The prognostic significance of single-lead ST-segment resolution in ST-segment elevation myocardial infarction patients treated with primary PCI – A substudy of the randomized TOTAL trial

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ABSTRACT

BACKGROUND ST-segment elevation myocardial infarction (STEMI) is associated with high morbidity and mortality worldwide. Simple electrocardiogram (ECG) tools, including ST-segment resolution (STR) have been developed to identify high-risk STEMI patients after primary percutaneous coronary intervention (PCI).

SUBJECTS AND METHODS We evaluated the prognostic impact of STR in the ECG lead with maximal baseline ST-segment elevation (STE) 30-60 minutes after primary PCI in 7,654 STEMI patients included in the TOTAL trial. Incomplete or no STR was defined as $< 70\%$ STR and complete STR as $\geq 70\%$ STR. The primary outcome was the composite of cardiovascular death, recurrent myocardial infarction (MI), cardiogenic shock, or new or worsening New York Heart Association (NYHA) class IV heart failure at 1-year follow-up.

RESULTS Of 7,654 patients, 42.9% had incomplete or no STR and 57.1% had complete STR. The primary outcome occurred in 341 patients (10.4%) in the incomplete or no STR group and in 234 patients (5.4%) in the complete STR group. In Cox regression analysis, adjusted hazard ratio for STR $< 70\%$ to predict the primary outcome was 1.56 (95% confidence interval 1.32-1.89; $P < .001$) (model adjusted for all baseline comorbidities, clinical status during hospitalization, angiographic findings, and procedural techniques).

CONCLUSION In a large international study of STEMI patients, STR $< 70\%$ 30-60 minutes post primary PCI in the ECG lead with the greatest STE at admission was associated with an increased rate of the composite of cardiovascular death, recurrent MI, cardiogenic shock, or new or worsening NYHA class IV heart failure at 1-year follow-up. Clinicians should pay attention to this simple ECG finding. (Am Heart J 2024;269:149–157.)

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Background

After diagnosis of ST-segment elevation myocardial infarction (STEMI), reperfusion therapy should take place as soon as possible. Within certain time frames, primary percutaneous coronary intervention (PCI) is the guideline-recommended choice.[1] However, even after primary PCI, mortality for STEMI patients remains relatively high.[2] Practical tools for early identification of high-risk STEMI patients are needed, as they may potentially facilitate attempts to find successful therapies. The 12-lead electrocardiogram (ECG) is a simple, cheap, and widely available laboratory method for diagnosis and risk stratification. Simple ECG methods, including estimation

of ST-segment resolution (STR), have been developed for risk stratification. Lack of STR is assumed to reflect microvascular dysfunction at the myocardial tissue level, thus predicting adverse outcome, even after successful restoration of epicardial coronary artery blood flow.[3-8] Estimation of STR, both in a single lead and in multiple leads have been used, though single-lead STR seems to provide as good risk assessment as the more complex, multiple-lead STR.[5]

The Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI (TOTAL) determined the effect of primary PCI with routinely performed upfront manual thrombectomy in STEMI patients. In the TOTAL trial, routinely performed upfront manual thrombectomy did not reduce the risk of adverse outcome, but as a disadvantage, increased the risk of the key safety outcome.[9]

The aims of this prespecified substudy of the TOTAL trial were to assess the prognostic impact of single-lead STR 30-60 minutes after primary PCI and its correlation to angiographic data and the treatment assignment in STEMI patients. To the best of our knowledge, this is the largest study to assess the impact of single-lead STR on patient outcome in STEMI.

