

# The Sum of ST-Segment Elevation Is the Best Predictor of Microvascular Obstruction in Patients Treated Successfully by Primary Percutaneous Coronary Intervention. Cardiovascular Magnetic Resonance Study

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**Introduction and objectives.** The usefulness of ST-segment elevation resolution (STR) for predicting epicardial reperfusion is well established. However, it is still not clear how ST-segment changes are related to microvascular obstruction (MVO) observed by cardiovascular magnetic resonance (CMR) after primary percutaneous coronary intervention (pPCI) for ST-segment elevation myocardial infarction (STEMI).

**Methods.** The study involved 85 consecutive patients admitted for a first STEMI and treated by pPCI who had a patent infarct-related artery. An ECG was recorded on admission and 90 min and 6, 24, 48 and 96 h after pPCI. Thereafter, STR and the sum of ST-segment elevation (sumSTE) in all leads were determined.

**Results.** Overall, CMR revealed MVO in 37 patients. In infarcts with MVO, sumSTE was greater both before and after revascularization than in infarcts without MVO ( $P \leq .001$  at all times). In contrast, there was no significant difference in the magnitude of STR between infarcts with and without MVO 90 min after revascularization ( $P = .1$ ), though there was after 6 h ( $P < .05$  at all times). The area under the receiver operating characteristic curve for detecting MVO was greater for sumSTE than STR ( $P < .05$  for all measurements). On multivariate analysis, after adjusting for clinical, angiographic and ECG characteristics, a sumSTE  $>3$  mm 90 min after pPCI was an independent predictor of MVO on CMR, while an STR  $\geq 70\%$  was not (odds ratio=3.1; 95% confidence interval, 1.2-8.4;  $P = .02$ ).

**Conclusions.** MVO was associated with a significantly increased sumSTE at all times after revascularization. The difference in the magnitude of STR between infarcts

with and without MVO was significant only  $>6$  h after revascularization. The best predictor of MVO was a sumSTE  $>3$  mm 90 min after pPCI.

**Key words:** Cardiovascular magnetic resonance. Microvascular obstruction. ST-segment resolution. Sum of ST-segment elevation. ST-segment elevation myocardial infarction.

## La suma de la elevación del segmento ST predice mejor la obstrucción microvascular en pacientes tratados con éxito con una intervención coronaria percutánea primaria. Un estudio de resonancia magnética cardiovascular

**Introducción y objetivos.** La utilidad de la resolución del segmento ST (RST) para la predicción de la reperusión epicárdica está bien establecida. La asociación de los cambios del segmento ST con la obstrucción microvascular (OMV) observada en la resonancia magnética cardiovascular (RMC) tras una intervención coronaria percutánea primaria (ICPp) en el infarto de miocardio con elevación del ST (IMEST) no se ha aclarado todavía.

**Métodos.** Estudiamos a 85 pacientes consecutivos ingresados por un primer IMEST y tratados con una ICPp que tenían una arteria relacionada con el infarto permeable. Se registró un ECG al ingreso, tras 90 min y tras 6, 24, 48 y 96 h de la ICPp. Se calculó la RST y la suma de la elevación del ST (sumEST) en todas las derivaciones.

**Resultados.** La RMC reveló una OMV en 37 pacientes. En los infartos con OMV, el valor de la sumEST antes y después de la revascularización fue mayor que en los infartos sin OMV ( $p \leq 0,001$  en todos los casos). En cambio, no hubo diferencias significativas en la cantidad de RST entre los infartos con y sin OMV a los 90 min de la revascularización ( $p = 0,1$ ), sino sólo a partir de las 6 h ( $p < 0,05$  en todos los casos). El área bajo la curva de características operativas del receptor para la detección de la OMV fue mayor para la sumEST que para la RST ( $p < 0,05$  en todas las determinaciones). En el análisis multivariable, ajustado respecto a las características clí-

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## ABBREVIATIONS

CMR: cardiovascular magnetic resonance  
 MVO: microvascular obstruction  
 pPCI: primary percutaneous intervention  
 STEMI: ST-segment elevation myocardial infarction  
 STR: ST-segment elevation resolution  
 sumSTE: sum of ST-segment elevation

nicas, angiográficas y electrocardiográficas, una sumEST > 3 mm a los 90 min de la ICPp, pero no una RST  $\geq$  70%, predijo de manera independiente la OMV observada en la RMC (*odds ratio* = 3,1; intervalo de confianza del 95%, 1,2-8,4; *p* = 0,02).

**Conclusiones.** La OMV se asoció a un valor significativamente superior de la sumEST en todos los momentos de valoración tras la revascularización. La diferencia en la cantidad de RST entre los infartos con OMV y sin OMV sólo fue significativa a partir de las 6 h tras la revascularización. La OMV se predijo mejor con una sumEST > 3 mm a los 90 min de la ICPp.

