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ST-segment resolution after primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction

Gjin Ndrepepa[1], Patricia Alger[1], Sebastian Kufner[1], Julinda Mehilli[1], Albert Schömig[1, 2], Adnan Kastrati[1]

[1]Deutsches Herzzentrum, Technische Universität, Munich, Germany
[2]1. Medizinische Klinik rechts der Isar, Technische Universität, Munich, Germany

Abstract

Background: *The association between ST-segment resolution and clinical outcome in patients with acute ST-segment elevation myocardial infarction (STEMI) after primary percutaneous coronary intervention (PPCI) remains unclear. Recent studies on the association between ST-segment resolution and mortality have given conflicting results. We undertook this study to assess whether ST-segment resolution in electrocardiograms recorded 90–120 min after initiation of PPCI predicts long-term mortality in patients with STEMI.*

Methods: *The study included 900 patients with STEMI presenting within the first 24 h after symptom onset who were treated with PPCI. The ST-segment resolution was assessed in electrocardiograms recorded 90–120 min after the first balloon inflation. The ST-segment resolution was dichotomized as follows: < 30% (no resolution), 30% to ≤ 70% (partial resolution) and > 70% (complete resolution). The primary endpoint was five-year mortality.*

Results: *ST-segment resolution was < 30% in 263 (29.0%) patients, between 30% and ≤ 70% in 356 (40.0%) patients and > 70% in 281 (31.0%) patients. There were 62 deaths during the follow-up. In patients with ST-segment resolution < 30%, 30 to ≤ 70% and > 70%, the Kaplan-Meier estimates of mortality were 8.3% (n = 17 deaths), 11.5% (n = 29 deaths) and 6.8% (n = 16 deaths), respectively; unadjusted hazard ratio (HR) = 0.88, 95% confidence interval (CI) 0.46–1.67, p = 0.695 for ST-segment resolution > 70%* vs *< 30%; adjusted HR = 0.91, 95% CI 0.61–1.33; p = 0.607, for ST-segment resolution > 70%* vs *ST-segment resolution < 30%.*

Conclusions: *In patients with STEMI undergoing PPCI, ST-segment resolution in electrocardiograms recorded 90–120 min after initiation of PPCI did not predict long-term mortality.* (Cardiol J 2012; 19, 1: 61–69)

Key words: acute myocardial infarction, electrocardiogram, percutaneous coronary intervention, ST-segment resolution

Address for correspondence: Gjin Ndrepepa, MD, Deutsches Herzzentrum, Lazarettstrasse 36, 80636 Munich, Germany, tel: +49-89-12181535, fax: +49-89-12184053, e-mail: ndrepepa@dhm.mhn.de

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Introduction

Previous studies have convincingly demonstrated that ST-segment elevation resolution is an important predictor of increased risk of death and congestive heart failure in patients with acute ST--segment elevation myocardial infarction (STEMI) treated with fibrinolytic therapy [1, 2]. The current theory holds that ST-segment resolution or recovery after reperfusion therapy signifies effective microvascular perfusion [3], myocardial tissue perfusion [4] and myocardial salvage [5]. The most solid evidence on the predictive value of ST-segment resolution has come from thrombolytic studies. Primary percutaneous coronary intervention (PPCI) studies have also suggested the existence of an association between ST-segment resolution and improved survival [3, 6–10]. There are, however, great differences between thrombolysis and PPCI in terms of degree of restoration of epicardial blood flow (60% with thrombolysis *vs* close to 95% with PPCI) and the speed of blood flow restoration. Furthermore, PPCI studies that have investigated the association between the degree of ST-segment resolution and outcome have had great differences in the timing of ST-segment resolution analysis, have used various cut-offs for the assessment of ST-segment recovery, and in most studies ST-segment resolution analysis was not performed in an independent electrocardiographic (ECG) core laboratory [3, 7––9]. The limited value of ST-segment resolution to predict myocardial salvage in anterior infarction [11], uncertainty about the best cut-off point criteria for ST-segment resolution [12] and importantly, the contradictory nature of the most recent evidence on the association between ST-segment recovery and prognosis [10, 13], show that the clinical value of ST-segment resolution after PPCI remains unclear.

