) with nonextensive infarct size and MVO, 15 of 56 patients (27%) with extensive MVO and nonextensive infarct size, 14 of 42 patients (33%) with extensive infarct size and nonextensive MVO, and 17 of 73 patients (23%) with extensive infarct size and MVO ($P < .001$ for the trend) (Fig 2). When these four categories of infarct size and MVO were incorporated into the multiple regression analysis, the presence of nonextensive infarct size and MVO appeared as the only independent predictor of reverse remodeling (3.18; range, 1.77–5.70; $P < .001$) (Table 2). A steady deterioration in ejection fraction and dilation in LVESVI, LVEDVI, and LV mass at 6 months after STEMI was detected along the four categories of infarct size and MVO (Fig 4).

Reverse Remodeling and MACE

During a mean follow-up period of 186 weeks ± 113 (range, 12–250 weeks), 56 first MACE took place, including 12 deaths, 21 reinfarctions, and 23 readmissions for heart failure. Reverse remodeling showed a nonsignificant trend toward a lower probability of MACE occurring during the follow-up period (16 of 211 [7%] vs 40 of 296 [13%]; $P = .055$) (Fig 5).

Discussion

The main findings of the present study were as follows: *(a)* in a large prospective series of patients with a first STEMI treated with PCI, sequential cardiac MR imaging depicted reverse remodeling in almost one-half of cases and *(b)* late gadolinium-enhanced imaging contributes the most relevant information in the prediction of reverse remodeling. The presence of simultaneous nonextensive infarct size and nonextensive MVO at 1-week cardiac MR imaging predicted the occurrence of reverse remodeling to best advantage.

Incidence and Structural Consequences of Reverse Remodeling after STEMI

Little information is available on reverse remodeling after STEMI. Only three studies, all of which are based on echocardiography, have specifically addressed this issue (17,18,20). So far, there have been no reports analyzing the incidence, consequences, and prediction of reverse remodeling with cardiac MR imaging in patients with STEMI.

A significant decrease of LVESVI (> 10% at 6-month cardiac MR imaging) was detected in almost one-half (42%) of patients in our prospective study of 507 patients. Reverse remodeling was not futile in terms of structural consequences on the LV:

