# Impact of the Residual SYNTAX Score on Outcomes of Revascularization in Patients with ST-Segment Elevation Myocardial Infarction and Multivessel Disease



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#### ABSTRACT

Primary percutaneous coronary intervention (P-PCI) has become the preferred reperfusion strategy in ST-elevation myocardial infarction (STEMI) when performed by an experienced team in a timely manner. However, no consensus exists regarding the management of multivessel coronary disease detected at the time of P-PCI.

**AIM:** The aim of this study was to evaluate the use of the residual SYNTAX score (rSS) following a complete vs. culprit-only revascularization strategy in patients with STEMI and multivessel disease (MVD) to quantify the extent and complexity of residual coronary stenoses and their impact on adverse ischemic outcomes.

**METHODS:** Between October 1, 2012, and November 30, 2013, we enrolled 120 consecutive STEMI patients with angiographic patterns of multivessel coronary artery disease (CAD) who had a clinical indication to undergo PCI. The patients were subdivided into those who underwent culprit-only PCI (60 patients) and those who underwent staged-multivessel PCI during the index admission or who were staged within 30 days of the index admission (60 patients). Both the groups were well matched with regard to clinical statuses and lesion characteristics. Clinical outcomes at one year were collected, and the baseline SYNTAX score and rSS were calculated.

**RESULTS:** The mean total stent length  $(31.07 \pm 12.7 \text{ mm vs.} 76.3 \pm 14.1 \text{ mm})$  and the number of stents implanted per patient  $(1.34 \pm 0.6 \text{ vs.} 2.47 \pm 0.72)$  were higher in the staged-PCI group. The rSS was higher in the culprit-only PCI group  $(9.7 \pm 5.7 \text{ vs.} 1.3 \pm 1.99)$ . The angiographic and clinical results after a mean follow-up of  $343 \pm 75$  days demonstrated no significant difference in the occurrence of in-hospital Major Adverse Cardiac and Cerebrovascular Events (MACCE) between both the groups (6.7% vs. 5%, P = 1.000). However, patients treated with staged PCI with an rSS  $\leq 8$  had significant reductions in one-year MACCE ( $10.7\% \text{ vs.} 30.5\%, P = 0.020^{*}$ ), death/Myocardial infarction (MI)/Cerebrovascular accident (CVA) (5% vs. 13.8%,  $P = 0.016^{*}$ ), and repeat revascularization (4.8% vs. 25%,  $P = 0.001^{*}$ ). We found that culprit-only, higher GRACE risk scores at discharge and an rSS  $\geq 8$  were independent predictors of MACCE at one year. **CONCLUSIONS:** Staged PCI that achieves reasonable complete revascularization (rSS  $\leq 8$ ) improves mid-term survival and reduces the incidence of repeat PCI in patients with STEMI and MVD. Nonetheless, large-scale randomized trials are required to establish the optimal revascularization strategy for these high-risk patients.

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KEYWORDS: multivessel CAD, STEMI, syntax score