The aim of the present study was to assess whether the degree of ST-segment resolution is a predictor of long-term mortality in patients with STEMI treated with PPCI.

Methods

Patients

The study included a consecutive series of 900 patients with acute STEMI who presented within the first 24 h after symptom onset and who were treated with PPCI between January 2002 and December 2007 in the Deutsches Herzzentrum in Munich. The diagnosis of STEMI required: chest pain lasting ≥ 20 min and ST-segment elevation of ≥ 1 mm in at least two extremity ECG leads or ≥ 2 mm in at least two contiguous precordial leads or left bundle branch block (LBBB) of new onset. The diagnosis was confirmed with coronary angiography at the time of PPCI. The source sample out of which the study patients were obtained consisted of 1,026 patients. Patients with mechanical failures (n = 24), patients with missing ECG or with technically inadequate recordings (n = 45) and those presenting with LBBB, even though the diagnosis of acute MI was established based on clinical and biomarker data and confirmed by angiography (n = 57) were excluded. Patients with cardiogenic shock were also excluded. Thus, 900 patients with STEMI and technically adequate ECG before and 90–120 min after PPCI were included in this study. All patients gave informed consent for participation in the study. The study was conducted according to the principles of the Declaration of Helsinki and approved by the institutional ethics committee.

ST-segment resolution

All included patients had technically adequate 12-lead ECG, before and 90–120 min after the first balloon inflation. The sum of ST-segment elevation was measured 20 ms after the end of the QRS complex in: leads I, aVL, and V1 through V6 for anterior infarction; leads II, III, aVF for inferior infarction and leads V5 to V6 for lateral infarction. The ST--segment elevation resolution was calculated as the initial sum of ST-segment elevation minus the sum of ST-segment elevation on the second ECG divided by the initial sum of ST-segment elevation and expressed as a percentage. Patients were divided into three groups according to the degree of ST--segment resolution: < 30% (no resolution); 30% to ≤ 70% (partial resolution); and > 70% (complete resolution). Analysis of ST-segment elevation resolution was performed in the ECG core laboratory by personnel unaware of reperfusion status or follow-up information.

Angiographic examination and definitions

Coronary angiography was performed according to standard criteria. Offline analysis of digital angiograms was performed in the core laboratory using an automated edge detection system (CMS, Medis Medical Imaging Systems, Neuen, the Netherlands) by personnel blinded to the clinical diagnosis. Primary PCI (mostly with stent implantation) and periprocedural care were performed according to the standard criteria. Bare metal stents were mostly used. Antiplatelet therapy consisted of clopidogrel (600 mg as a loading dose followed by

75 mg/day for a minimum of four weeks and a maximum of six months) and aspirin (200 mg/day indefinitely).

Epicardial blood flow in the infarct-related artery and myocardial perfusion grade were graded according to the Thrombolysis in Myocardial Infarction (TIMI) group definitions: TIMI 0, no reperfusion; TIMI 1, penetration without perfusion; TIMI 2, partial reperfusion; TIMI 3, complete perfusion. Myocardial perfusion grade (MPG) was defined as follows: MPG 0, contrast fails to enter the microvasculature; MPG 1, contrast slowly enters but fails to exit the microvasculature; MPG 2, delayed entry and exit of contrast of dye from the microvasculature; and MPG 3, normal entry and exit of dye from the microvasculature [14]. The left ventricular ejection fraction (LVEF) was measured on left ventricular angiograms using the area-length method [15]. Collateral circulation was quantified according to Rentrop's classification [16]. Glomerular filtration rate (GFR) was calculated using the Cockroft-Gault-formula [17]. Severity of heart failure in the acute stage of STEMI was assessed according to the Killip classification [18].