**Palabras clave:** *Resonancia magnética cardiovascular. Obstrucción microvascular. Resolución del segmento ST. Suma de la elevación del segmento ST. Infarto de miocardio con elevación del segmento ST.*

## INTRODUCTION

In ST-segment elevation myocardial infarction (STEMI), the timely re-establishment of blood flow in the infarct related artery via primary percutaneous coronary intervention (pPCI) is crucial. However, in spite of Thrombolysis in Myocardial Infarction (TIMI) flow grade 3 in the epicardial coronary artery, perfusion at tissue level may be impaired; a phenomenon referred to as microvascular obstruction (MVO). Cardiovascular magnetic resonance (CMR) allows for a comprehensive assessment of STEMI patients<sup>1</sup> with accurate detection of MVO.<sup>2,3</sup>

Several studies have shown that the presence of MVO is associated with adverse outcome, unfavourable left ventricular remodelling and higher mortality.<sup>4,6</sup>

Monitoring of ST-segment changes, especially ST-segment resolution (STR), has been employed in the past as a simple measure of epicardial reperfusion quality in STEMI.<sup>7</sup> Furthermore, STR has been used as a surrogate end-point for MVO in the past<sup>7,8</sup> but the value of STR for detecting CMR-derived MVO is conflicting<sup>9,10,11</sup> and the relationship between ST-segment changes and MVO remains to be clarified.

We analyzed the usefulness of STR and the extent of the sum of ST-segment elevation (sumSTE) for detecting CMR-derived MVO in a consecutive group of patients with STEMI treated with pPCI and re-established TIMI flow grade 3 in the infarct related artery.

## METHODS

### Patients

We prospectively included 100 consecutive patients admitted to a university hospital for a first STEMI treated with pPCI within 12 hours after the onset of chest pain. The inclusion criteria were: *a*) stable clinical course without complications during hospitalization; *b*) no contraindications to CMR; and *c*) TIMI flow grade 3 in the infarct related artery after revascularization. We excluded 4 patients because of claustrophobia and 7 patients due to TIMI flow grade  $\leq$  2 after pPCI. Patients with inconclusive ECG (bundle branch block or ventricular pacing) were excluded (4 cases). Therefore, the final study group comprised 85 patients. All patients gave written informed consent and the study protocol was approved by the local ethics committee.

### Percutaneous Coronary Intervention and Angiography

pPCI was performed within 12 hours of symptom onset in all patients. TIMI flow grade<sup>12</sup> before and after the procedure was assessed. Myocardial blush grade<sup>13</sup> was evaluated after pPCI. Angiographic data was analyzed by an experienced investigator unaware of patient identity, ECG and CMR results using standard software (HM3000, Philips, Best, The Netherlands).

### ECG Analysis

A standard 12 lead ECG was recorded upon admission and at 90 minutes, 6 hours, 24 hours, 48 hours, and 96 hours after pPCI at a paper speed of 25 mm/s and an amplification of 10 mm/mV. ECG data was evaluated by an observer unaware of patient identity, angiographic data and CMR results. The isoelectric line was defined as the level of the preceding TP-segment. Extent of ST-segment elevation was measured 20 ms after the J-point in every lead. The following ECG parameters were determined:

– Sum of ST-segment elevation (sumSTE): sumSTE was manually calculated as the sum of ST-segment elevation in all leads using previously validated algorithms as the sum of elevation in V1–6,

I, and aVL for anterior infarction and as the sum of elevation in leads II, III, aVF, V5, and V6 for non-anterior infarction.<sup>7,14,15</sup> For dichotomic univariate analysis of sumSTE we implemented cut-off values established on the basis of the area under the receiver operating characteristics curves (AUC) for predicting MVO by maximizing the observed overall diagnostic accuracy (minimizing the number of false positives plus the number of false negatives).

– ST-segment resolution: STR was defined as the percent reduction in the sumSTE obtained on admission and each time point following pPCI. Complete STR was considered for a reduction of  $\geq 70\%$ .<sup>7,15</sup>

### Cardiovascular Magnetic Resonance Imaging

CMR (1.5-T scanner, Sonata Magnetom, Siemens, Erlangen, Germany) was performed at least 48 hours after cardiac catheterization in accordance with our laboratory protocol.<sup>16,17</sup> Images were acquired by a phased-array body surface coil during breath-holds and were ECG-triggered. Cine images (steady-state free precession sequence; repetition time / echo time: 3.2/1.6 ms, flip angle: 61 degrees, matrix: 256×128, slice thickness: 6 mm, temporal resolution: 26 ms) were acquired in 2-, 3-, 4-chamber views and every 1 cm in short-axis views.

Late enhancement imaging was performed in the same projections used for cine images at least 10 minutes after administering 0.1 mmol/kg of gadolinium-diethylenetriaminepentaacetic acid (Magnograf, Juste S.A.Q.F., Madrid, Spain). A segmented inversion recovery imaging with steady state free precession sequence was used (repetition time / echo time: 2.5/1.1 ms, slice thickness: 6 mm, flip angle: 50 degrees, matrix: 195×192) nullifying myocardial signal.