Methods

TOTAL Trial

The TOTAL trial was an international, randomized controlled trial that determined the effect of primary PCI with a strategy of routinely performed upfront manual thrombectomy in patients with STEMI. The study inclusion period was from August 2010 to July 2014. The study population consisted of 10,732 STEMI patients who were randomized to undergo either primary PCI alone or primary PCI with routinely performed upfront manual thrombectomy. Patients who were randomized within 12 hours of the symptom onset and referred for primary PCI were eligible for the inclusion. The exclusion criteria included prior coronary artery bypass surgery and fibrinolytic therapy for the index STEMI. Informed consent was obtained from each patient. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. The TOTAL trial is registered with ClinicalTrials.gov, number NCT01149044. The TOTAL trial was funded by Medtronic and the Canadian Institutes of Health Research. This substudy did not receive any specific funding. The study design and the inclusion and exclusion criteria have been described in detail previously.[9,10]

An ECG was recorded from all eligible patients right before randomization (baseline ECG) and 30-60 minutes after primary PCI (post-PCI ECG). All ECGs were analyzed by the independent core laboratory at the Heart Center, Tampere University Hospital, Finland. The investigators were blinded to all clinical and angiographic findings and the treatment assignment.

Study Population

For this substudy, we selected all patients who had undergone primary PCI with or without thrombectomy for the index STEMI and had baseline and post-PCI ECGs available without missing STR data on post-PCI ECG (n = 9,858). We excluded patients with left bundle branch block (n = 62), other broad QRS (QRS > 120 ms) (n = 486), technically poor ECG (n = 703), and ECG not fulfilling the STEMI criteria (n = 953). The final study population consisted of 7,654 patients.

ECG Analysis

ST-segment elevation (STE) was measured at the J point (the junction between the end of the QRS complex and the beginning of the ST segment) using the TP segment as the reference. The accuracy of 0.1 mm (0.01 mV) was used. We included patients who had at least 2 contiguous leads with STE: ≥ 0.2 mV in leads V2 to V3 and/or ≥ 0.1 mV in the other leads.[1] A modified cut-point of ≥ 0.2 mV in leads V2 to V3 was used, because the investigators were blinded to patient detail.

STEMI was classified as anterior, inferior, and lateral or other in the case of STE in leads V1 to V6; II, III, aVF; and I, aVL, V5 to V6, respectively. Considering STE in the precordial leads, STEMI was classified as lateral or other, if V5 to V6 were the only precordial leads with STE. If there was any other precordial lead with STE (V1 to V4), STEMI was classified as anterior. If the criteria for both anterior and inferior STEMI was fulfilled, STEMI was classified as lateral or other.

STR was determined from the lead with the greatest STE in baseline ECG. The same lead was used in baseline and post-PCI ECG analyzes. STR was calculated using the following formula: $\frac{STE_{baseline}-STE_{post-PCI}}{STE_{baseline}} \times 100$ %. For statistical analysis, the study patients were divided into 2 groups: (1) incomplete or no STR (STR < 70%) and 2) complete STR (STR ≥ 70%).

Study Outcomes

The primary outcome was the composite of cardiovascular death, recurrent myocardial infarction (MI), cardiogenic shock, or new or worsening New York Heart Association (NYHA) class IV heart failure during 1-year follow-up. The key secondary outcome was the composite of the primary outcome, stent thrombosis, or target vessel revascularization within 1 year. All-cause mortality within 1 year was also defined as a secondary outcome. The key safety outcome was stroke and the net risk-benefit outcome was the primary outcome or stroke within 1 year. The study outcomes were described in detail previously.[9]

Statistical Analysis

Baseline and procedural characteristics of the whole study population and the 2 groups independently were summarized as mean with standard deviation or as median with interquartile range for continuous variables, and as counts with percentages for categorical variables. Differences between the groups were assessed using the Chi-square test for categorical variables, the 2-sample t-test for normally distributed continuous variables, and the 2-sample Wilcoxon rank-sum test for non-normally distributed continuous variables.