End points and follow-up

The primary end point of the study was five-year mortality. Non-fatal MI and target lesion revascularization at five years and LVEF at six months were secondary end points. The follow-up information was collected by a phone call at 30 days, a visit at six months, a phone call at one year and annual phone calls thereafter. Patients who had cardiac complaints underwent complete clinical, ECG, and laboratory evaluation. Information on deaths was obtained from hospital records, death certificates or phone contact with relatives of the patient or the patient's referring physician. The follow-up information was collected by personnel unaware of the status of reperfusion or ST-segment resolution at the end of the PPCI procedure. As standard practice in our institution, all patients were scheduled to undergo coronary angiography six months after the procedure or whenever they showed symptoms or signs of myocardial ischemia.

Statistical analysis

The normality of data distribution was analyzed using a Kolmogorov-Smirnov test. Data is presented as median (with 25^{th}–75^{th} percentiles), mean ± SD or counts and proportions (percentages). Categorical data was compared using a χ^2 test. Continuous data was compared using a Wilcoxon rank-sum test. Five-year mortality was estimated using the Kaplan-Meier method and log rank test. Linear regression analysis was used to determine intra- and interobserver variability in the measurement of ST-segment resolution. A multiple linear regression model was used to identify independent predictors of ST-segment resolution (entered in the model as a continuous variable). All variables of Tables 1 and 2 were entered into the model. Univariable and multivariable Cox proportional hazards models were used to assess the association between ST-segment resolution degree and five-year mortality. All variables (Tables 1 and 2) and ST-segment resolution (dichotomized at $< 30\%$, 30% to $\leq 70\%$ and $> 70\%$ resolution categories) were entered into the univariable Cox proportional hazards model with five-year mortality as a dependent variable. To identify independent correlates of five-year mortality, variables that showed a significant association with mortality in the univariable Cox model and ST-segment resolution (dichotomized at $< 30\%$, 30% to $\leq 70\%$ and $> 70\%$ resolution groups) were entered into the multivariable Cox proportional hazards model. All analyses were performed using S-plus statistical package (S-PLUS, Insightful Corp, Seattle, WA, USA). A two-sided $p < 0.05$ was considered to indicate statistical significance.

Results

Baseline characteristics

Baseline demographic and clinical characteristics are shown in Table 1. There were 263 (29.0%) patients with ST-segment resolution $< 30\%$, 356 (40.0%) patients with ST-segment resolution between 30% and $\leq 70\%$, and 281 (31.0%) patients with ST-segment resolution $> 70\%$. Patients in the group with ST-segment resolution $> 70\%$ featured a higher proportion of women, a smaller proportion of anterior infarct location, lower levels of C-reactive protein, a higher LVEF and presented earlier to hospital compared to other groups. Moreover, groups appear to differ regarding the values of GFR. Angiographic data is shown in Table 2. The group with ST-segment resolution $> 70\%$ had a lower proportion of patients with left anterior descendent artery occlusion and higher rates of post-interventional TIMI flow grade 3 and of MPG of 3. The remaining characteristics did not differ significantly between the groups. Overall median (interquartile range) time-to-admission and door-to balloon intervals were 4.0 (2.0 to 8.6) h and 1.25 (0.87 to 1.75) h, respectively. In a sample of 50 patients, the intra-observer (linear regression coefficient $R = 0.96$)

Table 1. Baseline characteristics in groups according to ST-segment resolution after percutaneous coronary intervention.