Figure 3

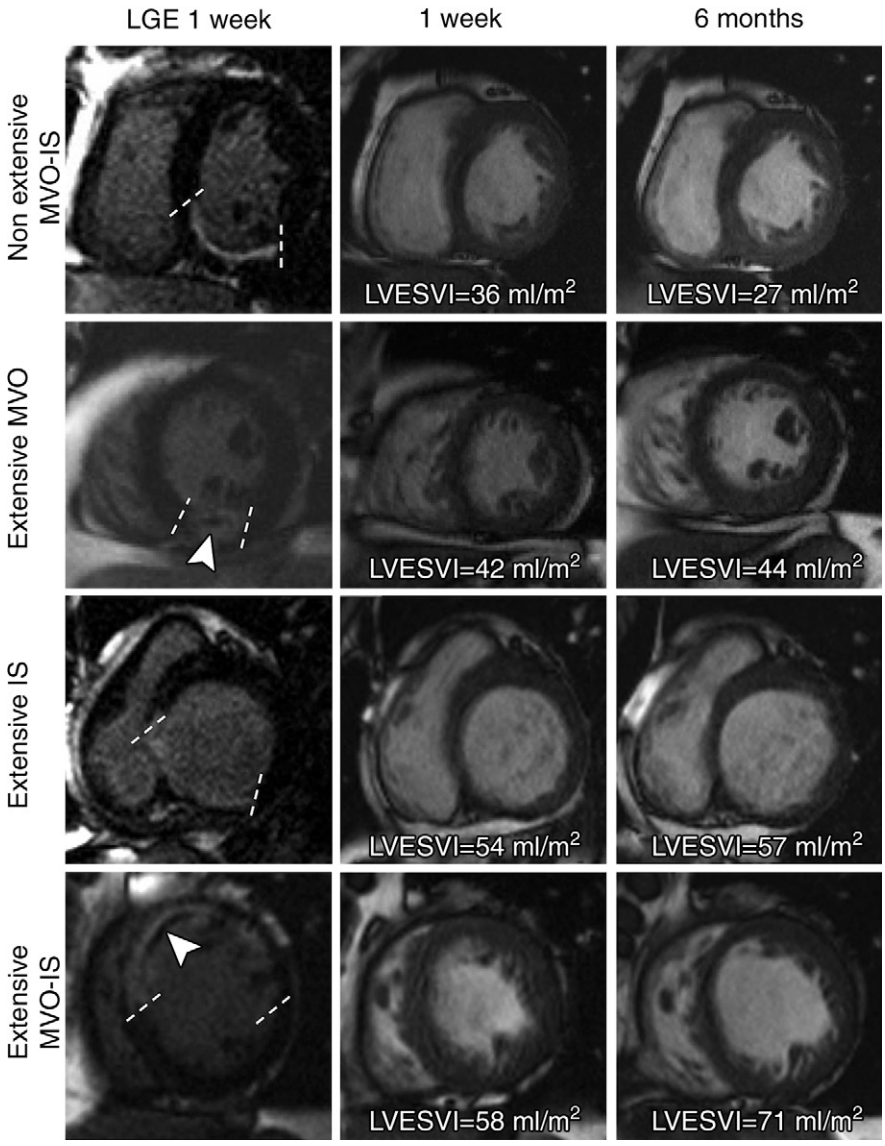


Figure 3: The four categories of infarct size *(IS)* and MVO and the typical course of LVESVI. Late gadolinium-enhanced *(LGE)* cardiac MR images obtained 1 week after STEMI (left column), short-axis cine MR images obtained 1 week after STEMI (middle column), and short-axis cine MR images obtained 6 months after STEMI (right column) show the course of reverse remodeling according to the magnitude of infarct size and microvascular obstruction. Characteristically, LVESVI decreased in patients with simultaneous nonextensive infarct size and MVO (top row), did not vary in those with extensive MVO and nonextensive infarct size (second row) or extensive infarct size and nonextensive MVO (third row), dilated in patients with simultaneous extensive infarct size and MVO (bottom row). Arrowheads = MVO, dashed lines = infarct size.

As expected, striking differences in terms of LVESVI variations were detected between patients with (median, −25%) and those without (median, 4%) reverse remodeling. Interestingly, this different course brought about a much bigger reduction in LV volumes and mass and a much more preserved LVEF at 6-month cardiac MR imaging in patients with reverse remodeling.

Predictors of Reverse Remodeling after STEMI

The magnitude of LV dilatation and systolic dysfunction 1 week after infarction did not relate to subsequent reverse remodeling. This implies that, even in patients with severely altered LV volumes or ejection fraction soon after STEMI, a substantial reduction of LVESVI cannot be dismissed. Thus, the state of LV volumes and LVEF before discharge is not enough to predict reverse remodeling.

Reverse remodeling is associated, to a lesser extent, with edema, hemorrhage, infarct size, and MVO and a trend toward a bigger myocardial salvage index. In a first multiple regression approach in which all continuous variables were treated as continuous, MVO and infarct size were the independent predictors of reverse remodeling. Then, a simpler multiple regression model dichotomizing infarct size and MVO (extensive vs nonextensive) via univariate ROC techniques revealed that, from a clinical perspective, the main predictor of reverse remodeling was the presence of simultaneous nonextensive infarct size and MVO. From 1-week to 6-month cardiac MR imaging, a substantial decrease in LVESVI was detected in only the patients with simultaneous nonextensive MVO (< 2.5% of LV mass) and infarct size (< 30% of LV mass). Thus, for reverse remodeling to take place, myocardial and microvascular integrity must be preserved (or not severely altered). Late gadolinium enhancement imaging represents an excellent tool for assessing these parameters and predicting reverse remodeling.