Cox proportional hazards model was used to perform multivariable analysis of the effect of STR on the risk of the clinical outcomes. Three nested adjusted models were created for the primary outcome. Model 1 was designed to reflect only the association between STR and primary endpoint with no additional adjustments besides age and sex (i.e., to depict the clinical utility of STR in risk stratification in clinical practice). Model 2 was additionally adjusted with information of prevalent conditions before hospitalization for STEMI for the purpose of providing information of the prognostic value of STR in reference to patient history. Model 3 was created to determine the prognostic value of STR independently of all baseline factors, factors depicting patient's clinical condition during hospitalization, angiographic findings, and procedural techniques. In models 1, 2, and 3, adjustments for the following covariates were used, respectively: (1) Age (per 10 year increment) and gender, (2) Age, gender, hypertension, diabetes, previous stroke, previous MI, previous PCI, peripheral artery disease, and current smoking, (3) Age, gender, hypertension, diabetes, previous stroke, previous MI, previous PCI, peripheral artery disease, current smoking, heart rate (per 10 bpm increment), Killip class $\geq$ 2, location of MI (nonanterior vs anterior), time from symptom onset to hospital arrival (6-12 hours vs $<$ 6 hours), time from symptom onset to procedure (per 10 minute increment), initial Thrombolysis in Myocardial Infarction (TIMI) thrombus grade (5 vs $<$ 5), TIMI 0 flow before PCI, TIMI flow $<$ 2 after PCI, proximal lesion (lesion located at least in 1 of the following: (1) Right coronary artery origin, (2) Right coronary artery proximal including right ventricle, (3) Left main coronary artery, (4) 3 mm after origin of left anterior descending artery, (5) Left circumflex artery proximal, (6) first 3 mm of the proximal left anterior descending artery), upfront manual thrombectomy, and bailout thrombectomy. The proportional hazards assumption of the Cox model and the linearity of continuous covariates were assessed using the Kolmogorov-type supremum test and restricted cubic spline method, respectively. No violation was detected. Hazard ratios (HR) and the corresponding 2-sided 95% confidence intervals (CI) were calculated. Kaplan–Meier curves were created to visualize differences between the groups in the rates of the primary outcome and cardiovascular death during 1-year follow-up. The effect of the treatment assignment on the primary outcome and its components in 1-year follow-up, subgrouped by STR was tested by the likelihood ratio test of an interaction term, using unadjusted Cox regression model. All analyzes were performed using SAS Version 9.4 (SAS Institute, Inc., Cary, NC). A 2-tailed *P*-value $<$ .05 was considered as statistically significant.

Results

Table 1 shows baseline and procedural characteristics of the study patients. Of 7,654 patients, 42.9% had incomplete or no STR and 57.1% had complete STR. The patients with incomplete or no STR were older, more often male, had higher heart rate, systolic blood pressure (BP), diastolic BP, and more frequently Killip class $\geq$ 2. Anterior infarct location was more frequent in the patients with incomplete or no STR, whereas the infarct more often was inferior in those with complete STR. The patients with incomplete or no STR more often had a history of stroke, hypertension, diabetes, or MI, and they were less often current smokers. Time from symptom onset to hospital arrival and from hospital arrival to procedure were longer in the patients with incomplete or no STR. Use of enoxaparin was less frequent and bailout use of glycoprotein IIb/IIIa inhibitor was more frequent in the patients with incomplete or no STR. The patients with incomplete or no STR had higher initial TIMI thrombus grades and lower pre-PCI and post-PCI TIMI flow grades.

The primary composite outcome of cardiovascular death, recurrent MI, cardiogenic shock, or new or worsening NYHA class IV heart failure during 1-year follow-up occurred in 341 patients (10.4%) with incomplete or no STR and in 234 patients (5.4%) with complete STR (HR 2.00; 95% CI 1.69–2.38; $P < .001$). When analyzed separately, the rates of cardiovascular death (165 [5.0%] vs 84 [1.9%]; HR 2.63; 95% CI 2.04–3.45; $P < .001$), recurrent MI (100 [3.0%] vs 98 [2.2%]; HR 1.39; 95% CI 1.05–1.85; $P = .020$), cardiogenic shock (87 [2.7%] vs 47 [1.1%]; HR 2.50; 95% CI 1.75-3.57; $P < .001$), and new or worsening NYHA class IV heart failure (91 [2.8%] vs 53 [1.2%]; HR 2.33; 95% CI 1.67-3.23; $P < .001$) were higher in those with $<$ 70% STR compared with those with $\geq$ 70% STR, respectively. The key secondary outcome (458 [14.0%] vs 382 [8.7%]; HR 1.67; 95% CI 1.45-1.89; $P < .001$), all-cause mortality (199 [6.1%] vs 106 [2.4%]; HR 2.56; 95% CI 2.00-3.23; $P < .001$), the key safety outcome (40 [1.2%] vs 27 [0.6%]; HR 2.00; 95% CI 1.23-3.33; $P = .005$), and the net risk-benefit outcome (361 [11.0%] vs 251 [5.7%]; HR 2.00; 95% CI 1.69-2.33; $P < .001$) also had higher rates in the incomplete or no STR group than in the complete STR group, respectively (Supplementary Table 1).