Characteristic	ST-segment resolution			P
	< 30% (n = 263)	30% to ≤ 70% (n = 356)	> 70% (n = 281)	
Age [years]	61.7 [49.8–70.2]	60.2 [50.8–70.2]	62.0 [53.6–72.4]	0.146
Women	49 (18.6)	74 (20.8)	85 (30.2)	0.002
Diabetes	58 (22.1)	55 (15.4)	47 (16.7)	0.089
Arterial hypertension	173 (65.8)	243 (68.3)	201 (71.5)	0.348
Body mass index [kg/m^2]	26.1 [24.1–28.3]	26.2 [24.1–28.7]	26.2 [24.3–28.6]	0.664
Hypercholesterolemia	134 (50.9)	181 (50.8)	151 (53.7)	0.730
Current smoker	110 (41.8)	159 (44.7)	128 (45.5)	0.657
Prior myocardial infarction	29 (11.0)	31 (8.7)	33 (11.7)	0.415
Prior coronary artery bypass surgery	6 (2.3)	8 (2.3)	11 (3.9)	0.376
Killip class:				0.120
I	204 (77.6)	264 (74.2)	212 (75.4)	
II	45 (17.1)	83 (23.3)	54 (19.2)	
III	14 (5.3)	9 (2.5)	15 (5.3)	
Infarct location:				< 0.001
Anterior	162 (61.6)	197 (55.3)	72 (25.6)	
Inferior	75 (28.5)	129 (36.2)	180 (64.1)	
Lateral	26 (9.9)	30 (8.5)	29 (10.4)	
C-reactive protein [mg/L]	5.0 [0.0; 12.8]	3.6 [0.0; 9.6]	2.6 [0.0; 7.2]	0.005
Glomerular filtration rate [mL/min]	88.5 [68.1; 114.8]	88.0 [66.8; 109.3]	84.1 [61.3; 103.9]	0.033
Peak creatine kinase MB [UI/L]	150.0 [68.0; 265.0]	144.0 [73.8; 308.3]	125.0 [65.0; 259.0]	0.149
Peak troponin T [μg/L]	3.9 [1.7; 7.4]	4.3 [1.9; 8.0]	3.6 [1.7; 6.6]	0.390
Left ventricular ejection fraction [%]	48.0 [39.1–54.0]	49.0 [41.3–55.0]	51.0 [44.0–57.0]	0.001
Time-to-admission interval [h]	6.9 [2.4; 12.1]	3.7 [2.0; 7.0]	3.1 [1.6; 5.3]	< 0.001
Sum of ST-segment elevation [mm]	6.3 ± 4.0	9.3 ± 6.5	9.4 ± 8.2	< 0.001
ST-segment resolution [%]	3.0 [–24.9–18.5]	50.5 [40.6–60.7]	86.4 [77.4–100.0]	< 0.001

Data is median [interquartile range], mean ± SD or counts (%)

and interobserver (linear regression coefficient R = 0.92) variability in the ST-segment resolution measurement were low.

Predictors of ST-segment resolution

Multiple linear regression model identified anterior infarct location (beta coefficient = –0.203; p < 0.001), time-to-admission interval (beta coefficient = –0.015; p < 0.001), GFR (beta coefficient = = –0.001; p = 0.038) and body mass index (beta coefficient = 0.012; p = 0.014) as independent correlates of ST-segment resolution. Female sex (beta coefficient = 0.071; p = 0.07) and current smoking (beta coefficient = 0.066; p = 0.08) were close to reaching statistical significance.

ST-segment resolution and clinical events

The median follow-up (25th; 75th percentile) was 4.0 (2.1–4.9) years. There were 62 deaths during the follow-up: 17 deaths in the group with ST-segment resolution < 30%, 29 deaths in the group with ST-segment resolution 30% to ≤ 70%, and 16 deaths in the group with ST-segment resolution > 70% (Kaplan-Meier estimates of mortality: 8.3%, 11.5% and 6.8%, respectively; odds ratio [OR] = 0.87, 95% confidence interval [CI] 0.43–1.77; p = 0.706 for ST-segment resolution > 70% *vs* ST-segment resolution < 30%; Fig. 1). Thirty-nine deaths were of cardiac origin: 12 deaths in the group with ST-segment resolution < 30%, 20 deaths in the group with ST-segment resolution 30% to ≤ 70% and seven deaths in the group with ST-segment resolution > 70% (Kaplan-Meier estimates of cardiac mortality: 5.9%, 7.4% and 2.8%, respectively; OR = 0.53, 95% CI 0.21–1.39; p = 0.188 for ST-segment resolution > 70% *vs* ST-segment resolution < 30%). There was a trend for lower cardiac mortality in patients with complete (> 70%) ST-segment reso-

Table 2. Angiographic characteristics in groups according to ST-segment resolution after percutaneous coronary intervention.

