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Predictive Value of the Residual SYNTAX Score in Patients with Cardiogenic Shock

Brief Title: residual SYNTAX score in cardiogenic shock

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A CULPRIT SHOCK sub-study demonstrates the first time that the residual SYNTAX score is independently associated with mortality in cardiogenic shock.

ABSTRACT

Background: In hemodynamically stable patients, complete revascularization (CR) following percutaneous coronary intervention (PCI) is associated with a better prognosis in chronic and acute coronary syndromes.

Objectives: Assess the extent and severity as well as the prognosis value of remaining coronary stenoses following PCI - using the residual SYNTAX score (rSS) - in patients with cardiogenic shock (CS) related to myocardial infarction (MI).

Methods: The CULPRIT-SHOCK trial compared a multivessel PCI (MV-PCI) to a culprit-lesion-only PCI (CLO-PCI) strategy in multivessel coronary artery disease patients presenting with MI-related CS. The rSS was assessed by a central Core Laboratory. The study population was divided in 4 groups according to tertiles of rSS of the population, isolating patients with rSS=0 (CR). The predictive value of rSS on the 30-day primary endpoint (mortality or severe renal failure), 30-day and 1-year mortality was assessed using multivariate logistic regression.

Results: Among the 587 patients with rSS available, the median rSS was 9.0 (interquartile range [IQR] 3.0-17.0); 102 (17.4%), 100 (17.0%), 196 (33.4%) and 189 (32.2%) patients had a rSS=0, $0 < rSS \leq 5$, $5 < rSS \leq 14$ and $rSS > 14$, respectively. CR was achieved in 75 (25.2%; 95%CI 20.3-30.5) and 27 (9.3%; 95%CI 6.2%-13.3%) in the MV-PCI and CLO-PCI strategy, respectively. After multiple adjustments, rSS was independently associated with 30-day and one-year mortality (aOR per 10 units [95%CI]: 1.49 [1.11-2.01] and 1.52 [1.11-2.07], respectively).

Conclusion: Among patients with multivessel disease and MI-related CS, complete revascularization is achieved only in one fourth of the patients using a MV-PCI strategy and, the residual SYNTAX score is independently associated with early and late mortality.

CONDENSED ABSTRACT: We aimed to assess the extent and severity as well as the prognostic value of remaining coronary stenoses following percutaneous coronary intervention (PCI) - using the residual SYNTAX score - in 587 patients of the CULPRIT-SHOCK trial in cardiogenic shock related to myocardial infarction. We found that 1) complete revascularization is achieved only in one fourth of the patients using a multivessel PCI strategy and 2) the residual SYNTAX score is independently associated with early and late mortality.

Key Words: cardiogenic shock, myocardial infarction, residual SYNTAX score

Abbreviations list

ACS: acute coronary syndrome

bSS: baseline SYNTAX score

CAD: coronary artery disease

CR: complete revascularization

CS: cardiogenic shock

CLO-PCI: culprit-lesion-only PCI

CTO: chronic total occlusion

MI: myocardial infarction

MV-PCI: multivessel PCI

PCI: percutaneous coronary intervention

rSS: residual SYNTAX score

In patients with cardiogenic shock (CS), the CULPRIT-SHOCK (Culprit Lesion Only percutaneous coronary intervention (PCI) versus Multivessel PCI in Cardiogenic Shock) trial demonstrated that a culprit-lesion-only PCI (CLO-PCI) with possible staged revascularization was more effective and safer than an immediate multivessel PCI (MV-PCI) strategy (1). Following these results, current European Society of Cardiology (ESC) guidelines on myocardial revascularization do no longer recommend routine non infarct-related-artery PCI (Class III, B) during primary PCI in this situation (2). This is in contrast with hemodynamically stable MI patients for whom the benefit of immediate or early complete revascularization (CR) following PCI or coronary artery bypass grafting has been shown to be associated with better cardiovascular outcomes (3–6).

Described fifteen years ago, the SYNTAX (SYNergy between PCI with TAXUS and Cardiac Surgery) score, an easy and friendly-to-use online tool, allows to quantitatively assess the extent and complexity of coronary artery disease (CAD), help the heart team choosing the more appropriate revascularization strategy and is independently associated with cardiovascular outcomes in elective PCI, acute coronary syndrome (ACS), myocardial infarction (MI) and also CS (2, 7–15). More recently, the usefulness of the residual SYNTAX score (rSS) - calculated following PCI - has been assessed in various clinical settings (16, 17). The predictive value of rSS has been demonstrated in hemodynamically stable patients with chronic coronary syndrome, ACS or MI (16–25). However, evidence remains scarce in patients with CS, with only one small trial published showing no impact of rSS on prognosis (26).