Table 1. Baseline and procedural characteristics of patients according to ST-segment resolution

Characteristics	All (N = 7,654)	STR < 70% (N = 3,283)	STR ≥ 70% (N = 4,371)	*P* value
Age, y, mean ± SD	60.8 ± 11.9	61.7 ± 12.2	60.1 ± 11.6	< .001
Gender (Male), *n* (%)	5,935 (77.5)	2,599 (79.2)	3,336 (76.3)	.003
Heart rate, bpm, mean ± SD	76.4 ± 17.5	78.1 ± 18.0	75.1 ± 16.9	< .001
Systolic BP, mmHg, mean ± SD	135.5 ± 26.6	136.3 ± 26.9	134.9 ± 26.4	.020
Diastolic BP, mmHg, mean ± SD	82.6 ± 16.5	83.5 ± 16.4	81.9 ± 16.6	< .001
BMI, kg/m^2, mean ± SD	27.7 ± 4.6	27.7 ± 4.6	27.6 ± 4.7	.391
Killip class ≥ 2, *n* (%)	308 (4.0)	187 (5.7)	121 (2.8)	< .001
Location of MI				< .001
Anterior, *n* (%)	2,981 (38.9)	1,691 (51.5)	1,290 (29.5)	
Inferior, *n* (%)	4,336 (56.7)	1,477(45.0)	2,859 (65.4)	
Lateral or other, *n* (%)	332 (4.3)	112 (3.4)	220 (5.0)	
Medical history				
Previous stroke, *n* (%)	223 (2.9)	111 (3.4)	112 (2.6)	.035
Hypertension, *n* (%)	3,817 (49.9)	1,705 (51.9)	2,112 (48.3)	.002
Diabetes, *n* (%)	1,366 (17.8)	732 (22.3)	634 (14.5)	< .001
Previous MI, *n* (%)	681 (8.9)	317 (9.7)	364 (8.3)	.043
Previous PCI, *n* (%)	638 (8.3)	277 (8.4)	361 (8.3)	.780
Peripheral artery disease, *n* (%)	174 (2.3)	77 (2.3)	97 (2.2)	.714
Current smoker, *n* (%)	3,490 (45.6)	1,365 (41.6)	2,125 (48.6)	< .001
Initial PCI procedure				
Time from symptom onset to hospital, min, median (IQR)	120.0 (71.0-210.0)	130.0 (75.0-234.0)	118.0 (70.0-195.0)	< .001
Time from hospital to procedure*, min, median (IQR)	51.0 (23.0-87.0)	55.0 (25.0-90.0)	48.0 (21.0-85.0)	< .001
PCI procedure time, min, median (IQR)	36.0 (27.0-50.0)	37.0 (27.0-51.0)	36.0 (27.0-49.0)	.028
Medication use				
Unfractionated heparin, *n* (%)	6,318 (82.5)	2,708 (82.5)	3,610 (82.6)	.905
Bivalirudin, *n* (%)	1,406 (18.4)	628 (19.1)	778 (17.8)	.137
Enoxaparin, *n* (%)	577 (7.5)	210 (6.4)	367 (8.4)	.001
Glycoprotein IIb/IIIa inhibitor				
Upfront, *n* (%)	1,946 (25.4)	824 (25.1)	1,122 (25.7)	.571
Bailout, *n* (%)	1,145 (15.0)	546 (16.6)	599 (13.7)	< .001
Initial TIMI thrombus grade				< .001
0, *n* (%)	181 (2.4)	70 (2.1)	111 (2.5)	
1, *n* (%)	382 (5.0)	118 (3.6)	264 (6.0)	
2, *n* (%)	206 (2.7)	80 (2.4)	126 (2.9)	
3, *n* (%)	811 (10.6)	297 (9.0)	514 (11.8)	
4, *n* (%)	1,028 (13.4)	425 (12.9)	603 (13.8)	
5, *n* (%)	5,042 (65.9)	2,291 (69.8)	2,751 (62.9)	
Pre-PCI TIMI flow				< .001
0-1, *n* (%)	5,735 (75.5)	2,579 (79.2)	3,156 (72.8)	
2, *n* (%)	919 (12.1)	363 (11.1)	556 (12.8)	
3, *n* (%)	938 (12.4)	316 (9.7)	622 (14.4)	
Upfront manual thrombectomy, *n* (%)	3,716 (48.5)	1,542 (47.0)	2,174 (49.7)	.016
Bailout thrombectomy, *n* (%)	268 (3.5)	142 (4.3)	126 (2.9)	< .001
Direct stenting, *n* (%)	2,237 (29.2)	824 (25.1)	1,413 (32.3)	< .001
Post-PCI TIMI flow				< .001
0-1, *n* (%)	126 (1.6)	87 (2.7)	39 (0.9)	
2, *n* (%)	392 (5.1)	236 (7.2)	156 (3.6)	
3, *n* (%)	7,074 (92.4)	2,933 (89.3)	4,141 (94.7)	