Characteristic	ST-segment resolution			P
	< 30% (n = 263)	30% to ≤ 70% (n = 356)	> 70% (n = 281)	
Door-to-balloon time [h]	1.25 [0.89; 1.82]	1.23 [0.85; 1.67]	1.33 [0.92; 1.83]	0.251
Occluded coronary artery:				< 0.001
Left main	1 (0.4)	0 (0.0)	1 (0.4)	
Left anterior descending	166 (63.1)	200 (56.2)	72 (25.6)	
Left circumflex	19 (7.2)	36 (10.1)	42 (16.0)	
Right coronary artery	73 (27.8)	116 (32.6)	160 (56.9)	
Bypass graft	4 (1.5)	4 (1.1)	6 (2.1)	
Number of affected coronary arteries:				0.089
1	106 (40.3)	141 (39.6)	92 (32.7)	
2	83 (31.6)	119 (33.4)	87 (31.0)	
3	74 (28.1)	96 (27.0)	102 (36.3)	
Multivessel disease	157 (60.0)	215 (60.4)	189 (67.3)	0.119
Pre-intervention TIMI flow grade:				0.471
0	127 (48.3)	182 (51.1)	123 (43.8)	
1	31 (11.8)	40 (11.2)	45 (16.0)	
2	60 (22.8)	76 (21.3)	68 (24.2)	
3	45 (17.1)	58 (16.3)	45 (16.0)	
Post-intervention TIMI flow grade:				0.019
0	8 (3.0)	4 (1.1)	5 (1.8)	
1	6 (2.3)	8 (2.2)	5 (1.8)	
2	35 (13.3)	34 (9.6)	14 (5.0)	
3	214 (81.4)	310 (87.1)	257 (91.4)	
Collateral grade:				0.908
0	197 (74.9)	255 (71.6)	208 (74.0)	
1	37 (14.1)	62 (17.4)	44 (15.7)	
2	21 (8.0)	26 (7.3)	22 (7.8)	
3	8 (3.0)	13 (3.7)	7 (2.5)	
Myocardial blush grade:				< 0.001
0	62 (23.6)	72 (20.2)	46 (16.4)	
1	28 (10.6)	28 (7.9)	9 (3.2)	
2	46 (17.5)	57 (16.0)	32 (11.4)	
3	127 (48.3)	199 (55.9)	194 (69.0)	
Type of intervention:				0.249
Stenting	231 (87.8)	324 (91.0)	258 (91.8)	
Balloon angioplasty	32 (12.2)	32 (0.0)	23 (8.2)	

Data is median [25th, 75th percentiles] or number of patients (%); TIMI — thrombolysis in myocardial infarction

lution *vs* those with incomplete (≤ 70%) ST-segment resolution (Kaplan-Meier estimates of five--year mortality 2.8% [seven deaths] and 6.8% [32 deaths], respectively; OR = 0.48, 95% CI 0.21––1.07, p = 0.07).

Non-fatal myocardial infarction occurred in 24 patients: eight infarctions in the group with ST--segment resolution < 30%, 14 infarctions in the group with ST-segment resolution 30% to ≤ 70%, and two infarctions in the group with ST-segment resolution > 70% (Kaplan-Meier estimates of infarction occurrence: 3.6%, 4.7% and 1.0%, respectively; odds ratio [OR] = 0.22, 95% CI 0.05–1.08; p = 0.088 for ST-segment resolution > 70% *vs* ST-segment resolution < 30%). Target lesion revascularization was required in 204 patients: 60 (25.5%) revascu-