The objectives of this CULPRIT-SHOCK sub-study were to assess, the 1) extent and severity of CAD following PCI, and 2) the prognostic value of the rSS, in a large prospective sample size of multivessel patients with CS related to acute MI.

METHODS

Study Population

The CULPRIT-SHOCK trial, conducted from April 2013 through April 2017 at 83 European centers, is the largest (n=706) randomized clinical trial performed to date in patients with CS related to acute MI. The study was approved by all local or national ethics committees. The design and results have been previously published (1, 27, 28). Briefly, the CULPRIT-SHOCK trial demonstrated that a CLO-PCI strategy (with possible subsequent planned PCI of non-culprit lesion) significantly reduced the rates of 30-day death or renal replacement therapy and 30-day mortality compared to an immediate MV-PCI strategy in patients with multivessel CAD and MI-related CS (1). At one year, the benefit of the CLO-strategy was confirmed with a slight attenuation in the mortality difference between groups (28).

Study Objectives

The first objective was to assess the extent and complexity of residual coronary stenoses following PCI, using the rSS and in particular the rate of CR reached in the MV-PCI strategy vs. in the CLO-PCI strategy. The score was calculated after the initial PCI or after subsequent PCI in the CLO-PCI group, if a planned staged revascularization of non-culprit lesions was performed.

The second objective was to evaluate the impact of the rSS on early and late prognosis.

Angiographic Core Laboratory

All coronary angiograms of the CULPRIT-SHOCK trial were anonymized and centrally analyzed by the ACTION Core Laboratory (Allies in Cardiovascular Trials, Initiatives and Organized Networks, Pitié-Salpêtrière Hospital, AP-HP, Paris, France). Patients with previous coronary artery bypass graft or with incomplete or missing coronary angiogram were excluded from this analysis.

Experienced and trained angiography readers assessed the SYNTAX score visually, blinded to clinical and procedural data (29). Each lesion $\geq 50\%$ diameter stenosis in a vessel ≥ 1.5 mm were scored using the online SYNTAX score tool (www.syntaxscore.com) (7). Two readers, blinded to the other, assessed the baseline (bSS) and rSS and entered the data in a dedicated computerized database. In case of discrepancy, an additional reading was performed by a senior interventional cardiologist to reach consensus. The bSS assessment was pre-specified and calculated prospectively once the coronary angiograms were received by the Core Lab (27). The rSS was calculated in addition, on the last frames of initial PCI angiogram or of the planned PCI angiogram in the CLO-PCI group, if a staged revascularization of non-culprit lesions was performed during index hospitalization. Inter- and intra-observer variabilities (tertil partitioning) to calculate the SYNTAX score were assessed for 2 readers in 50 and 20 angiograms, respectively. Cohen's Kappa statistics showed a high reliability for inter-observer ($K=0.79$; 95%CI 0.64-0.93) and intra-observer variability (reader 1: $K=0.84$; 95%CI 0.63-1.00 and reader 2: $K=0.78$; 95%CI 0.55-1.00).

Endpoints and definitions

Patients with CR had a post-PCI rSS=0 and act as a separate reference group. Patients were allocated in 4 groups according to tertiles of rSS of the population, isolating patients with CR: rSS=0, $0 < rSS \leq 5$, $5 < rSS \leq 14$ and $rSS > 14$.

The outcomes of interest were 30-day death or renal replacement therapy (primary endpoint of the CULPRIT-SHOCK trial), 30-day mortality and 1-year mortality rates. The 30-day secondary outcomes of the CULPRIT-SHOCK trial were also reported.

Statistical Analysis

Continuous variables are reported as median with interquartile range (IQR) and compared using the Kruskal-Wallis test. Categorical variables are reported as number and percentage and compared with Chi-square test or Fisher's exact test. As previously published, event rates were compared using Chi-square test or Fisher's exact test (1,27). Kaplan-Meier curves were also used to show event rates over time with classification according to the rSS and compared using long-rank test. Patients without event were censored at 30 days or 1-year. Correlation between bSS and rSS was assessed for each revascularization strategy using Pearson correlation coefficient and regression coefficient comparison was done (covariance analysis with interaction).