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### Introduction

Acute coronary syndrome (ACS) is a well-established major cause of death and disability in both developed and developing countries.<sup>1,2</sup> Primary percutaneous coronary intervention (P-PCI) has become the preferred reperfusion strategy in ST-elevation myocardial infarction (STEMI) when performed by an experienced team in a timely manner.<sup>3,4</sup> P-PCI has been shown to be superior to fibrinolysis in reducing morbidity and mortality in STEMI.<sup>5</sup> Approximately 40–65% of patients treated with P-PCI for STEMI have multivessel disease (MVD), which is an independent predictor of longterm mortality in these patients.<sup>6–8</sup> In previous registries, delayed complete revascularization (CR) appeared to confer a benefit, whereas other published observational studies have generally suggested that immediate CR is not only without benefit but may also be harmful.<sup>9,10</sup> No consensus exists regarding the management of MVD detected at the time of P-PCI. Current guidelines recommend against performing PCI for nonculprit vessels at the time of P-PCI unless there is a hemodynamic instability.<sup>11,12</sup> Various treatment strategies for nonculprit vessels have generated considerable interest and controversy. These include medical therapy and multivessel revascularization at the time of P-PCI and staged PCI. However, the achievement of CR is uncommon when treating ACS patients with multivessel coronary disease with PCI.<sup>13</sup> The SYNTAX score (SS) is an angiographic scoring tool for systematically quantifying the severity of each coronary lesion and assessing its individual characteristics.<sup>14</sup> This scoring tool is used worldwide to predict long-term outcomes in patients with coronary artery disease (CAD) undergoing elective PCI or coronary artery bypass graft (CABG) surgery. The SS is also useful for predicting short- and long-term outcomes in patients with STEMI who are treated with P-PCI. The residual SYNTAX score (rSS) has been shown to be an independent predictor of one-year ischemic events in patients with medium- to high-risk ACS<sup>13</sup> and of long-term adverse outcomes in patients with MVD undergoing PCI.<sup>15</sup>

### Aim

This study was designed to evaluate the use of the rSS following a complete vs. culprit-only revascularization strategy in patients with STEMI and MVD to quantify the extent and complexity of residual coronary stenoses and their impact on adverse ischemic outcomes.

### Methods

This single-center prospective study included 120 consecutive STEMI patients with angiographic patterns of multivessel CAD, with a baseline syntax score  $\leq$ 22 and a clinical indication to undergo PCI according to the guidelines.<sup>11,12</sup> Patients with a previous medical history of MI, CABG, or PCI and patients presenting with cardiogenic shock were excluded. The decision to undergo PCI was taken after "heart team" consultation. The included patients were divided into the following two groups:

Group I: 60 patients with MVD undergoing PCI for a culprit-vessel only.

Group II: 60 patients with MVD undergoing staged PCI for a culprit-vessel and another lesion in a staged procedure (within 5–30 days).

The decision to undergo culprit-only or staged PCI was based on the coronary anatomy, disease, age and comorbidities, patient's preference, operator's decision, and limited availability of staged intervention due to financial constraints in our country. The first 60 patients (in each group) who met the inclusion criteria/type of intervention were included.

### **Procedural Data**

All patients who underwent PCI received at least 300 mg of aspirin and a 600-mg loading dose of clopidogrel. Heparin was administered throughout the procedure to maintain an activated clotting time of  $\geq$ 250 seconds. DES selection and gly-coprotein IIb/IIIa inhibitors were used at the discretion of the operator. After the procedure, all the patients received 100 mg/day of aspirin indefinitely, as well as 150 mg for seven days and then 75 mg/day of clopidogrel for at least 12 months. Standard postintervention care was recommended.

### Angiographic Analysis

Angiographic imaging was performed in two orthogonal views after an intracoronary injection of nitrates.



Each lesion was measured before and after stenting on unoptically magnified cine angiographic frames, showing the lesion at its highest grade and using the guiding catheter as a reference. Measurements of the diameter of the guiding catheter, the minimal vessel lumen diameter, and the percent stenosis before and after stenting were performed by automatic contour edge detection; intravascular ultrasound imaging was not used routinely. The patients' angiography images were reviewed, and the SS and rSS were calculated by the same trained physician using a webbased calculator (www.syntaxscore.com). The physician was blinded to the clinical outcomes of the patients. All of the parameters and stenoses were assessed visually. The rSS was determined as the SS remaining after completion of PCI. In the case of staged-PCI procedures (defined as a second planned PCI procedure after the initial intervention), the final planned procedure was used as the entry point for this study.