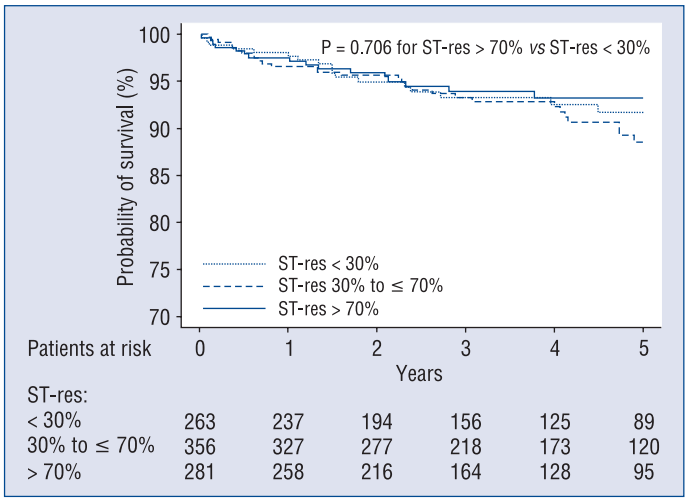

Figure 1. Kaplan-Meier curves of five-year survival in groups with ST-segment resolution (ST-res) < 30%, 30% to ≤ 70% and > 70%.

larizations in the group with ST-segment resolution < 30%, 87 (26.9%) revascularizations in the group with ST-segment resolution 30% to ≤ 70%, and 57 (22.6%) revascularizations in the group with ST-segment resolution > 70% (p = 0.423). Major adverse events (i.e. all-cause death, non-fatal MI or target lesion revascularization) occurred in 261 patients: 74 (31.6%) adverse events in the group with ST-segment resolution < 30%, 115 (37.0%) adverse events in the group with ST-segment resolution 30% to ≤ 70%, and 72 (28.2%) adverse events in the group with ST-segment resolution > 70% (p = 0.204).

The association between ST-segment resolution and mortality was also tested in the univariable and multivariable Cox proportional hazards model (see methods for variables entered into the models). Independent correlates of mortality from the univariable Cox model are shown in Table 3. ST-segment resolution was not independently associated with mortality either in the univariable (hazard ratio [HR] = 0.88, 95% CI 0.46–1.67, p = = 0.695 for ST-segment resolution > 70% *vs* ST--segment resolution < 30%) or the multivariable Cox model (HR = 0.91, 95% CI 0.61–1.33, p = 0.607 for ST-segment resolution > 70% *vs* ST-segment resolution < 30%).

ST-segment resolution and six-month left ventricular ejection fraction

Follow-up angiography was performed in 690 (77%) patients with no difference between groups (p = 0.181). In the groups with ST-segment resolution < 30% (n = 191), 30% to 70% (n = 281) and > 70% (n = 218), the six-month LVEF (median [25th–75th percentiles]) was 53.0% [45.0%; 60.0%], 51.0% [44.0%; 58.0%] and 55.0% [49.0%; 60.0%], respectively; p = 0.011]. The difference between the six-month and the baseline LVEF (delta LVEF) was 4.0% [–1.0% to 11.0%] in the group with ST--segment resolution < 30%, 2.0% [–2.2 to 9.0%] in the group with ST-segment resolution 30% to ≤ 70% and 1.6% [–2.0% to 10.0%] in the group with ST-segment resolution > 70% (p = 0.082) demonstrating no impact of ST-segment resolution on six-month LVEF.

Discussion

The main findings of this study can be summarized as follows: 1) In patients with STEMI treated with PPCI, the degree of ST-segment elevation resolution in ECG recorded 90–120 min after the first balloon inflation did not predict long-term all-cause mortality; 2) The degree of ST-segment resolution after PPCI in patients with STEMI had no impact on LVEF at six-months or on the occurrence of non-fatal MI or the need for target lesion revascularization up to five years after PPCI.

Previous studies of ST-segment resolution after PPCI have demonstrated an association between the degree of ST-segment resolution and clinical outcome [19]. These studies, however, were characterized by considerable methodological disparity in nearly all aspects of ST-segment resolution, which make their joint consideration rather problematic. The most recent evidence regarding the prognostic impact of ST-segment resolution after

Table 3. Correlates of five-year mortality and hazard ratios calculated by univariable Cox proportional hazards model.