After STEMI, the extent of hemorrhage and MVO are closely related. In our results, patients with reverse remodeling exhibited less extensive MVO and hemorrhage than did those without reverse remodeling; however, only MVO was an independent predictor of reverse remodeling. Accurately measuring hemorrhage is sometimes difficult; in fact, in the variability analyses, the MVO measurement was more reproducible than that of hemorrhage, a fact that may explain why higher MVO

Figure 4

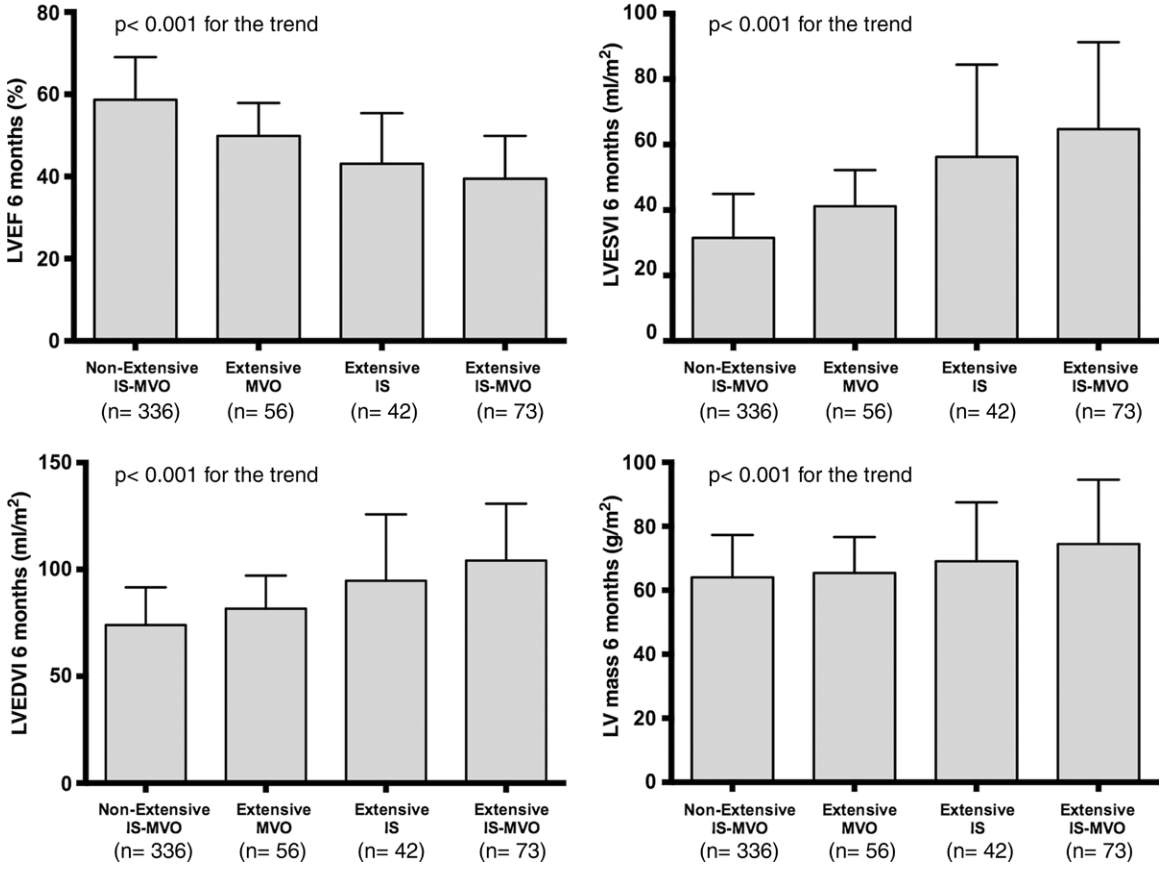


Figure 4: State of LV indexes at cardiac MR imaging 6 months after STEMI according to the magnitude of infarct size *(IS)* and MVO at 1-week cardiac MR imaging. Graphs show a steady deterioration in LVEF (top left) and dilation in LVESVI (top right), LVEDVI (bottom left), and LV mass (bottom right) at 6 months in the four categories of MVO and infarct size.