Multivariate logistic regression models were used to evaluate the independent association between rSS (as continuous variable) and outcomes. In each model, rSS was adjusted on baseline clinical and procedural characteristics possibly associated with outcomes in univariate analysis ($p < 0.2$) and are detailed in **Supplemental Table 1**.

Sensitivity analyses were performed for each outcome, adjusting rSS on consistent covariates as well as the effective revascularization strategy undergone by the patients (to account for crossover [11.1%] among the groups of randomization). Results are interpreted in term of adjusted Odds Ratio (aOR) with their associated 95% confidence intervals (95%CI). Interaction between rSS and revascularization strategy (randomization group) was evaluated for each outcome using logistic regression. Area under the curve of rSS was performed for each endpoint (receiver operating characteristic [ROC] curve analysis). A p-value < 0.05 was considered significant unless otherwise specified. All statistical analyses were performed with SAS release 9.4 (SAS Institute Inc, Cary, NC) statistical software package.

RESULTS

Among the 706 patients randomized in the CULPRIT-SHOCK trial, 686 were analyzed according to the intention to treat principle. From this group, 99 patients (14.4%) were excluded by the Core Laboratory because of previous coronary artery bypass graft (n=33), missing (n=23), incomplete (n=27) or unreadable (n=16) coronary angiogram. Thus, 587 (85.6%) patients were analyzed in this sub-study. The median bSS before PCI was 24.5 (IQR 17.0 - 32.0). Immediate MV-PCI was performed in 298 patients (50.8%). Among the 289 patients (49.2%) randomized in the CLO-PCI arm, 48 patients (16.6%) underwent a staged PCI within 9 (IQR 4-18) days after randomization. In the global population the median rSS was 9.0 (IQR 3.0 - 17.0) and complete revascularization (rSS=0) was achieved in 102 patients (17.4%). Among patients with incomplete revascularization, 100 (20.6%), 196 (40.4%) and 189 (39.0%) had $0 < rSS \leq 5$, $5 < rSS \leq 14$ and $rSS > 14$, respectively.

Clinical and procedural characteristics

Clinical and procedural characteristics are shown in **Table 1** and **Table 2**. Patients with CR were younger, more often active smoker and were more prone to have a double vessel disease (>50%) with a lower bSS (17.3; IQR 12.0-22.5), very few CTO (<1%) and a higher post-PCI TIMI 3 flow grade (91.2%).

Baseline and residual SYNTAX score correlation

Figure 1 shows the level of completeness of revascularization assessed by rSS according to bSS for each revascularization strategy. CR was achieved in 25.2% (95%CI 20.3-30.5) in the MV-PCI group and 9.3% (95%CI 6.2-13.3) in the CLO-PCI group. Strong correlations were present between bSS and rSS in CLO-PCI (r=0.68) and MV-PCI (r=0.59) groups, without any significant difference between the two groups (**Figure 2**). Intriguingly, rSS was found to be

greater than bSS in 1.0% and 3.4% of the patients in the CLO-PCI and MV-PCI groups, respectively.

Clinical outcomes

The median duration of follow-up for survival was 181 [2-365] days. Thirty-day outcomes and 1-year mortality are shown in **Table 3** and **Figure 3**. There was a stepwise increase in outcomes rates according to increased rSS in the whole study population as within each randomization group separately (**Supplemental Figure 1**). After multivariable analysis, including bSS in the model, no independent association of rSS with 30-day primary endpoint was found. However, rSS was independently associated with 30- and 1-year mortality, on top of bSS (**Central Illustration**).

Results remained consistent after sensitivity analysis when adjusting for the effective revascularization strategy used (**Supplemental Figure 2**). No significant interactions were observed between the rSS and the revascularization strategy for the primary endpoint ($p=0.64$), 30-day and 1-year mortality ($p=0.81$ and $p=0.87$, respectively).

ROC curve analyses demonstrated moderate discrimination accuracy for the 30-day primary endpoint (c-statistics = 0.62; 95% CI 0.57; 0.66), 30-day mortality (c-statistics = 0.63; 95% CI 0.59; 0.68) and 1-year mortality (c-statistics = 0.64; 95% CI 0.59; 0.68).

DISCUSSION

The association of the rSS with mortality has been widely established in chronic or acute coronary syndromes and ST-segment elevation MI patients. We report the first study in a large sample size evaluating the prognostic value of the rSS in CS related to acute MI. We found that 1) although using a MV-PCI strategy, CR is achieved in only one fourth of the patients; 2) the

rSS is associated with early and late mortality, independently of all clinical characteristics and bSS.