Variable	Hazard ratio [95% CI]	P
Age (for 10-year increase)	2.32 [1.86–2.90]	< 0.001
Female sex	2.21 [1.32–3.70]	0.003
Diabetes	2.18 [1.27–3.75]	0.004
Body mass index (for 5 kg/m^2 increase)	0.66 [0.46–0.95]	0.025
Previous myocardial infarction	1.98 [1.03–3.79]	0.040
Anterior infarct location	1.76 [1.06–2.94]	0.030
Killip class (for 1 class increase)	2.24 [1.58–3.15]	< 0.001
Glomerular filtration rate (for 30 mL/min decrease)	2.82 [2.06–3.84]	< 0.001
Baseline C-reactive protein (for 5 mg/L increase)	1.05 [1.03–1.07]	0.019
Time-to-admission interval (for 1 h increase)	1.04 [1.01–1.08]	0.023
Left ventricular ejection fraction (for 10% decrease)	1.40 [1.11–1.75]	0.003
Multivessel disease (*vs* single vessel)	2.14 [1.18–3.88]	0.013
Collateral circulation (for 1 class increase)	0.65 [0.43–0.99]	0.044
Post-intervention TIMI grade (for 1 grade decrease)	1.57 [1.16–2.13]	0.003
Myocardial blush grade (for 1 grade decrease)	1.33 [1.10–1.61]	0.002
ST-segment resolution (for > 70% *vs* < 30% resolution)	0.88 [0.46–1.67]	0.695

CI — confidence interval; TIMI — thrombolysis in myocardial infarction

PPCI has been contradictory [10, 13]. A recent analysis of 4,866 patients in the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial demonstrated that the degree of ST-segment resolution 30 min (median 32 min) after PPCI was closely associated with the rates of 90-day death or composite end point of 90-death, heart failure or shock [10]. It is worth noting that all six different methods used to calculate ST-segment recovery provided strong prognostic information regarding the clinical outcome [10]. Contrary to the findings of the APEX-AMI trial, a recent report from the DANish Acute Myocardial Infarction-2 (DANAMI-2) trial came to the opposite conclusions [13]. The DANAMI-2 trial analysis included 1,421 patients treated with fibrinolysis or PPCI in whom the degree of ST-segment resolution at 90 min and 4 h after PPCI was assessed. In groups with no (< 30%), partial (30% to 70%), and complete (> 70%) ST--segment resolution, there were significant differences in 30-day and 4.2-year mortality in patients treated with fibrinolysis, but not in those treated with PPCI. The authors concluded that ST-segment resolution remains an important predictor of prognosis after fibrinolysis, but may be overemphasized as a surrogate end point after PPCI [13].

In the present study, we also could not find an association between the degree of ST-segment resolution in the ECG recorded 90–120 min after a PPCI procedure and all-cause mortality, non-fatal MI or the need for repeat revascularization up to five years after PPCI. Similarly, we could not find any association between the degree of ST-segment resolution in the 90–120-min ECG and LVEF six months after a PPCI procedure. In this regard, our results support those of the DANAMI-2 trial and provide further proof of the limited value of ST-segment resolution after PPCI in patients with STEMI, at least if ST-segment resolution analysis is based on ECG obtained 90 min (or more) after PPCI.

The exact reasons for concordance of the results with the DANAMI-2 trial [13] and the discordance with the APEX-AMI trial [10] are not known. However, a tentative explanatory hypothesis may be raised. Despite the fact that ST-segment elevation was recognized as a sign of coronary occlusion more than 90 years ago by Pardee [20], the underlying mechanisms of ST-segment elevation and resolution in the course of myocardial ischemia or necrosis remain unclear. As previously demonstrated experimentally by Kleber et al. [21], ST-segment elevation becomes maximal 10–15 min after coronary occlusion and declines afterwards to almost complete resolution in the center of the ischemic zone at 2 h of coronary occlusion.