### Cardiovascular Magnetic Resonance Imaging Data analysis

CMR studies were analyzed by an experienced observer blinded to all patient, angiographic and ECG data using customized software (QMASS MR 6.1.5, Medis, Leiden, The Netherlands). Segment location was defined according to the 17-segment model<sup>18</sup>. Left ventricular mass (g/m<sup>2</sup>), ejection fraction (%), and volumes (mL/m<sup>2</sup>) were quantified by manual definition of endocardial borders of all short-axis slices in cine-images. Late gadolinium enhancement was considered in the case of signal intensity  $> 2$  standard deviations with respect to a remote non-infarcted area in late gadolinium enhancement imaging.<sup>16,19</sup> Infarct size was calculated as the percentage of left ventricular mass showing late gadolinium enhancement.<sup>17</sup>

Microvascular obstruction: on a segmental basis MVO was visually defined in late enhancement imaging as a lack of contrast uptake in the core of a segment surrounded by tissue showing late enhancement<sup>2</sup> (Figure 1). On a patient basis, significant microvascular obstruction was considered if it was detected in at least 1 segment. Intraobserver variability for the detection of MVO using this criterion in our laboratory was 1%.

### Statistical Analysis

All data were tested for normal distribution using the one-sample Kolmogorov-Smirnov test. Continuous normally distributed data were expressed as the mean (standard deviation) and compared using Student's *t* test. Non-parametric data were expressed as the median with the interquartile range (IQR) and were compared with the Mann-Whitney *U* test. Group percentages were compared using the  $\chi^2$  test or Fisher's exact test where appropriate.

Receiver operating characteristic curve analysis for predicting MVO was performed for STR and sumSTE at all time points. The areas under the receiver operating characteristic curve were compared.

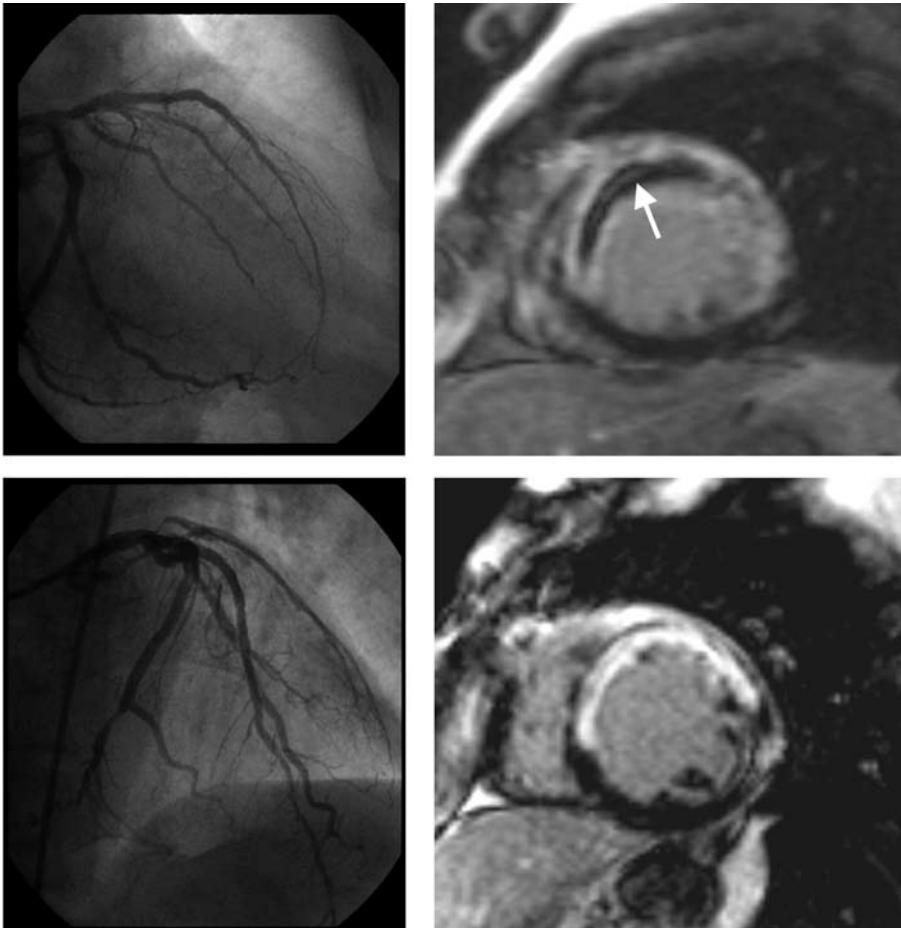
In order to determine the predictive value of sumSTE and STR, a logistic regression model was applied, adjusted by variables showing a *P*-value  $< .1$  in univariate analyses (Table 1). These variables were: systolic blood pressure, anterior infarction and peak creatine kinase MB. Odds ratios with the respective 95% confidence intervals were computed.

Statistical significance was considered for 2-tailed *P*-value  $< .05$ . SPSS 13.0 (SPSS Inc, Chicago, Illinois, USA) and STATA 9.0 (StataCorp, College Station, Texas, USA) were used.