Numerous observational studies and meta-analyses suggest a benefit of achieving CR following PCI or coronary artery bypass grafting on cardiovascular outcomes and mortality (3, 4). However, due to the retrospective nature of most of the studies, the small sample size and the lack of consensus for the definition of CR, evidence remains limited (29). More recently, several randomized trials have been conducted in ST-segment elevation MI patients without hemodynamic compromise. These trials relatively consistently demonstrated a prognostic benefit of adopting a MV-PCI strategy resulting in less repeat revascularization and recurrent MI and even, in a pooled analysis, in a reduced cardiovascular mortality compared to a CLO-PCI strategy (5, 6, 31–34). However, in all these trials there was no clearly defined staged PCI strategy in the CLO-PCI arm, which is different from the CULPRIT-SHOCK trial.

In CS, revascularization of non-culprit lesions during the index PCI was formerly recommended, mainly based on pathophysiological considerations (35). The results of the CULPRIT-SHOCK trial have shown a deleterious impact of immediate MV-PCI and led to a downgrading of the former recommendation to routinely perform immediate PCI of non-culprit lesions during primary PCI in CS (1, 2).

The CULPRIT-SHOCK trial inclusion criteria selected patients with a high CAD burden with multivessel disease including CTO presence in one out of five patients. Indeed, the median bSS was 24.5, higher than in previous studies where it ranged from 12 to 16 in ACS or MI with stable hemodynamic situation and 22 in the only study in CS (5, 9, 16, 23, 26). Following PCI, the median rSS was 9.0, also higher in comparison to previous studies where it ranged from 2 to 5.5 in stable ACS patients and 7 in CS (10,15–25,36). In our study as in others, the rSS is

strongly correlated to the bSS (16, 17, 22, 24, 36). It reflects the extent and severity of CAD in MI-related CS and emphasizes the challenge of achieving optimal revascularization in patients with multivessel and complex coronary disease. Indeed, in the MV-PCI arm of the CULPRIT-SHOCK trial, CR could be only achieved in one fourth of the patients in agreement with one other report (26). This is lower in comparison to the rates of CR achieved in hemodynamically stable patients ranging from 37 to 52% and up to 90% in the recent COMPLETE trial including patients with ST-segment elevation MI without cardiogenic shock (5, 8, 17, 18, 21, 22, 24, 36). Although, taking into consideration unfavorable anatomical conditions (i.e., CTO, small vessel disease) for which revascularization might be challenging, hopeless or futile, the optimal level of achievable rSS in CS remains unknown.

Généreux and al. were the first to show that the rSS is a strong independent predictor of cardiovascular outcomes in ACS. In CS, the only reported work by Javainen & al. included a small number (n=61) of patients and did not show any association between rSS and cardiovascular outcomes (26). In contrast, we report a strong association between rSS and early and late mortality in a large group of CS. Importantly, unlike other studies, this association remains consistent on top of the bSS and after adjustment for the effective revascularization strategy (36). Obviously, rSS is associated to mortality with a higher magnitude in CS compared to ACS patients, ie. rSS > 8 is associated with roughly 50% early mortality rate in CS, but only 5 to 10% in ACS.

There is an apparent discrepancy between a high rSS being an independent predictor of cardiovascular outcomes as shown in our study and the results of the CULPRIT-SHOCK trial demonstrating a benefit from CLO-PCI in comparison to the MV-PCI strategy. We can speculate on these discrepancies in patients in CS, which may relate to 1) a more severe CAD pattern at

baseline, 2) a less achievable CR following PCI, and 3) a higher risk of harmful complementary PCI. Indeed, primary PCI led to a worsening of coronary anatomy in 1 to 3% of the patient in whom rSS was higher than bSS, in the CLO-PCI and MV-PCI strategy, respectively. A condition that has never been described in hemodynamic stable patients (17, 22, 24). This may be explained by taking into account - for rSS but not bSS assessment - the hidden stenoses downstream of the culprit coronary total occlusion after they have been revealed following successful PCI. However, the management of the non-culprit lesion appears as a key determinant of prognosis. In the acute setting, there is an obvious risk to overestimate the non-culprit lesion severity and therefore perform PCI of non-flow limiting stenosis which may cause even harm (37). Furthermore, in CS TIMI 3 flow is less often achievable and the increased thrombotic and inflammatory activities favor an enhanced risk of stent thrombosis after PCI compared to hemodynamic stable patients (38–41). In the CLO-PCI arm of the CULPRIT-SHOCK trial, planned non-culprit stenosis PCI were performed in about half of the surviving patients. Therefore, rSS appears more as a global marker of severity that outweighs the benefit of revascularization.

Both more complete and safer revascularization may be the goal of future clinical research in this area. Mechanical circulatory support devices may represent an answer to this double injunction, whether it should be used in the acute setting for myocardial salvage, in non-acute staged revascularization or both to achieve a more complete revascularization remains a matter of debate. However to date, their benefit has been confined to some hemodynamic improvements without any clinical benefit demonstrated in any randomized trial (42) and there were some concerns in recent observational trials (43, 44). The eagerly awaited, ongoing or future, ANCHOR (NCT04184635), ECLS-SHOCK (NCT03637205), EUROSHOCK

(NCT03813134) and DanGer Shock (NCT01633502) trials will compare veno-arterial extracorporeal membrane oxygenation or Impella to conventional therapy and hopefully break the glass ceiling of mortality rate in CS.

Limitations

Several limitations should be discussed. First, in CS, multivessel CAD is generally observed in three quarters of the populations, however in the CULPRIT-SHOCK trial it was part of the inclusion criteria and led to include a population at higher risk by excluding patients with single vessel CAD. Second, some values are missing: Left ventricular ejection fraction was only available in one half of the patients. Third, this study is out of the scope of functional assessment of non-culprit stenosis using fractional flow reserve (45). Finally, despite careful adjustment, potential unmeasured confounders may remain.

CONCLUSION

In patients with multivessel CAD and CS related to acute MI, complete revascularization is seldom achieved. The rSS is independently associated with early and late mortality.

Clinical Perspectives

Competency in Patient Care and Procedural Skills: Even with a multivessel PCI strategy, complete revascularization is achieved in only one-fourth of patients with acute myocardial infarction complicated by cardiogenic shock. The residual SYNTAX score is independently associated with early and late mortality.

Translational Outlook: Randomized trials are needed to evaluate the utility of mechanical circulatory device to facilitate complete revascularization in patients with infarct-related cardiogenic shock.

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Figure Legends

Figure 1: rSS according to baseline SYNTAX score in A) culprit-only PCI and B) multivessel PCI strategy. The higher is the bSS and more the CLO-PCI strategy is used, the higher is the rSS. CR is rare and correlated to the severity of baseline CAD and the revascularization strategy. SYNTAX score categories: low ≤ 22 , intermediate 22-32, high ≥ 33 .

Figure 2: Correlation between baseline and residual SYNTAX score. Using Pearson correlation coefficient, a strong correlation was observed between bSS and rSS in CLO-PCI and MV-PCI groups, without any difference between the 2 revascularizations strategies.

Figure 3: Kaplan Meier curves of early and late outcomes according to residual SYNTAX score. A) 30-day death and renal replacement therapy, B) 30-day death, C) one-year death. A stepwise increase in CV outcomes is observed according to rSS.

Central Illustration: Association between residual SYNTAX score and early and late outcomes. (Top) Median rSS according to bSS in the CULPRIT SHOCK trial assessed by the independent ACTION Core Laboratory. PCI allows to reduce the SYNTAX score from 24.5 (bSS) to 9.0 (rSS) in CS. **(Middle)** Rates of rSS>bSS and CR observed in each randomization group. rSS was higher than bSS in 1 to 3.4% and CR was achieved in 10% and 25% in the CLO-PCI and MV-PCI group, respectively. **(Bottom)** Multivariate logistic regression models evaluating the independent association between rSS and CV outcomes. rSS is an independent predictor of early and late mortality. bSS, baseline SYNTAX score; CLO-PCI, culprit-lesion-only PCI; CR, complete revascularization; MV-PCI, multivessel PCI; PCI, percutaneous coronary intervention; RRT, renal replacement therapy; rSS, residual SYNTAX score. aOR: Adjusted odd ratio are per 10 units; CI: confidence interval; Number of included patients for

each outcomes are: 30-day death or RRT, N=528; 30-day death, N=544; 1-year Death, N=528;

Covariables of adjustment for each outcome are detailed in Supplemental Table 1.

Table 1: Baseline clinical characteristics according to residual SYNTAX score

	rSS = 0 (N=102)	0 < rSS ≤ 5 (N=100)	5 < rSS ≤ 14 (N=196)	rSS > 14 (N=189)	Total (N=587)	p-value
Age, years	64.0 (57.0-75.0)	70.0 (57.0-77.5)	69.0 (60.0-78.0)	70.0 (63.0-78.0)	69.0 (60.0-78.0)	0.0018
Male gender	79/102 (74.5%)	73/100 (73.0%)	157/196 (80.1%)	137/189 (72.5%)	443/587 (75.5%)	0.313
BMI, kg/m ²	26.4 (24.4-29.5)	27.1 (24.5-29.3)	26.6 (24.7-29.4)	26.6 (24.2-29.4)	26.6 (24.5-29.4)	0.764
Cardiovascular risk factors						
Current smoking	37/100 (37.0%)	28/97 (28.9%)	52/189 (27.5%)	34/183 (18.6%)	151/569 (26.5%)	0.008
Hypertension	54/101 (53.3%)	61/99 (61.6%)	115/195 (59.0%)	121/185 (65.4%)	351/590 (60.5%)	0.241
Hypercholesterolemia	37/101 (36.6%)	32/97 (33.0%)	59/194 (30.4%)	64/185 (34.6%)	192/577 (33.3%)	0.711
Diabetes Mellitus	23/101 (22.8%)	34/97 (35.1%)	64/196 (32.7%)	58/184 (31.5%)	179/578 (31.0%)	0.239
Past Medical History						
Previous MI	11/101 (10.9%)	20/98 (20.4%)	27/194 (13.9%)	34/187 (18.2%)	92/580 (15.9%)	0.196
Previous Stroke	3/101 (3.0%)	6/98 (6.1%)	11/194	18/188	38/581	0.157

			(5.7%)	(9.6%)	(6.5%)	
Known PAD	7/101 (6.9%)	10/98 (10.2%)	19/194 (9.8%)	28/188 (14.9%)	64/581 (11.0%)	0.174
Previous PCI	13/101 (12.9%)	21/98 (21.4%)	28/194 (14.4%)	37/187 (19.8%)	99/580 (17.1%)	0.212
Hemodynamics and signs of impaired organ perfusion						
Mean BP, mm Hg	76.2 (63.3- 91.8)	76.7 (65.0- 94.0)	76.7 (63.3- 92.0)	73.3 (62.3- 93.3)	76.0 (63.3- 93.3)	0.911
Heart rate, bpm	91.0 (73.0- 106.0)	87.0 (70.0- 104.0)	90.0 (70.0- 107.0)	90.0 (73.0- 109.5)	90.0 (72.0- 107.0)	0.844
Altered mental status	69/101 (68.3%)	74/100 (74.0%)	130/196 (66.3%)	122/189 (64.6%)	395/586 (67.4%)	0.420
Cold clammy skin and limbs	66/100 (66.0%)	79/100 (79.0%)	140/192 (72.9%)	118/188 (62.8%)	403/580 (69.5%)	0.019
Oliguria	25/100 (25.0%)	23/99 (23.2%)	57/187 (30.5%)	40/184 (21.7%)	145/570 (25.4%)	0.251
Arterial lactate > 2mmol/l	59/101 (58.4%)	68/97 (70.1%)	128/190 (67.4%)	124/185 (67.0%)	379/573 (66.1%)	0.313
LVEF*, %	38.0 (30.0- 48.0)	30.0 (25.0- 45.0)	32.5 (25.0- 40.0)	34.0 (20.0- 40.0)	35.0 (25.0- 40.0)	0.201
Presentation						
Fibrinolysis	5/102 (4.9%)	5/100 (5.0%)	9/194 (4.6%)	11/189	30/585	0.961

				(5.8%)	(5.1%)	
Resuscitation	57/102 (55.9%)	54/100 (54.0%)	108/195 (55.4%)	96/189 (50.8%)	315/586 (53.8%)	0.786
STEMI	65/100 (65.0%)	70/97 (72.2%)	123/188 (65.4%)	108/184 (58.7%)	366/569 (64.3%)	0.154
- Anterior STEMI	37/64 (57.8%)	37/69 (53.6%)	62/123 (50.4%)	54/107 (50.5%)	190/363 (52.3%)	0.765
IABP-SHOCK II score**	2.0 (1.0-3.0)	3.0 (1.0-4.0)	3.0 (1.0-4.0)	3.0 (1.0-4.0)	3.0 (1.0-4.0)	0.423

Values are median (Q1-Q3) or n/N (%). BMI, Body mass index; BP, blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; rSS, residual SYNTAX score; STEMI, ST-segment elevation MI; TIMI, Thrombolysis in myocardial infarction.

*LVEF was only available in 223 patients

** IABP SHOCK II was only available in 292 patients

Table 2: Procedural characteristics according to residual SYNTAX score

	rSS = 0 (N=102)	0 < rSS ≤ 5 (N=100)	5 < rSS ≤ 14 (N=196)	rSS > 14 (N=189)	Total (N=587)	p- value
Number of affected vessels						<0.001
- Single VD	3/102 (2.9%)	1/100 (1.0%)	1/196 (0.5%)	0/189 (0.0%)	5/587 (0.9%)	
- Double VD	54/102 (52.9%)	50/100 (50.0%)	81/196 (41.3%)	33/189 (17.5%)	218/587 (37.1%)	
- Triple VD	45/102 (44.1%)	49/100 (49.0%)	114/196 (58.2%)	156/189 (82.5%)	364/587 (62.0%)	
Baseline SYNTAX score	17.3 (12.0-22.5)	19.0 (14.0-24.5)	22.8 (18.0-29.3)	32.5 (26.5-39.5)	24.5 (17.0-32.0)	<0.001
Culprit vessel*						0.275
- RCA	37/102 (36.3%)	28/100 (28.0%)	47/196 (24.0%)	52/189 (27.5%)	164/587 (27.9%)	
- LM	9/102 (8.8%)	7/100 (7.0%)	11/196 (5.6%)	16/189 (8.5%)	43/587 (7.3%)	
- LAD	38/102 (37.3%)	44/100 (44.0%)	99/196 (50.5%)	74/189 (39.2%)	255/587 (43.4%)	
- LCx	18/102 (17.6%)	21/100 (21.0%)	39/196 (19.9%)	47/189 (24.9%)	125/587 (21.3%)	

CTO \geq 1*	1/102 (1.0%)	6/100 (6.0%)	36/196 (18.4%)	81/189 (42.9%)	124/587 (21.1%)	<0.001
Procedural Characteristics						
Femoral access	88/102 (86.3%)	81/100 (81.0%)	150/196 (76.5%)	162/189 (85.7%)	481/587 (81.9%)	0.070
DES in culprit lesion	97/102 (95.1%)	92/98 (93.9%)	180/192 (93.8%)	158/167 (94.6%)	527/559 (94.3%)	0.962
Aspiration thrombectomy	17/102 (16.7%)	17/100 (17.0%)	29/196 (14.8%)	24/189 (12.7%)	87/587 (14.8%)	0.723
Pre-PCI TIMI Flow*						0.065
- TIMI 0	46/100 (46.0%)	42/100 (42.0%)	89/196 (45.4%)	92/187 (49.2%)	269/583 (46.1%)	
- TIMI 1	3/100 (3.0%)	16/100 (16.0%)	22/196 (11.2%)	15/187 (8.0%)	54/583 (9.3%)	
- TIMI 2	12/100 (12.0%)	18/100 (18.0%)	20/196 (10.2%)	17/187 (9.1%)	67/583 (11.5%)	
- TIMI 3	40/100 (40.0%)	26/100 (26.0%)	65/196 (33.2%)	63/187 (33.7%)	193/583 (33.1%)	
Post-PCI TIMI Flow*						<0.001
- TIMI 0	0/102 (0.0%)	0/99 (0.0%)	7/190 (3.7%)	33/185 (17.82)	40/576 (6.9%)	
- TIMI 1	0/102 (0.0%)	0/99 (0.0%)	7/190 (3.7%)	17/185	24/576	

- TIMI 2	9/102 (8.8%)	15/99 (15.2%)	20/190 (10.5%)	13/185 (7.0%)	57/576 (9.9%)	
- TIMI 3	93/102 (91.2%)	84/99 (84.8%)	156/190 (82.1%)	122/185 (65.9%)	455/576 (79.0%)	
Immediate MV-PCI	78/102 (76.5%)	50/100 (50.0%)	102/196 (52.0%)	83/189 (43.9%)	313/587 (53.3%)	<0.001
Staged PCI	15/102 (14.7%)	11/100 (11.0%)	13/196 (6.6%)	9/189 (4.8%)	48/587 (8.2%)	0.015
Total contrast volume, ml	220.0 (169.0- 294.0)	200.0 (150.0- 300.0)	230.0 (158.0- 300.0)	220.0 (150.0-300.0)	220.0 (155.0- 300.0)	0.958
Total duration of fluoroscopy, min	13.4 (8.2- 20.0)	14.4 (8.3- 22.5)	14.3 (9.4- 24.1)	18.0 (11.1- 27.5)	15.2 (9.3- 24.5)	0.005
Resuscitation						
Catecholamine	84/102 (82.4%)	90/99 (90.9%)	177/196 (90.3%)	174/188 (92.6%)	525/585 (89.7%)	0.049
Mechanical Circulatory support	19/102 (18.6%)	20/100 (20.0%)	54/196 (27.6%)	68/189 (36.0%)	161/587 (27.4%)	0.003
Mild hypothermia	36/101 (35.6%)	33/100 (33.0%)	71/195 (36.4%)	61/189 (32.3%)	201/585 (34.4%)	0.829
Mechanical ventilation	77/102 (75.5%)	78/99 (78.8%)	160/196 (81.6%)	160/188 (85.1%)	475/585 (81.2%)	0.216

Antithrombotics in cath lab						
Aspirin	72/101 (71.3%)	78/100 (78.0%)	144/196 (73.5%)	142/189 (75.1%)	436/586 (74.4%)	0.720
Clopidogrel	17/101 (16.8%)	21/100 (21.0%)	42/196 (21.4%)	28/189 (14.8%)	108/586 (18.4%)	0.330
Prasugrel	19/101 (18.8%)	19/100 (19.0%)	21/196 (10.7%)	25/189 (13.2%)	84/586 (14.3%)	0.127
Ticagrelor	28/101 (27.7%)	19/100 (19.0%)	47/196 (24.0%)	46/189 (24.3%)	140/586 (23.9%)	0.541
GP IIb/IIIa inhibitors	21/101 (20.8%)	25/100 (25.0%)	41/196 (20.9%)	46/189 (24.3%)	133/586 (22.7%)	0.764
Cangrelor	4/101 (4.0%)	1/100 (1.0%)	8/196 (4.1%)	2/189 (1.1%)	15/586 (2.6%)	0.150
UFH	81/101 (80.2%)	87/100 (87.0%)	160/196 (81.6%)	149/189 (78.8%)	477/586 (81.4%)	0.392
LMWH	16/101 (15.8%)	9/100 (9.0%)	24/196 (12.2%)	33/189 (17.5%)	82/586 (14.0%)	0.192
Bivalirudin	10/101 (9.9%)	6/100 (6.0%)	9/196 (4.6%)	12/189 (6.3%)	37/586 (6.3%)	0.362

Values are median (Q1-Q3) or n (%). CTO, chronic total occlusion; DES, drug-eluting stent; GP, glycoprotein; LAD, left anterior descending; LCx, left circumflex; LM, left main; LMWH, low molecular weight heparin; MV-PCI, multivessel-PCI; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; RCA, right coronary artery; rSS, residual SYNTAX score; TIMI, Thrombolysis in myocardial infarction; UFH, unfractionated heparin; VD, vessel disease.

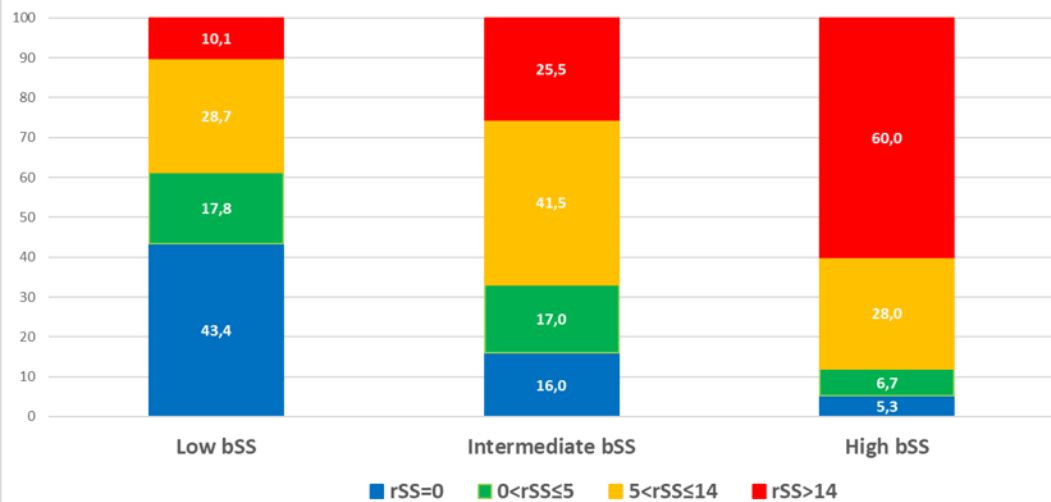
* