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Worst lead ST deviation and resolution of ST elevation at one hour for prediction of myocardial salvage, infarct size, and microvascular obstruction in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention

Anne Line Stensjøen MD, PhD[1] | Anders Hommerstad MD[1] | Sigrun Halvorsen MD, PhD[1,2] | Håkan Arheden MD, PhD[3] | Henrik Engblom MD, PhD[3] | David Erlinge MD, PhD[4] | Alf-Inge Larsen MD, PhD[5,6] | Maria Sejersten Ripa MD, DMSc[7,8] | Peter Clemmensen MD, DMSc[8,9,10,11] | Dan Atar MD, PhD[1,2] | Trygve S. Hall MD, PhD[1]

[1]Department of Cardiology, Oslo University Hospital Ullevål, Oslo, Norway

[2]Institute of Clinical Sciences, University of Oslo, Oslo, Norway

[3]Department of Clinical Sciences, Clinical Physiology, Skåne University Hospital, Lund, Sweden

[4]Department of Clinical Sciences, Cardiology, Lund University, Lund, Sweden

[5]Department of Cardiology, Stavanger University Hospital, Stavanger, Norway

[6]Department of Clinical Science, University of Bergen, Bergen, Norway

[7]Novo Nordisk A/S, Søborg, Denmark

[8]Department of Cardiology, The Heart Centre, University of Copenhagen, Rigshospitalet, Copenhagen, Denmark

[9]Department of Medicine, Division of Cardiology, Nykoebing-Falster Hospital, University of Southern Denmark, Odense, Denmark

[10]Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark

[11]Department of General and Intervention Cardiology, University Heart Center, Hamburg-Eppendorf, Germany

Correspondence
Anne Line Stensjøen, Oslo University Hospital HF, Ullevål Hospital,

Abstract

Background: ECG changes after revascularization predicts improved outcome for patients with ST-elevation myocardial infarction (STEMI). Worst lead residual (WLR) ST deviation and resolution of worst lead ST elevation (rST elevation) are simple measures that can be obtained early after PCI. The objective of the current study was to investigate whether simple ECG measures, obtained one hour following PCI, could predict cardiac magnetic resonance (CMR)-derived myocardial salvage index (MSI), infarct size (IS), and microvascular obstruction (MVO) in patients with STEMI included in the MITOCARE trial.

Methods: The MITOCARE trial included 165 patients with a first-time STEMI presenting within six hours of symptom onset. The current analysis included patients that had an ECG recorded at baseline and one hour after PCI and underwent CMR imaging after 3–5 days. Independent core laboratories determined WLR ST deviation, rST elevation, and the CMR variables (MSI, IS, and MVO).

Results: 83 patients with a mean age of 61 years were included. 83.1% were males and 41% had anterior infarctions. In logistic regression models, WLR ST deviation was a statistically significant predictor of IS (OR 2.2, 95% CI 1.3–3.8) and MVO (OR 2.8, 95% CI 1.5–5.2), but not of MSI (OR 0.8, 95% CI 0.5–1.2). rST elevation showed a trend toward a significant association with IS (OR 0.3, 95% CI 0.1–1.0), but not with the other CMR variables.

Hjertemedisinsk avdeling, P.O. Box 4956 Nydalen, N-0424 Oslo, Norway.
Email: alinesten@gmail.com

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Conclusion: WLR ST deviation one hour after PCI was a predictor of IS and MVO. WLR ST deviation, a measure easily obtained from ECGs following PCI, may provide important prognostic information in patients with STEMI.

KEYWORDS
cardiac magnetic resonance, cardiology, electrocardiography, ST-elevation myocardial infarction

1 | INTRODUCTION

Cardiac magnetic resonance (CMR) imaging is considered to be the best in vivo surrogate for infarct size (IS) and the gold standard for diagnosing microvascular obstruction (MVO) after reperfusion therapy (Allencherril et al., 2019; Ibanez et al., 2019). However, CMR is rarely utilized in clinical practice when treating patients with ST-elevation myocardial infarction (STEMI).