## RESULTS

The baseline characteristics and angiographic data of all patients are displayed in Table 1. The mean age was 60 (13) years (range, 31-90) with the majority of the patients being male (81%). Median time from pain onset to revascularization was 210 minutes [141-420]. Abnormal TIMI flow grade (0-2) was present in 87% prior to pPCI with an occluded infarct related artery in 78% of the cases. A stent was placed in 96% of patients and TIMI flow grade 3 in the infarct related artery was established in all cases. Myocardial blush grade 2-3 was observed in 77% after pPCI.

The evolution of sumSTE and STR over time in the entire patient population is displayed in Figure 2. The median sumSTE on arrival was 9.0 mm [6.0-14.0] and dropped to 3.0 mm [0.0-6.0] after pPCI (Figure 2A). Accordingly, the median STR at 90



**Figure 1.** Coronary angiography and late gadolinium enhancement cardiovascular magnetic resonance imaging of two patients with an anterior myocardial infarction. After primary percutaneous intervention, TIMI flow grade 3 was established in the left anterior descending artery (left upper and lower panel). In one patient, on cardiovascular magnetic resonance imaging (right upper panel), late enhancement sequences show a large area of transmurular necrosis along the anteroseptal wall with a lack of contrast arrival in the core of the infarcted area (arrow). While infarct size was comparable, no evidence of microvascular obstruction was present in the other patient (right lower panel).

min after pPCI was 71% [22-100] (Figure 2B). Both indexes showed a progressive normalization over time. The percentage of patients displaying complete STR ( $\geq 70\%$ ) steadily increased over time (53% at 90 min, 67% at 6h, 73% at 24h, 74% at 48h, and 77% at 96h).

### Cardiovascular Magnetic Resonance Imaging Results

CMR imaging was performed 6 (2) days after pPCI. The clinical course between both examinations was stable in all patients. MVO was present in 37 patients (44%). Clinical and angiographic characteristics of the patients with and without evidence of MVO on CMR imaging are displayed in Table 1.

Patients with MVO-infarctions were younger (56 [14] years vs 63 [12];  $P=.02$ ), had more anterior infarctions (68% vs 33%;  $P=.002$ ), a larger median peak creatine kinase MB 334 [162-503] ng/mL vs 85 [44-197];  $P<.0001$ ) and there was a trend towards a lower systolic blood pressure (119 [26] mmHg vs 130 [25];  $P=.05$ ).

On CMR imaging, patients with MVO-infarctions showed a larger infarct size (37 [23%] vs 11 [9];  $P<.0001$ ), a lower left ventricular ejection fraction (44 [13%] vs 59 [12];  $P<.0001$ ) and larger end-systolic (54 [31] mL/m<sup>2</sup> vs 29 [14];  $P<.0001$ ) and end-diastolic (93 [33] mL/m<sup>2</sup> vs 70 [18];  $P<.0001$ ) left ventricular volumes and mass (81 [19] g/m<sup>2</sup> vs 65 [15];  $P<.0001$ ).

### Relationship of SumSTE and STR With Microvascular Obstruction

In MVO-infarctions, the extent of sumSTE was significantly larger before and at all time points after revascularization compared to non-MVO-infarctions ( $P\leq.001$  at all time points). In patients with MVO-infarctions, the median sumSTE at 24 hours after revascularisation smoothly reached 3 mm and did not drop further during the following measurements. In patients without MVO the median sumSTE at 6 hours reached 0 mm (Figure 3A). The amount of STR did not differ significantly at 90 min after pPCI between MVO

**TABLE 1. Baseline Characteristics and Angiographic Data**

	Total	Microvascular Obstruction		P-Value
		Absent	Present	
Patients	85	48	37	
Men (%)	69 (81)	40 (83)	29 (78)	.6
Age, mean (SD), y	60 (13)	63 (12)	56 (14)	.02
Median time to revascularization, min	210 [141-420]	190 [140-326]	240 [145-510]	.22
Median peak creatine kinase-MB, ng/mL	299 [62-408]	85 [44-197]	334 [162-503]	<.0001
Heart rate, bpm	79 (17)	78 (17)	79 (18)	.8
Systolic blood pressure, mm Hg	125 (26)	130 (25)	119 (26)	.05
Risk factors				
Active smoker (%)	44 (52)	21 (44)	23 (62)	.09
Hypertension (%)	40 (47)	22 (46)	18 (49)	.8
Diabetes mellitus (%)	12 (14)	4 (8)	8 (22)	.08
Dyslipidemia (%)	34 (40)	19 (40)	15 (41)	.9
Anterior infarction (%)	41 (48)	16 (33)	25 (68)	.002
TIMI flow grade 3 before PCI (%)	11 (13)	6 (13)	5 (14)	.9
Myocardial blush grade 2-3 after PCI (%)	65 (77)	36 (75)	29 (78)	.7
Affection of the proximal LAD (%)	22 (26)	9 (19)	13 (35)	.09
Glycoprotein IIb/IIIa inhibitors (%)	53 (62)	28 (58)	25 (68)	.4
Stent placement (%)	82 (96)	46 (96)	36 (97)	.9
Vessel occlusion prior to PCI (%)	66 (78)	35 (73)	31 (84)	.2

Bpm indicates beats per minute; PCI, primary percutaneous intervention; LAD, left anterior descending artery; TIMI, Thrombolysis in Myocardial Infarction.