### **Patient Follow-up**

Clinical follow-up was conducted for all patients at 1, 3, 6, 9, and 12 months and every 3 months thereafter either during outpatient department visits or by direct telephone contact with the patients. All the patients were contacted for follow-up to assess the presence of angina and the occurrence of adverse events, such as death, nonfatal myocardial infarction, need for repeat percutaneous intervention in the target lesion, or CABG. For all patients who revealed cardiac symptoms, clinical evaluation was performed. Non-invasive testing for myocardial ischemia was conducted for all patients unless contraindicated at 12-month follow-up visit. Follow-up coronary angiography was performed in all patients with recurrent angina or positive noninvasive testing. All data collected were stored in a regularly updated computer database.

### **Study Outcomes and Definitions**

The study outcome was a composite of major adverse cardiac events (MACE; a composite of cardiac death, MI, or ischemia-driven target lesion revascularization [ID-TLR]), death (cardiac and noncardiac), MI, ID-TLR, and stent thrombosis. Periprocedural MI was defined as an increase in the serum levels of creatine kinase-MB or creatine kinase three or more times the local upper limit of normal with preference given to creatine kinase-MB values or a persistent ST-segment elevation >1 mm in two contiguous electrocardiographic limb leads or equal to 2 mm in two contiguous precordial leads. In patients who had increased creatine kinase or creatine kinase-MB at presentation, a diagnosis of MI required at least a twofold increase in enzyme levels after the procedure. Stent thrombosis was defined as definite or probable stent thrombosis according to the definitions of the Academic Research Consortium.<sup>16</sup>

#### Table 1. Baseline clinical characteristics.

	STAGED-PCI (n = 60)		CULPRIT ONLY (n = 60)		Ρ
	NO.	%	NO.	%	
Sex					
Male	44	73.3	50	83.3	0.161
Female	16	26.7	10	16.7	
Age					
$\text{Mean}\pm\text{SD}$	56.7 ± 10	0.79	$59.53 \pm 10.86$		0.326
Hypertension	30	50	28	46.7	0.715
Diabetes	26	43.3	28	46.7	0.174
Smoking	30	50	42	70	0.025*
Dyslipidemia	24	40.0	36	60.0	0.028*
Family history of CAD	16	26.7	12	20.0	0.388
Chest pain to ER (min.)					
$Mean\pmSD$	$241.5\pm203.3$		$334.0\pm298.4$		0.101
Killip class					
1	54	90.0	56	93.3	0.509
П	6	10.0	4	6.7	
Pulse					
$Mean\pmSD$	84.67 ± 14.74		$82.90 \pm 11.93$		0.612
Systolic BP					
$Mean\pmSD$	$130.33\pm21.73$		$125.33\pm23.15$		0.392
Diastolic BP					
Mean ± SD	80.67 ± 13.18		$80.0\pm12.39$		0.841
GRACE risk score					
Low	36	60	26	43.3	0.079
Intermediate	20	33.3	32	53.3	
High	4	6.7	2	3.3	

**Notes:** \*Statistically significant at P < 0.05 by chi-square test. Age, pulse, systolic blood pressure (SBP), Diastolic blood pressure (DBP), and chest pain to Emergency Room (ER) were analyzed by the Student's *t*-test. **Abbreviation:** MCP, Monte Carlo significance.

#### **Statistical Analysis**

Count and percentage were used to describe and summarize the qualitative data. The arithmetic mean and standard deviation (SD) were used as measures of central tendency and dispersion, respectively, for the quantitative data. The quantitative data between the two groups were compared using the Student's t-test, while categorical variables were compared using the Pearson's chi-square test, and if >20% of cells have expected cell count <5, we used Fisher's exact test if  $2 \times 2$  table and Monte Carlo significance test if more than  $2 \times 2$  tables. Univariate analysis was conducted to determine factors related to the occurrence of Major Adverse Cardiac and Cerebrovascular Events (MACCE) at one year, and significant variables by univariate analysis were entered in a binary logistic regression model by enter method; odds ratio with 95% CI were calculated. All statistical analyses were performed using the SPSS software (version 20.0; SPSS, Inc.). A value of P < 0.05 was considered statistically significant.