ST-segment resolution on the electrocardiogram (ECG) is a marker of reperfusion and begins to occur immediately after re-establishment of coronary blood flow to an ischemic area. Early ST-segment resolution predicts improved outcome and has been shown to be associated with final infarct size (Buller et al., 2008; van 't Hof, Liem, de Boer, & Zijlstra, 1997; Kim et al., 2008; Schroder, Wegscheider, Schroder, Dissmann, & Meyer-Sabellek, 1995). A previous study on STEMI patients supports that different metrics of ST-segment recovery predict infarct size and ejection fraction evaluated with CMR at four months after the infarction (Hallén, Sejersten, Johanson, Atar, & Clemmensen, 2010). In their work, Hallén et al. found that worst lead residual (WLR) ST-segment deviation, which is easily obtained from an ECG following reperfusion, performed equal to or better than more advanced measures of ST-segment resolution in patients treated with primary percutaneous coronary intervention (PCI). In the MITOCARE project, core laboratories assessed protocol-specified observations from ECGs and CMR images in patients with STEMI (Atar et al., 2015; Mitocare Study Group, 2012).

In the present substudy, we aimed to investigate whether WLR ST deviation and resolution of worst lead ST elevation (rST elevation) at one hour after revascularization could predict myocardial salvage index (MSI), IS, and MVO obtained by CMR after 3–5 days.

2 | MATERIAL AND METHODS

2.1 | Patient population

The MITOCARE study was a multi-center, randomized trial evaluating the efficacy and safety of TRO40303 for the reduction of reperfusion injury in 165 patients undergoing primary PCI for STEMI. TRO40303 did not show any significant effect on reperfusion injury (Atar et al., 2015). All subjects had a first-time STEMI (defined as nitrate-resistant pain for at least 30 min and new ST elevation at J-point in two contiguous leads with standard cut-off points), presenting within 6 hr of the onset of chest pain and had occlusion of the culprit artery (Mitocare Study Group, 2012). Patients were included in the current analysis if they had an ECG recorded at baseline and one hour after PCI and underwent CMR imaging 3–5 days after their event. Patients were not considered if the ECGs showed significant confounders (defined as ventricular pacing, ventricular rhythm or LBBB) or if the CMR investigation was incomplete. The study complies with the Declaration of Helsinki and was approved by regulatory agencies and local ethics committees. All patients provided written informed consent.

2.2 | ECG analysis

ECG analyses were performed by an ECG core laboratory at Rigshospitalet (Copenhagen, Denmark), by investigators blinded to all patient data (Sejersten et al., 2017). For the current study, standard 12-lead ECGs recorded at baseline and one hour after revascularization were used. ST-segment deviation from the TP segment was measured manually to the nearest 0.5 mm at the J-point in all 12 leads. If the TP segment was not distinct, the PR segment was used as the isoelectric line. For the current study, two ECG measures were assessed. WLR ST deviation was defined as the absolute mm magnitude of residual ST deviation in the most affected lead on the one-hour ECG, without reference to the baseline ECG. In addition, rST elevation was calculated from baseline and one-hour ECG, using the worst lead ST elevation at baseline, and the same lead at the one-hour ECG (reported as resolution relative to the ST elevation at baseline).

2.3 | Cardiovascular magnetic resonance imaging

In the MITOCARE study, the main secondary endpoint was the MSI, calculated from CMR measures of IS and myocardium at risk. CMR images were obtained 3–5 days after revascularization using whole-body 1.5T magnetic resonance scanners with ECG-gated image acquisition. All CMR analyses were performed by a core laboratory (Imacor AB, Lund, Sweden), blinded to clinical data. Measures of left ventricular ejection fraction, IS (as percentage of left ventricular volume), MSI ((1-IS)/myocardium at risk), and MVO (as percentage of

left ventricular volume) were obtained for all patients, as previously described (Atar et al., 2015; Heiberg et al., 2008).

2.4 | Statistical analysis

Continuous variables are presented as mean (*SD*) or median (range) as appropriate. IS, MSI, and MVO were dichotomized using median values, and separate logistic regression models were applied to assess the associations between the ECG variables and the dichotomized CMR variables. WLR ST deviation and rST elevation were treated as continuous variables in all regression models. Results are reported as odds ratios (OR) with 95% confidence intervals (CI) and *p*-values < .05 were considered statistically significant. All statistical analyses were performed using IBM SPSS statistics version 26.