According to current knowledge, ischemia leads to an increase in extracellular potassium concentration (due to ischemia-induced intracellular potassium loss) leading to a current of injury flow-

ing from ischemic to normal myocardium which provides the electrophysiological basis of ST-segment elevation in the ECG. The difference in the transmembrane potential between ischemic and normal myocardium build up only the electromotive force of the current of injury [22]. In addition, the flow of current requires a low-resistance pathway or intact (at least functional) cell-to-cell coupling [22]. Upon brisk restoration of massive coronary blood flow in the infarct-related artery by PPCI, there is an abrupt increase in intracellular Ca^{2+}. The excess of Ca^{2+} may damage cell-to-cell communication and lead to cellular uncoupling due to calcium induced inhibition of gap junction conductance [23]. As a consequence, resistance to current flow is abruptly increased which leads to an attenuation of the current of injury and a decline in the ST-segment elevation in the ECG. Moreover, the reperfusion-accentuated excess of intracellular Ca^{2+} invigorates cell death by causing hypercontracture of cardiomyocytes which almost exclusively occurs within the first minutes of reperfusion [24]. Reperfusion-induced cell death and cell-to-cell uncoupling may markedly attenuate the current of injury through reducing its driving force (cell death) and increased resistance in its pathway of flowing. These two factors may cause a quick ST-segment resolution in the ECG, which is not due to myocardial salvage. Thus, it is reasonable to summarize that ST-segment resolution after PPCI reflects not only myocardial salvage [5], which reduces the current of injury by restoring the transmembrane potential of salvaged cells, but also reperfusion-induced accentuation of cardiomyocyte death and cell-to-cell uncoupling.

The timing of ST-segment resolution analysis may provide a further explanation of discrepancies between the studies. In the present study and the DANAMI-2 study [13], the ST-segment resolution analysis was performed late (more than 90 min) after PPCI. Conversely, in the APEX-AMI trial [10], the ST-segment resolution analysis was performed early (median 32 min) after PPCI. Based on the results of these studies, it may be hypothesized that an early ST-segment analysis after PPCI, as carried out in the APEX-AMI trial [10] and other studies [25], may reflect more closely the myocardial salvage, known to be a predictor of improved survival after PPCI [26]. In late ST-segment analyses, like the ones performed in the DANAMI-2 trial [13] and the present study, the prognostic power of ST-segment resolution related to myocardial salvage may be offset by components of ST-segment resolution related to reperfusion-induced cell death and damage of cell-to-cell coupling. Further studies are needed to corroborate this hypothesis.

Limitations of the study

The present study has several limitations. Serial ECG recordings were not performed. As a consequence, the speed of ST-segment resolution could not be assessed. Although data was prospectively collected, the ECG for ST-segment resolution measurements were retrospectively analyzed. The data on LVEF was available only in patients in whom repeat angiography was performed (77%). Due to the time of patient recruitment for the present study, the age and gender-specific criteria of the ST-segment analysis recommended by American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society [27] were not used for the diagnosis of STEMI. Although time-to-admission and door-to-balloon intervals were within the range of previous studies in patients with STEMI, the inclusion of patients up to 24 h following symptom onset may indicate that some patients may be included after the infarction process has already completed, at least in terms of ST-segment dynamics. Although the present study did not demonstrate an association between the degree of ST-segment resolution and five-year mortality, factors such as younger age of patients, small infarcts, low event rate, long time-to-treatment interval and intervention of other confounding factors during the five-year follow-up may have minimized the predictive value of ST-segment resolution. Since long-term mortality may be predicted by multiple factors, some of them unrelated to reperfusion, the power of reperfusion markers to predict long-term mortality may be attenuated.

Conclusions

In patients with STEMI undergoing PPCI, ST-segment resolution in ECG recorded 90–120 min after the initiation of PPCI (first balloon inflation) did not predict long-term mortality, non-fatal MI or target lesion revascularization. The degree of ST-segment resolution was not associated with an improvement of LVEF at six months after PPCI. Further studies are needed to assess the optimal timing of ST-segment resolution and its prognostic impact in patients with STEMI after PPCI.

Conflict of interest: none declared

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