### **Ethics Statement**

This study complied with the Declaration of Helsinki and was reviewed and approved by the ethics committee of the Faculty of Medicine, Alexandria University (review report serial number 0302694). All patients were informed about the technique and informed consents were obtained from them.

### Results

This study included 120 patients, 60 patients in the staged-PCI group and 60 patients in the culprit-vessel PCI group, from October 2012 to November 2013 at the International Cardiac Center and Alexandria Main University Hospital. The baseline characteristics of both the groups are presented in Table 1.

There was no significant difference between the two groups with regard to the angiographic characteristics, baseline GRACE risk score, and baseline SS (20.07 ± 5.77 vs. 17.85 ± 6.84; P = 0.180), as shown in Table 2. The mean total stent length (31.07 ± 12.7 mm vs. 76.3 ± 14.1 mm) and the number of stents implanted per patient (1.34 ± 0.6 vs. 2.47 ± 0.72) were higher in the staged-PCI groups.

Table 2. Baseline angiographic characteristics.

	STAGED-PCI (n = 60)		CULPRIT ONLY (n = 60)		Ρ
	NO.	%	NO.	%	
No. of diseased vessels					
Two-vessel CAD	30	50.0	42	70.0	0.114
Three-vessel CAD	30	50.0	18	30.0	
Culprit vessel					
LAD/diagonal	42	70.0	26	43.3	0.037*
Ramus intermedius	0	0.0	2	3.3	1.000
LCX/OM	6	10.0	16	26.7	0.018*
RCA	12	20.0	16	26.7	0.542
Left main	0	0.0	0	0.0	_
No. of lesions					
1	52	86.7	48	80.0	0.672
2	6	10.0	10	16.7	
3	2	3.3	2	3.3	_
Thrombus containing lesion	26	43.3	26	43.3	1.000
TIMI flow grade pre-PCI					
0	27	45	28	46.6	0.980
1	24	40.0	22	36.6	
11	5	8.3	6	10	
111	4	6.6	4	6.6	_
LVEF%	50.50	± 6.70	$51.43 \pm 8.64$		0.642
Baseline SYNTAX score	$20.07\pm5.77$		17.85 ± 6.84		0.18

**Notes:** \*Statistically significant at P < 0.05 by chi-square test. left ventricular ejection fraction (LVEF)% and baseline syntax score were compared by the Student's *t*-test.

Abbreviations: FEP, Fisher's exact test significance; MCP, Monte Carlo significance test.



Angiographic and procedural data are shown in Tables 2 and 3, respectively.

**Residual SYNTAX score.** The rSS in the culpritvessel PCI group was significantly higher than that in the staged-PCI group: mean =  $9.53 \pm 5.32$  vs. mean =  $1.30 \pm 1.99$ , respectively, and P < 0.001 (Table 3).

**In-hospital outcome.** There was no significant difference in the in-hospital MACCE between both the groups (6.7% vs. 3.35%; P = 1.000). There was also no significant difference between both the groups with regard to minor and major bleeding complications, as shown in Table 4.

**Mid-term outcome.** After a mean follow-up of  $343 \pm 75$  days, the composite MACCE endpoint at one year (death, reinfarction, need for revascularization, and stroke)

was higher in the culprit-vessel PCI group (16.66% vs. 5%; P = 0.04). In the culprit-vessel PCI group, four patients (6.7%) had reinfarction, seven patients (11.7%) underwent nontarget vessel revascularization, and four patients (6.7%) underwent target vessel revascularization (two patients had in-hospital cardiac arrest). In the staged-PCI group, MACCE was lower at one year, mainly due to significantly lower non-target vessel revascularization (3.33% vs. 18.3%; P = 0.008) during the follow-up period (Table 4).