TABLE 1 Descriptives in ECG/CMR population and total MITOCARE population

	ECG/CMR population (*n* = 83)	Total study population (*n* = 165)
Age, years, mean (*SD*)	61.0 (11.6)	61.9 (11.6)
Male	83.1%	83.6%
BMI, mean (*SD*)	27.4 (3.5)*	27.7 (4.0)**
Cardiovascular risk factors		
Hypertension	26.5%	29.1%
Diabetes	4.8%	7.3%
Smoking	44.7%†	46.6%‡
Killip class (grade)	(*n* = 67)	(*n* = 121)
1	95.5%	95.0%
2–4	4.5%	5.0%
Infarct location		
Anterior	41.0%	39.4%
Posterior	59.0%	60.6%
Culprit vessel		
LAD	39.8%	37.6%
RCA, dominant or balanced	47.0%	49.1%
LCx, dominant or balanced	13.3%	13.3%
Time from pain to balloon inflation, minutes, median (range)	(*n* = 78) 177 (76–453)	(*n* = 152) 178 (47–2855)
TIMI grade flow after PCI	(*n* = 83)	(*n* = 164)
0 or 1	10.8%	9.8%
2 or 3	89.2%	90.2%
Received study treatment	56.6%	51.5%

Abbreviations: BMI, Body mass index; CMR, Cardiac magnetic resonance; ECG, Electrocardiogram; TIMI, Thrombolysis in myocardial infarction.

*n = 81.

**n = 151.

†n = 76.

‡n = 148.

3 | RESULTS

83 patients with valid ECGs at baseline and one hour after PCI and complete CMR studies were included. 64 patients were excluded due to lack of analyzable CMR images, three due to lacking baseline ECGs, seven due to lacking or confounded one hour ECGs, and eight due to missing both CMR and ECG data. The characteristics of evaluated patients in comparison with the total study population are reported in Table 1. The mean age for the included patients was 61 years. 83.1% were male and 41% had anterior myocardial infarctions. The median WLR ST deviation was 1 mm (0–6 mm), and the median rST elevation was 0.75 (−1.0 to 1.25). Values for the CMR variables are presented in Table 2.

Logistic regression analyses showed that WLR ST deviation was a significant predictor of IS (OR 2.2, 95% CI 1.3–3.8) and MVO (OR 2.8, 95% CI 1.5–5.2), but not of MSI (OR 0.8, 95% CI 0.5–1.2). rST elevation trended toward significant association with IS (OR 0.3, 95% CI 0.1–1.0), but not with MVO or MSI (Table 3).

4 | DISCUSSION

4.1 | Infarct size

We found that WLR ST deviation was predictive of IS evaluated by CMR after 3–5 days, while rST elevation trended toward statistical significance. A previous report by Hallén et al, supports that WLR ST deviation and single lead ST resolution predict IS obtained by CMR (Hallén et al., 2010). In their study, they found that WLR ST deviation had great performance in predicting IS obtained by CMR four months after revascularization. Late gadolinium enhancement CMR images are currently considered the best in vivo measure of IS (Ibanez et al., 2019). Interestingly, recent data indicate that assessment of IS as early as 3–5 days after infarction predicts all-cause mortality and heart failure hospitalization (de Waha et al., 2017). The

TABLE 2 Median values for CMR variables (*n* = 83)

CMR variable	Median	Range
Infarct size (%LV)	15.0	2.3–43.7
Microvascular obstruction (%LV)	0.033	0.0–16.1
Myocardial salvage index (%)	54.7	16.9–89.3
Left ventricular ejection fraction (%)	48.3	18.8–64.5

Abbreviations: %LV, Percentage of left ventricle volume; CMR, Cardiac magnetic resonance; Myocardial salvage index, 1-(Infarct size/Myocardium at risk).

TABLE 3 Univariate logistic regression for prediction of CMR variables (n = 83)

CMR variable	Odds ratio (95% CI) with increasing WLR ST deviation	Odds ratio (95% CI) with increasing rST elevation
Infarct size (%LV)	2.2 (1.3–3.8)	0.3 (0.1–1.0)
Microvascular obstruction (%LV)	2.8 (1.5–5.2)	0.4 (0.1–1.2)
Myocardial salvage index (%)	0.8 (0.5–1.2)	2.2 (0.7–7.0)

Abbreviations: %LV, Percentage of left ventricle volume; CMR, Cardiac magnetic resonance; Myocardial salvage index, 1-(Infarct size/Myocardium at risk); rST elevation, Resolution of worst lead ST elevation; WLR, Worst lead residual.

association between WLR ST deviation and IS in our study are further supported by a paper by Rommel et al., reporting a significant association between CMR evaluated IS at 1–4 days after PCI and residual worst lead ST elevation (Rommel et al., 2014). In the latter study, residual ST elevation also showed a significant association with a combined clinical endpoint.