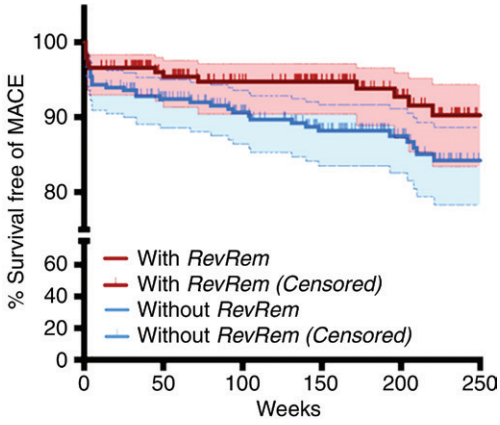
values predict reverse remodeling in the present study (Table E2 [online]). Moreover, in a recent multicenter study, MVO—and not hemorrhage—was an independent prognosticator of cardiac events (10).

It should be emphasized that the categorization of the study group into four subgroups (simultaneous nonextensive infarct size and MVO, extensive MVO and nonextensive infarct size, extensive infarct size and nonextensive MVO, and simultaneous extensive infarct size and MVO) on the basis of the best cut-off values for infarct size and MVO was not perfect for predicting reverse remodeling. The fact that a combined analysis of infarct size and MVO was insufficient to accurately predict the probability of reverse remodeling probably reflects that reverse remodeling is a multifactorial process, and further studies will be needed to better understand its pathophysiologic characteristics.

Regarding the clinical impact of reverse remodeling, our exploratory data indicate that, beyond its salutary effects on LV performance, this process might portend benefits to patients with STEMI. Similar to two previous studies that used echocardiography, the event rate almost halved in the group of patients with reverse remodeling (17,18). The prognostic utility of cardiac MR imaging soon after STEMI has already been validated and was not the primary objective of the present study (10–13,21). Recently, Eitel et al (10) demonstrated that the presence of simultaneous extensive infarct size and MVO soon after STEMI is strongly associated with a higher mortality rate within the following year. Thus, the presence of simultaneous nonextensive infarct size and MVO at late gadolinium-enhanced MR imaging seems to be beneficial both for promoting reverse remodeling and preventing cardiac events.

The analysis was performed in a single sample of patients, and the proposed models used thresholds derived from that same single sample (via a separate analysis). For this reason, the threshold results and the role of the newly found best prognostic category for reverse remodeling may be nongeneralizable. An independent and broader separate

Figure 5



N at risk:

With RevRem	296	246	196	146	96	1
Without RevRem	211	161	111	61	31	0

Figure 5: Kaplan-Meier curves with 95% confidence intervals (dashed lines) show the survival free of MACE (solid lines) in patients both with and without reverse remodeling *(RevRem)*. In patients with reverse remodeling, there was a nonsignificant trend toward less MACE (ie, cardiac death, reinfarction, or readmission for heart failure) than in those without reverse remodeling. Patients were censored from the survival analysis the moment of the first MACE ($n = 56$), the moment they were lost to follow-up ($n = 27$), or 5 years after the inclusion of the first patient in the study group. At all time points, the number of patients at risk are shown at the foot of x-axis. Censored patients are shown on the survival curves.

validation study is needed to establish the optimal threshold values of infarct size and MVO used for dichotomization. We cannot completely dismiss that the presence of undetected small areas of previous chronic myocardial infarction may have influenced our results.

Cardiac MR imaging permits a comprehensive assessment of reverse remodeling after STEMI. In this scenario, reverse remodeling occurs in almost one-half of patients. The extent of infarct size and MVO at cardiac MR imaging 1 week after infarction contributes valuable information for its prognostication.

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