STR, ST-segment resolution; SD, standard deviation; bpm, beats per minute; BP, blood pressure; BMI, body mass index; MI, myocardial infarction; PCI, percutaneous coronary intervention; IQR, interquartile range; TIMI, Thrombolysis in Myocardial Infarction

*Time from hospital to access site sheath insertion

Table 2 shows the adjusted multivariable analysis of the effect of STR on the risk of the primary outcome. HR for < 70% STR to predict the primary outcome in models 1, 2, and 3 was 1.89 (95% CI 1.61-2.27; $P < .001$), 1.85 (95% CI 1.56–2.17; P < .001), and 1.56 (95% CI 1.32-1.89; $P < .001$), respectively. In model 3, the other independent variables to predict the primary outcome were age, female gender, diabetes, previous stroke, previous MI, peripheral artery disease, heart rate, Killip class ≥ 2, anterior infarct location, TIMI flow < 2 after PCI, and proximal lesion. In contrast, hypertension, previous PCI, current smoking, time from symptom onset to hospital arrival (6-12 hours vs < 6 hours), time from symptom onset to procedure, initial TIMI thrombus grade (5 vs < 5),

Table 2. Adjusted multivariable analysis of effect of ST-segment resolution on the risk of the primary outcome

	Model #1		Model #2		Model #3	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
STR < 70%	1.89 (1.61-2.27)	< .001	1.85 (1.56-2.17)	< .001	1.56 (1.32-1.89)	< .001
Age, per 10 year increment	1.49 (1.39-1.60)	< .001	1.48 (1.36-1.60)	< .001	1.47 (1.36-1.59)	< .001
Gender (female)	1.35 (1.13-1.62)	.001	1.37 (1.14-1.65)	< .001	1.33 (1.10-1.60)	.003
Hypertension	-	-	0.94 (0.78-1.12)	.463	0.92 (0.77-1.10)	.387
Diabetes	-	-	1.51 (1.24-1.82)	< .001	1.40 (1.15-1.70)	.001
Previous stroke	-	-	2.15 (1.59-2.92)	< .001	2.16 (1.59-2.94)	< .001
Previous MI	-	-	1.67 (1.20-2.32)	.003	1.53 (1.10-2.12)	.015
Previous PCI	-	-	0.90 (0.62-1.29)	.555	0.97 (0.67-1.40)	.871
Peripheral artery disease	-	-	1.80 (1.24-2.62)	.004	1.89 (1.29-2.76)	.002
Current smoking	-	-	1.09 (0.90-1.32)	.359	1.09 (0.90-1.32)	.366
Heart rate, per 10 bpm increment	-	-	-	-	1.14 (1.09-1.19)	< .001
Killip class ≥ 2	-	-	-	-	1.96 (1.50-2.57)	< .001
Location of MI (nonanterior vs anterior)	-	-	-	-	0.83 (0.70-0.99)	.037
Time from symptom onset to hospital arrival (6-12 hours vs < 6 hours)	-	-	-	-	0.90 (0.65-1.25)	.528
Time from symptom onset to procedure*, per 10 min increment	-	-	-	-	1.01 (1.00-1.02)	.050
Initial TIMI thrombus grade (5 vs < 5)	-	-	-	-	1.10 (0.86-1.42)	.442
TIMI 0 flow before PCI	-	-	-	-	1.08 (0.82-1.40)	.593
TIMI flow < 2 after PCI	-	-	-	-	1.76 (1.18-2.62)	.010
Proximal lesion	-	-	-	-	1.27 (1.07-1.50)	.006
Upfront manual thrombectomy	-	-	-	-	0.98 (0.83-1.16)	.832
Bailout thrombectomy	-	-	-	-	1.35 (0.91-2.01)	.156