All patients treated by staged PCI (n = 60) and 24 patients in the culprit-vessel PCI group had an rSS <8. Thirty six patients in the culprit-vessel PCI group had an rSS  $\geq$ 8: 8 patients had total occlusion of one vessel and 28 patients had remaining stenosis (small vessel disease, distal vessel,

#### Table 3. Procedural techniques, materials, and complications.

	STAGED-PCI				
	(n = 60) NO.	%	(n = 60) NO.	%	
Door -to- balloon (min.)	58.83 ± 25.92			72.67 ± 32.10	
GPIIb/IIIa Inhibitor (In hospital)	32	53.3	26	43.3	0.438
Thrombus aspiration	26	43.3	24	40	1.000
Balloon pre-dilatation	30	50	36	60.0	0.436
Stent use	60	100.0	60	100.0	_
Type of stent BMS	0	0	2	3.3	0.792
DES	60	100	58	96.6	
Reference vessel diameter (mean $\pm$ SD)	3.13 ± 0.44	1	$3.08\pm0.3$	6	0.630
Number of treated vessels					
1-vessel	0	0	60	100	<0.001*
2-vessel	36	60	0	0	
3-vessel	24	40	0	0	
Number of stents implanted/pt					
1	0	0	54	90	<0.001*
2	32	53.33	6	10	
3	28	46.66	0	0	
Number of stent implanted/pt (mean $\pm$ SD)	$2.47 \pm 0.72$	2	$1.34\pm0.6$		0.043*
Mean total stent length mm (mean $\pm$ SD)	76.3 ± 14.1		31.07 ± 12	.7	<0.001*
TIMI flow grade pre-PCI					
0	0	0	0	0	
1	0	0	0	0	0.832
II	1	1.66	6	10	
	59	98.33	60	100	
Residual SYNTAX score					
Low (0–22)	60	100.0	54	90.0	0.237
Intermediate (23–32)	0	0.0	6	10.0	
High (>32)	0	0.0	0	0.0	
Mean residual SYNTAX score	1.30 ± 1.99	9	9.70 ± 5.70	)	<0.001*
Procedure success	58	96.6	56	93.3	0.679

**Notes:** \*Statistically significant at *P* < 0.05. Quantitative variables were compared by the Student's *t*-test. **Abbreviations:** FEP, Fisher's exact test; MCP, Monte Carlo significance test.

	STAGED-PCI (n = 60)		CULPRIT ONLY (n = 60)		Р	
	NO.	%	NO.	%		
In-Hospital MACCE	3	5	4	6.7	1.000	
Death	2	3.33	1	1.7	1.000	
Re-infarction	0	0	2	3.33	0.496	
TVR	1	1.7	1	1.7	1.000	
Non TVR	0	0	0	0	-	
Repeat revascularization	1	1.66	1	1.66	1.000	
Stroke	0	0	0	0	-	
Death/MI/stroke	2	3.33	3	5.00	0.773	
Major bleeding	0	0	0	0	_	
Minor bleeding	2	3.33	0	0	0.487	
FU- MACCE(1-year)	6	10	14	23.3	0.040*	
Death	1	1.7	2	3.33	1.000	
Re-infarction	2	3.33	5	5.3	0.439	
TVR	1	1.7	4	6.7	0.046*	
Non TVR	1	1.66	7	11.7	0.016*	
Repeat revascularization	2	3.33	11	18.3	0.008	
Stroke	0	0	0	0	-	
Death/MI/stroke	3	5.00	7	11.7	0.030*	

Table 4. In-hospital and mid-term outcomes.

**Note:** \*Statistically significant at *P* < 0.05. **Abbreviation:** FEP, Fisher's exact test.

or side branch); it should be noticed that the mean syntax score of this study population was  $\leq$  22. Comparing patients with an rSS <8 (84 patients) with the remaining 36 patients in the culprit-vessel PCI group with an rSS  $\geq$ 8, there were significant reductions in one-year MACCE (10.7% vs. 30.5%; P = 0.020), death/MI/CVA (5% vs. 13.9%; P = 0.016), and repeat revascularization (4.8% vs. 25%; P = 0.002; Table 5). We found that the type of intervention (culprit-only), diabetes mellitus, intermediate/high GRACE risk score at discharge, and rSS  $\geq$ 8 were independent predictors of MACCE at one vear (Table 6).