4.2 | Microvascular obstruction

MVO is defined as absent or inadequate myocardial perfusion despite successful epicardial reperfusion (Allencherril et al., 2019; van Kranenburg et al., 2014). This has been associated with reduced left ventricular function evaluated by CMR at follow-up (Nijveldt et al., 2008), and adverse clinical outcome (Allencherril et al., 2019). A previous study comparing dynamic ECG changes between patients with and without MVO found that patients with MVO had a higher single lead maximum ST elevation before PCI, while at one hour after PCI there was only a trend toward a significant association (Weaver et al., 2011). Repeated ECGs after PCI showed an increasing correlation between MVO and maximum ST elevation, suggesting that the optimal timing for measuring residual ST elevation was 48–72 hr post-PCI (Weaver et al., 2011). In the current study, we found a significant association between WLR ST deviation one hour after PCI and MVO, but not for rST elevation and MVO. Compared with Weaver et al., the current study included more patients, which may explain the significant association found for WLR ST deviation at one hour after PCI in our study. While the association between MVO and residual ST elevation might appear stronger later in the clinical course, the use of an earlier ECG measurement for risk prediction may have important clinical implications.

4.3 | Myocardial salvage index

There was no statistically significant association between WLR ST deviation or rST elevation and MSI in the current study. Previous analyses have compared myocardium at risk or myocardial salvage to more advanced ECG scores based on pre-PCI ECGs and found significant associations (Schoos et al., 2013; Sejersten et al., 2017). Residual ST elevation after revascularization is thought to represent impaired myocardial reperfusion at the microcirculatory level (Claeys et al., 1999; van 't Hof et al., 1997) and does not necessarily reflect the volume of myocardium at risk before revascularization (McLaughlin et al., 2004). While it may be presumed that rST elevation have a stronger association with MSI than WLR ST deviation, neither of the variables showed a statistically significant relationship to MSI. It is possible that a more comprehensive ECG scoring is needed to reflect the myocardium at risk, and hence the resulting MSI (Schoos et al., 2013). However, in contrast to the current study, others have found a significant correlation between MSI and residual worst lead ST elevation (Rommel et al., 2014). Our sample size may explain why we did not reproduce the finding of a significant relationship between MSI and WLR ST deviation. Furthermore, we believe that there are distinct differences between the two studies. While we measured residual ST deviation at one hour, Rommel et al. evaluated only residual ST elevation. Also, myocardium at risk and hence MSI were assessed differently, as we applied a contrast-enhanced steady-state free precession sequence instead of a T2-weighted triple inversion-recovery sequence (Atar et al., 2015; Eitel et al., 2013; Rommel et al., 2014). In addition, the AIDA STEMI trial included patients up to 12 hr after pain onset, resulting in a longer median time to treatment (Atar et al., 2015; Rommel et al., 2014). How these differences affect the relationship between WLR ST deviation and MSI warrant further investigation.

4.4 | Strengths and limitations

The main strengths of the current study are the prespecified ECG and CMR analyses performed by core laboratories. WLR ST deviation is easily obtainable in clinical practice, and few patients are excluded due to confounders in ECG. A limitation of our study is that some participants were not available for complete CMR examinations. This reduced the number of patients in our study and could limit the external validity of our findings. However, the included patients had similar baseline characteristics compared with the total population (Table 1). Furthermore, the difficulties of obtaining CMR images in clinical practice underscores the need for more simple tools for risk stratification of patients after successful PCI.

5 | CONCLUSIONS

WLR ST deviation was a significant predictor of IS and MVO, while rST elevation trended toward a significant association with IS. Measures of WLR ST deviation obtained from ECGs obtained one hour following PCI may provide important prognostic information in patients with STEMI.

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CONFLICTS OF INTEREST

HA is a shareholder of Imacor AB, Lund, Sweden, which performs core laboratory analysis of CMR images. HA and HE have been employed by Imacor AB on a part-time basis. MSR is employed by Novo Nordisk A/S. The other authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

ALS, AH, DA and TSH substantially contributed to conception and design. SH, HA, HE, DE, AIL, MSR, PC and DA contributed to acquisition of data. ALS, AH, DA and TSH analyzed the data. All authors were involved in drafting the manuscript or revising it. All authors have reviewed and approved the final version.

ETHICS

The study complies with the Declaration of Helsinki and was approved by regulatory agencies and local ethics committees. All patients provided written informed consent.

ORCID

Anne Line Stensjøen https://orcid.org/0000-0001-8482-8101
Dan Atar https://orcid.org/0000-0003-1513-8793
Trygve S. Hall https://orcid.org/0000-0002-6185-7783

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