STR, ST-segment resolution; MI, myocardial infarction; PCI, percutaneous coronary intervention; bpm, beats per minute; TIMI, Thrombolysis in Myocardial Infarction

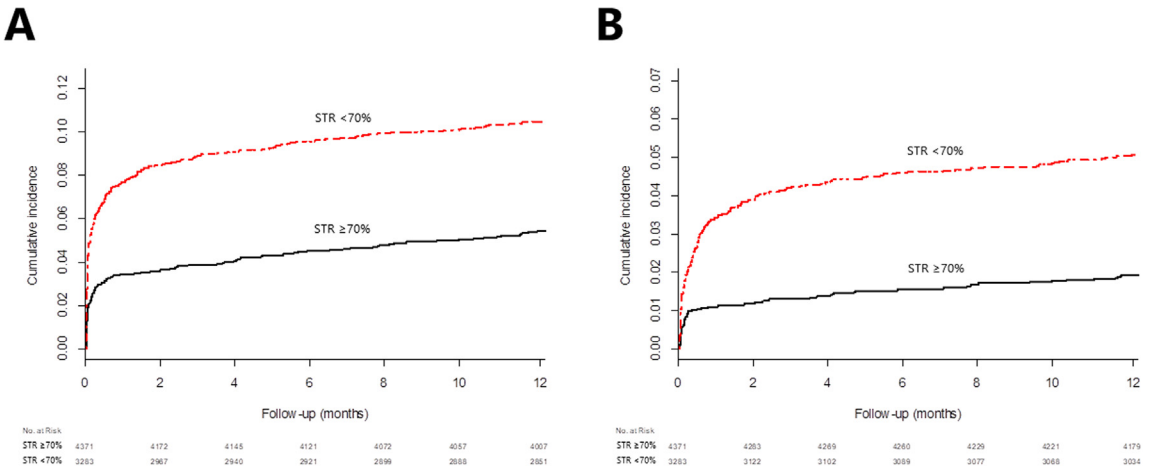
*Time from symptom onset to access site sheath insertion

Table 3. Effect of treatments on the primary outcome and components, subgrouped by ST-segment resolution