### Discussion

P-PCI is the standard of care for patients with STEMI. In up to 30% of such patients, significant stenoses are observed in one or more noninfarct-related arteries (N-IRA) during index angiography. The optimal management of patients found to have MVD, while undergoing P-PCI for STEMI remains unresolved.<sup>1-9</sup> The results of this study included 120 STEMI patients with MVD who were equally subdivided into two groups, those who underwent culprit-only and staged PCI, and found no significant difference in the occurrence of inhospital MACCE between both the groups (6.7% vs. 3.35%; P = 0.492). However, the composite MACCE endpoint at one year (death, reinfarction, need for revascularization, and

Table 5. Relationship between the rSS and one-year MACCE, repeated hospitalization, and angina.

	RESI	Р			
	<8 (n = 84)		≥8 <u>(n = 36)</u>		
	NO.	%	NO.	%	
Repeated hospitalization	0	0.0	12	33.3	<0.001*
Angina	0	0.0	20	55.6	<0.001*
MACCE(1-year)	9	10.7	11	30.5	0.020*
Death	1	1.2	2	5.6	0.214
Re-infarction	4	4.8	3	8.3	0.427
TVR	1	1.2	4	11.1	0.028*
Non TVR	3	3.6	5	13.8	0.025*
Repeat revascularization	4	4.8	9	25	0.001*
Stroke	0	0	0	0	-
Death/MI/stroke	5	6	5	13.9	0.016*

**Note:** \*Statistically significant at P < 0.05 by Fisher's exact test. **Abbreviation:** FEP, Fisher's exact test.

stroke) was higher in the culprit-vessel PCI group (16.66% vs. 6.66%; P = 0.014). When analyzing the outcomes according to the level of completeness of revascularization using the cutoff rSS  $\leq 8$ , there were significant reductions in one-year MACCE (10.7% vs. 30.5%; P = 0.020), death/MI/CVA (5% vs. 13.9%, P = 0.016), and repeat revascularization (4.8% vs. 25%, P = 0.002). We found that the type of intervention (culprit-only), diabetes mellitus, intermediate/high GRACE risk score at discharge, and rSS  $\geq$ 8 were independent predictors of MACCE at one year.

Recently, the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial reported that in patients with STEMI and multivessel CAD undergoing infarct artery PCI, preventive PCI in noninfarct coronary arteries with major stenoses significantly reduced ischemic events by ~65%, with CR during the index procedure.<sup>17</sup> The results of the Complete Versus Lesion-Only Revascularization in Patients Undergoing Primary Percutaneous Coronary Intervention for STEMI and Multivessel Disease (CvLPRIT)<sup>18</sup> were consistent with those observed in the PRAMI trial. CvLPRIT and PRAMI were similar in general design. Both assessed the safety and benefit of total revascularization intended around the time of P-PCI. CvLPRIT demonstrated that in a population of patients with STEMI treated by contemporary P-PCI, in-hospital CR of angiographically significant N-IRA lesions improved clinical outcomes compared with the treatment of culprit lesion only.

Prior meta-analyses of complete versus culprit-only revascularization for patients with MVD undergoing P-PCI for STEMI have reported varying results due to differences in study designs, comparisons of different groups, and different analytical methods.<sup>19-22</sup> Vlaar et al found that staged PCI resulted in lower short- and long-term mortality compared with MVD-PCI or IRA-PCI.<sup>19</sup> Bangalore et al found that MVD-PCI compared



Table 6. Multivariate logistic regression model for the predictors of MACCE at one year.