Values are displayed as the mean (standard deviation) (compared with Student t test), absolute numbers with percentages in parenthesis (compared using  $\chi^2$  test) or the median with the interquartile range in square parenthesis (compared using the Mann-Whitney U test).

and non-MVO infarctions ( $P=.1$ ). In the following measurements patients with non-MVO infarctions had a significant larger amount of STR than did patients with MVO infarctions ( $P\leq.02$  from 6 h to 96 h) (Figure 3B).

Table 2 shows the areas under the receiver operating characteristic curve of sumSTE and STR at all time points for predicting MVO. SumSTE yielded a significantly larger area under the curve at every measurement compared to the corresponding STR at that time point.

Since STR is habitually dichotomized according to complete ( $\geq 70\%$ ) versus incomplete ( $< 70\%$ ) the following analyses were carried out: When dichotomized according to complete STR ( $\geq 70\%$  vs  $< 70\%$ ) there was no significant difference in the prevalence of MVO between the 2 groups at 90 minutes (36% vs 52%;  $P=.1$ ). Only from 24 hours after revascularization onwards, patients with complete STR displayed a significantly lower prevalence of MVO (Table 3).

According to the best cut-off derived from the area under the receiver operating characteristic curve, sumSTE at 90 minutes after pPCI was dichotomized (sumSTE  $\leq 3$  vs sumSTE  $> 3$  mm). Patients with sumSTE  $> 3$  mm had a higher prevalence of MVO than patients with sumSTE  $\leq 3$  (63% vs 28%;  $P=.001$ ). The diagnostic accuracy of sumSTE  $> 3$  and complete

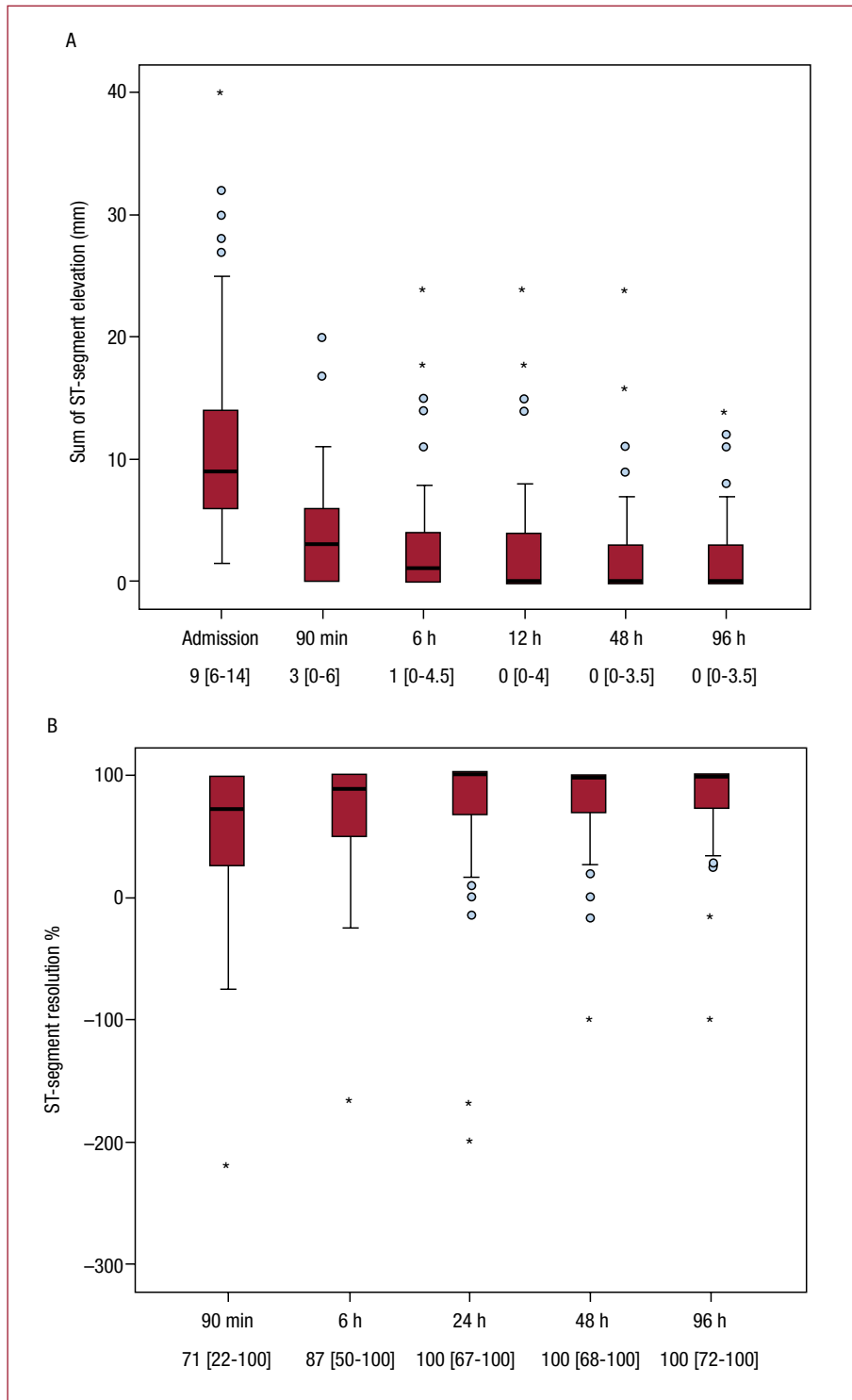
STR ( $\geq 70\%$ ) at 90 minutes after pPCI is displayed in Table 4. SumSTE  $> 3$  mm yielded a higher diagnostic accuracy for predicting MVO than STR  $\geq 70\%$ .