Outcomes	Subgroup	Thrombectomy		PCI alone			
		Events/patients	Event rate (%)	Events/patients	Event rate (%)	HR (95% CI)	*P* value for interaction
Primary outcome	STR ≥ 70%	125/2,253	5.5	109/2,118	5.1	1.08 (0.83-1.40)	.404
	STR < 70%	159/1,581	10.1	182/1,702	10.7	0.94 (0.76-1.16)	
CV death	STR ≥ 70%	46/2,253	2.0	38/2,118	1.8	1.14 (0.74-1.75)	.478
	STR < 70%	77/1,581	4.9	88/1,702	5.2	0.94 (0.69-1.28)	
Recurrent MI	STR ≥ 70%	48/2,253	2.1	50/2,118	2.4	0.90 (0.61-1.34)	.447
	STR < 70%	51/1,581	3.2	49/1,702	2.9	1.12 (0.76-1.66)	
Cardiogenic shock	STR ≥ 70%	28/2,253	1.2	19/2,118	0.9	1.39 (0.77-2.49)	.162
	STR < 70%	38/1,581	2.4	49/1,702	2.9	0.83 (0.54-1.27)	
Class IV heart failure	STR ≥ 70%	31/2,253	1.4	22/2,118	1.0	1.33 (0.77-2.29)	.426
	STR < 70%	44/1,581	2.8	47/1,702	2.8	1.00 (0.67-1.52)	

PCI, percutaneous coronary intervention; STR, ST-segment resolution; CV, cardiovascular; MI, myocardial infarction

Figure 1



Kaplan-Meier curves according to ST-segment resolution (STR) for A) the primary outcome and B) cardiovascular death.

TIMI 0 flow before PCI, upfront manual thrombectomy, and bailout thrombectomy were not independently predictive.

Table 3 shows that there was no difference on the effect of primary PCI with routinely performed thrombectomy and primary PCI alone on the primary outcome or its components between the STR groups. Of 3283 patients with incomplete or no STR, 1,581 (48.2%) were randomized to primary PCI with routinely performed thrombectomy and 1,702 (51.8%) to primary PCI alone. In 4,371 patients with complete STR, the corresponding numbers were 2,253 (51.5%) and 2,118 (48.5%), respectively.

Figure 1 demonstrates the effect of STR on the primary outcome and cardiovascular death. The curves between the groups separate at an early stage, and they tend to stay parallel after that.

Discussion

In this large, prospective substudy of the TOTAL trial with 7,654 STEMI patients, STR < 70% 30-60 minutes after primary PCI in the ECG lead with maximal baseline STE, was associated with an increased rate of the primary composite outcome of cardiovascular death, recurrent MI, cardiogenic shock, or new or worsening NYHA class IV heart failure during 1-year follow-up. The differences in outcome between the patients with < 70% and ≥ 70% STR remained statistically significant after adjustments for preprocedural risk factors, clinical status during hospitalization, angiographic findings, and procedural techniques. More specifically without any adjustment, the risk for the primary outcome was approximately 2-fold among the patients with incomplete or no STR. As in the main TOTAL trial, routinely performed upfront manual thrombectomy had no effect on the patient progno-

sis, when the patients were categorized based on the completeness of STR.

Complete STR is considered as a sign of epicardial coronary artery patency and restored blood flow at the myocardial tissue level. In primary PCI, lack of STR has been associated with microvascular obstruction, and is associated with adverse cardiovascular events and higher mortality rates in short-term and long-term follow-up.[5-8,11-16] Despite attempts to find therapeutic measures to prevent or treat microvascular obstruction, so far no clearly effective method has been reported.[1,17-21]

The 2 study groups showed clear differences in baseline and procedural characteristics. As in previous studies, patients with incomplete or no STR were older, more frequently male, less frequently current smokers, and had higher rates of comorbidities, such as hypertension or diabetes than those with complete STR. With respect to the procedure, the patients with incomplete or no STR had lower TIMI flow grades both before and after PCI, which was in line with our study. Also, patients with incomplete or no STR have had longer times from symptom onset to certain end-points (i.e., time to prehospital ECG and time to balloon). This was also the case in our study, and reminds us of the importance of short delays in STEMI treatment.[3,6,8,12,13,22]

Interestingly, in the adjusted multivariable analysis, time from symptom onset to hospital arrival (6-12 hours vs < 6 hours), time from symptom onset to procedure, initial TIMI thrombus grade (5 vs < 5), and TIMI 0 flow before PCI were not independently predictive for the primary outcome. Furthermore, both STR < 70% and TIMI flow < 2 after PCI independently predicted the primary outcome, which could indicate that lack of STR is a sign of impaired blood flow at the myocardial tissue level, regardless of the epicardial blood vessel patency.