	В	S.E.	WALD	ODDS RATIO	95% CI FOR OR	P-VALUE
Type of intervention (culprit-only)	4.024	0.755	28.410	0.0180	0.004-0.079	<0.001**
Diabetes Mellitus	2.290	0.675	11.520	9.872	2.63-37.04	0.001*
GRACE score			10.616			0.005*
GRACE score (Intermediate)	1.055	0.450	5.496	2.871	1.188–6.94	0.019*
GRACE score (High)	2.843	1.043	7.426	17.172	2.222–132.7	0.006*
RSS ≥8	-2.790	0.712	15.365	0.0610	0.015-0.245	<0.001**

**Notes:** Nagelkerke  $R^2 = 0.73$ , Model  $\chi^2_{(5)} = 95.2$ , P < 0.001. \*P < 0.05; \*\*P < 0.001. Reference categories intervention: staged PCI; DM: nondiabetic; GRACE score: low risk; rSS: <8.

with IRA-PCI resulted in similar long-term mortality, but a lower long-term rate of MACE.<sup>20</sup> A recent meta-analysis demonstrated that MVD-PCI compared with IRA-PCI resulted in worse outcomes in cohort studies, but not in the randomized clinical trials.<sup>21</sup> This is in line with our findings. Furthermore, Bainey et al found that staged-multivessel PCI was superior to multivessel PCI during the index procedure. The difference in outcome between the IRA-only and MVD-PCI groups may be due to revascularization, as differences in baseline may also play an important role.<sup>22</sup> However, in real-world practice, CR in patients with STEMI and MVD is often not obtained.

Our results show that quantifying the extent and complexity of residual atherosclerosis after PCI can help to identify patients with MVD who are at increased risk for adverse long-term clinical outcomes. Our results are in parallel with the previous published data showing that an rSS <8 is a suitable threshold for the definition of "reasonable" incomplete revascularization (ICR) and confirms the results of the SYN-TAX trial.<sup>13-15</sup> Généreux et al reported that the 30-day and one-year rates of ischemic events were significantly higher in the ICR group, specifically in patients with moderate- and high-risk ACS undergoing PCI with an rSS >8.<sup>13</sup> Witberg et al studied 148 consecutive patients with triple-vessel/left main CAD treated by PCI. Patients with reasonable ICR (rSS <8) had significant reductions in three-year MACCE and repeat revascularization.<sup>23</sup> To date, the published trials and meta-analyses have been unable to define a comprehensive common strategy for all STEMI patients with MVD. Because these patients are very heterogeneous, any revascularization strategy should be individualized in this high-risk group of STEMI patients with impaired outcome related to the extent of CAD. However, the use of the available risk stratification scores and staged and ischemia-driven revascularization of the N-IRA with the achievement of "reasonable" CR may be the best treatment strategy for STEMI patients with MVD. The current ongoing COMPLETE and COMPARE ACUTE trials are studying these issues.

### Conclusions

Staged PCI that achieved reasonable CR (rSS  $\leq$ 8) in patients with STEMI and MVD improved mid-term survival and

reduced the need for repeat PCI. The rSS may improve the determination of an objective level of reasonable ICR. Such findings are of value in guiding the clinician to reduce the level of reversible myocardial ischemia by treating obstructive lesions in a manner that stays within the threshold of reasonable ICR. Nevertheless, large randomized trials are required to establish the optimal revascularization strategy for these high-risk patients.

### Limitations

This study was a prospective single-center study and therefore lacks randomization and intention to treat data. As an observational study, it is subject to selection bias. For example, patients may have been allocated to one treatment option because of the characteristics that would have made that option more preferable. Because of the limited sample size, the patients in our study might not be representative of the entire population of acute STEMI patients who undergo P-PCI. To confirm our findings, a study with a larger sample of patients is required. However, the results of our analysis should be considered hypothesis generating.

### **Author Contributions**

Conceived and designed the experiments: ML. Analyzed the data: ML. Wrote the first draft of the manuscript: ML. Contributed to the writing of the manuscript: ML. Agree with manuscript results and conclusions: ML, SA, MS. Made critical revisions and approved final version: ML, SA, MS. All authors reviewed and approved of the final manuscript.

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