### Multivariable Analysis

A multivariate logistic regression model for predicting MVO at 90 minutes after pPCI, adjusted for those variables showing a  $P$ -value  $< .1$  in the univariate analyses, was performed. The variables included were: age, diabetes, smoker, systolic blood pressure, anterior infarction, median peak creatine kinase MB, involvement of the proximal left anterior descending artery, sumSTE  $> 3$  mm at 90 min and STR  $\geq 70\%$  at 90 min. Anterior infarction (OR, 4.2; 95% CI, 1.8-11.2;  $P=.04$ ) and sumSTE  $> 3$  mm at 90 min after pPCI (OR, 3.1; 95% CI, 1.2-8.4;  $P=.02$ ) were the only parameters associated with the presence of MVO on CMR imaging.

### DISCUSSION

The main finding of the present study is that monitoring of ST-segment characteristics is useful for predicting MVO in patients with STEMI treated with pPCI and re-established TIMI flow grade 3 in the infarct related artery. The amount of SumSTE at 90 min after pPCI was shown to be a simple



**Figure 2.** A: sum of ST-segment elevation (mm).B: extent ST-segment resolution (%) on admission and after revascularization in the entire group of patients. Data at the bottom of the graphs indicate the median with the interquartile range.

predictor of MVO even after adjustment for baseline characteristics and angiographic data.

### Microvascular Obstruction

In spite of restoration of epicardial blood flow in STEMI, impairment at the microvascular

level can occur, a phenomenon referred to as MVO.<sup>20,21</sup> It has been demonstrated that patients with MVO-infarctions have poor recovery of left ventricular function and are at high risk for development of heart failure and death.<sup>20</sup> Several non-invasive and invasive indexes such as angiographic parameters,<sup>9,10</sup>

**TABLE 2. Area Under the Receiver Operating Characteristic Curve of ST-Segment Elevation and ST-Segment Resolution at All Time Points for Predicting Microvascular Obstruction**

Time	Sum of ST-Segment Elevation	ST-Segment Resolution	P-Value
	AUC (95% Confidence Interval)	AUC (95% Confidence Interval)	
Admission	0.728 (0.621 to -0.819)	–	–
90 min	0.699 (0.59 to -0.794)	0.602 (0.49 to -0.707)	.006
6 h	0.706 (0.597 to -0.8)	0.647 (0.536 to -0.748)	.01
24 h	0.704 (0.596 to -0.798)	0.666 (0.555 to -0.764)	.048
48 h	0.708 (0.599 to -0.801)	0.665 (0.555 to -0.764)	.02
96 h	0.714 (0.605 to -0.807)	0.672 (0.562 to -0.77)	.03

AUC indicates area under the receiver operating characteristic curve.

**TABLE 3. Prevalence of Microvascular Obstruction According to Complete ST-Segment Resolution ( $\geq 70\%$ ) at Every Time Point**

Time	Prevalence of MVO		P-Value
	STR $< 70\%$	STR $\geq 70\%$	
90 min	52%	36%	.1
6 h	57%	37%	.08
24 h	65%	36%	.01
48 h	68%	35%	.007
96 h	70%	35%	.006

MVO indicates microvascular obstruction; STR, ST-segment resolution.

myocardial contrast echocardiography,<sup>20,22</sup> or scintigraphy<sup>23</sup> have been used for the evaluation of MVO.