Our results were in line with previous studies. In a substudy of the APEX-AMI trial, complete single-lead STR 30 minutes after primary PCI was associated with lower incidence of total mortality, cardiogenic shock, and congestive heart failure during 90-day follow-up in adjusted analysis.[5] The study population consisted of 4,866 STEMI patients, and the results were consistent when STR was analyzed both in 2 (≥ 50% and < 50%) and 3 categories (≥ 70%, 30% to < 70%, and < 30%). Interestingly, this study showed that patients with < 30% STR had a distinctively high mortality rate (8.0%), while the difference in mortality rates between the 30% to < 70% and ≥ 70% STR patients was surprisingly small (3.4% vs 2.9%, respectively). This could indicate that only minor decrease in the level of STE post-PCI could identify very high-risk STEMI patients. In a more recent study, Fabris et al [6] explored the clinical impact of single-lead complete STR in 1,456 STEMI patients. In their substudy of the ATLANTIC trial, complete STR was defined as ≥ 70% STR in an ECG recorded 1 hour after primary PCI. In logistic regression analysis, they found that 30-day rates of total mortality, definite stent thrombosis, and composite major adverse cardiovascular and cerebrovascular events were lower in patients with complete STR. Compared to this substudy of the ATLANTIC trial, which also represents the current era of STEMI treatment, the sample size of our trial was multiple, and we adjusted the analyzes by other prognostic factors, such as preprocedural risk factors, clinical status during hospitalization, and angiographic findings. In particular, we showed that the results are consistent even when considering culprit artery patency post-PCI.

As seen in previous studies, there was a clear positive association between < 70% STR and anterior infarct location.[11-13] In the multivariable analysis, STR < 70% retained its independence to predict the primary outcome when the infarct location was taken into account, and in the subgroup analysis, we found no interaction when the incomplete or no STR and complete STR patients were subgrouped to nonanterior and anterior STEMI location (Supplementary Table 2).

In the present study, upfront manual thrombectomy was more often performed in the patients with complete STR. However, the difference was relatively small (49.7% vs 47.0%) and this borderline significant observation could be a false positive finding which is supported by the fact that the original trial showed that upfront thrombectomy does not improve the outcome. It appears that although routinely performed thrombus aspiration improves STR, it has no positive effect on patient outcome, and thrombus aspiration should only be considered in specific situations.[1,9,21]

The Kaplan-Meier analysis (Figure 1) showed that the curves illustrating the difference in the rates of the primary outcome and cardiovascular death between the STR groups separate already at an early stage, and they tend to stay rather parallel after that. Thus, possible actions to improve patient prognosis should start as soon as possible, probably during the initial hospital stay. Studies randomizing patients into different treatment groups based on the ECG findings in STEMI are extremely rare. Different high-risk ECG features have been described, but due to the lack of randomized studies, no firm conclusions about therapeutic consequences can usually be drawn. In a small, placebo-controlled pilot study adenosine seemed to accelerate recovery of myocardial reperfusion based on ECG and invasive end-points.[23] At this point, no specific recommendations for the treatment of patients with incomplete or no STR can be given.

Limitations

Because of the study design in the TOTAL trial, half of the patients received upfront manual thrombecomy; this may have increased the number of patients in the complete STR group. It should also be mentioned that due to the exclusion criteria and use of only the 12 standard ECG leads, the study results do not necessarily apply to the whole STEMI population. It could have been of inter-

est to explore the association between continuously assessed STR and clinical outcome. However, the patients were categorized into the 2 study groups at the ECG core laboratory, and we have no information of the exact numerical values for STR; this could be examined in future studies.

Conclusion

In STEMI patients, STR < 70% in the ECG lead with maximal baseline STE, 30-60 minutes after primary PCI, is associated with worse outcome compared to patients with ≥ 70% STR. The results were consistent after adjustments, including post-PCI artery patency. Clinicians should pay attention to this simple ECG finding. Future research to improve the prognosis of this high-risk STEMI population is needed.

Disclosures

None reported

CRediT authorship contribution statement

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2023.12.009.

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