CMR has become the gold standard in cardiovascular imaging and allows for a comprehensive assessment of a wide range of parameters in patients with STEMI,<sup>1</sup> including infarct size and MVO.<sup>2,3</sup> The presence of MVO on CMR imaging has been shown to predict less functional recovery<sup>24</sup> and post infarction complications independent of infarct size.<sup>21</sup>

## ST-Segment Analysis for Assessing Microvascular Perfusion. Role of ST-Segment Resolution

The ECG, as a widely available, rapid and simple method, has been applied as a tool for assessing the success of reperfusion after thrombolysis.<sup>25</sup> STR is useful for predicting the patency of the infarct related artery and thus epicardial reperfusion but its relationship to perfusion on the microcirculatory level remains unclear. Several studies investigating microvascular perfusion assessed by myocardial contrast echocardiography or angiographic blush scores have shown that a lack of STR is indicative of MVO.<sup>13,14,26</sup>

So far, the relationship between STR and CMR-derived MVO has been barely explored in STEMI patients with a patent infarct related artery after pPCI and existing data on the association of CMR-derived MVO with STR is conflicting.<sup>9,10,11</sup>

Two studies in the past reported no significant relationship with STR and CMR-derived MVO.<sup>9,10</sup> While in another study CMR-derived MVO analyzed in first pass perfusion and late enhancement was related to incomplete STR, defined as  $\geq 70\%$ .<sup>11</sup>

In our series of patients, there was not a significant association of STR with MVO at 90 min after pPCI neither as a continuous nor as a binary variable. Nevertheless, in the following measurements patients with MVO-infarctions displayed a significant lower amount of STR that did patients without MVO-infarctions. Accordingly, after 24 hours after revascularization and onwards, patients with complete STR ( $\geq 70\%$ ) had a significantly lower prevalence of MVO.

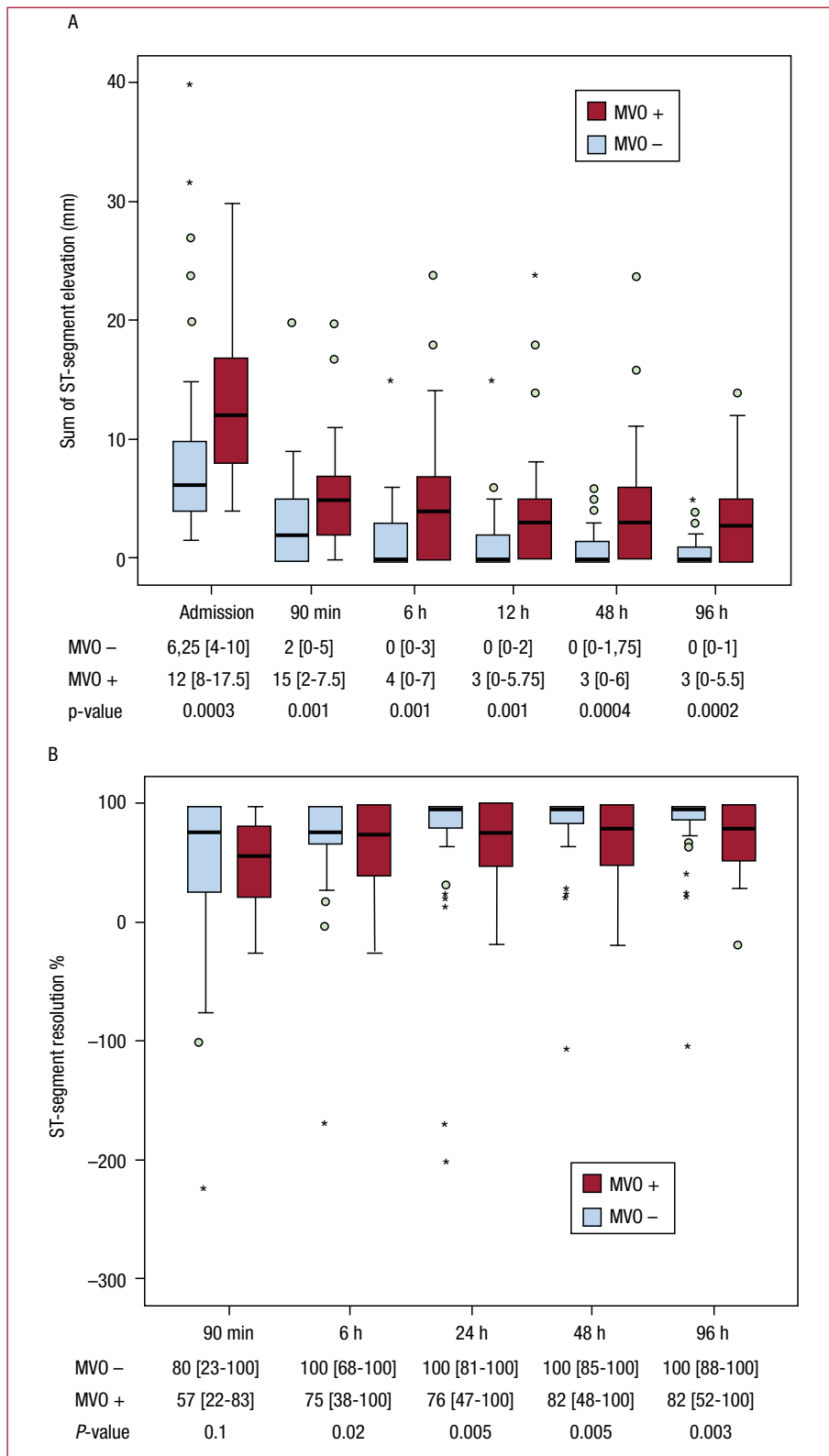
## Sum of ST-Segment Elevation and Microvascular Obstruction

In the present study, SumSTE was significantly larger throughout all measurements in patients with MVO-infarctions. When dichotomized ( $> 3$  mm vs  $\leq 3$  mm) sumSTE at 90 minutes after pPCI yielded a higher diagnostic accuracy for detecting MVO than complete STR and accordingly MVO was more frequent in patients displaying a high sumSTE

**TABLE 4. Diagnostic Accuracy of Sum of ST-Segment Elevation ( $> 3$  mm) and Complete ST-Segment Resolution ( $\geq 70\%$ ) at 90 Minutes After Percutaneous Coronary Intervention for Detecting Microvascular Obstruction**

	Sensitivity	Specificity	PPV	NPV	Accuracy
sumSTE $> 3$ mm	24/37 (65%)	34/48 (71%)	24/38 (63%)	34/47 (72%)	58/85 (68%)
STR $\geq 70\%$	21/37 (57%)	29/48 (60%)	21/40 (53%)	29/45 (64%)	50/85 (59%)

NPV, negative predictive value; PPV, positive predictive value; STR, ST-segment resolution; sumSTE indicates sum of ST-segment elevation.



**Figure 3.** A: time course of the sum of ST-segment elevation (mm). B: ST-segment resolution (%) according to the presence of microvascular obstruction on cardiovascular magnetic resonance imaging. The sum of ST-segment elevation was significantly higher at all time points in patients with microvascular obstruction (MVO) compared to patients without MVO. For ST-segment resolution there was no statistically significant difference at the first measurement after revascularization between the 2 groups. During the following measurements patients without MVO displayed a significant larger amount of STR. Data at the bottom of the graphs indicate the median with the interquartile range and the P-value for comparison of patients with and without MVO.

(>3 mm)(63% vs 28%;  $P=0.001$ ). In a multivariate analysis adjusted for clinical and angiographic parameters, the presence of an elevated sumSTE (>3 mm) at 90 minutes after revascularization was an independent predictor of MVO. Of note, sumSTE

on admission yielded the largest AUC for predicting MVO. The exact implications of this finding remain to be determined.

STR highly depends on pre-procedural extent of sumSTE.<sup>27</sup> As a relative measure, STR reflects



resolution of the initial sumSTE not taking into account the absolute extent of sumSTE neither on admission nor after pPCI, thus not incorporating the remaining microvascular injury after revascularization. At the first measurement after revascularization we did not detect a significant association of STR with MVO neither as a continuous variable nor as a binary variable using a well established cut-off ( $\geq 70\%$  vs  $< 70\%$ ). Nevertheless at 24 hours after revascularization the association of STR with MVO reached statistical significance. The lower discriminative value of STR might be owed to several reasons. For example, a patient who displays complete STR might still have a significant amount of sumSTE after pPCI and thus have a higher probability of MVO. Of note and of implications for clinical practice is, that sumSTE constitutes a simple index that yields a better diagnostic accuracy and can be obtained with one single measurement compared with 2 measurements (on arrival and at a later time point) necessary in order to determine STR for predicting MVO. Moreover, the information on the status of the microcirculation after pPCI offered by sumSTE is already available at an early time point (90 minutes after revascularization) when this information is most appreciated by the clinician.

It has been demonstrated that myocardial microcirculation displays a dynamic behaviour within the first days and months after STEMI.<sup>16</sup> These dynamic changes in abnormal perfusion are likely reflected by the smooth normalization in the extent of sumSTE observed in our study, advocating the ECG as a non-invasive tool for assessing the status of the microcirculation in the first phase after STEMI. This observation highlights the value of serial electrocardiographic examinations after STEMI since the behaviour of the microcirculation, mirrored by ST-segment changes, displays marked differences between patients with MVO and without MVO.

### Limitations and Strengths of the Study

The results of our study have to be interpreted with caution because of the small sample size. Nevertheless, CMR is a highly reproducible modality with a very low interobserver and intraobserver variability accounting for a smaller number of patients necessary to detect significant differences. Since CMR data were evaluated by one experienced observer, interobserver variability for the CMR indexes is not available.

Of note, myocardial blush grade was not significantly associated with the presence of CMR-derived MVO. The focus of the present study was to investigate the association of ST-segment changes with MVO. A possible explanation for the finding

that myocardial blush grade was not associated with MVO might be that this variable is more operator-dependent and might have yielded better results if evaluated in a core laboratory.

### CONCLUSIONS

Our study demonstrates the value of ST-segment monitoring for prediction of CMR-derived MVO. MVO was best predicted by the extent of sumSTE. Therefore, the assessment of ST-segment changes should not only involve the evaluation of STR after pPCI but should also focus on the remaining sumSTE. This simple bedside measure provides information on the quality of microvascular reperfusion after pPCI.

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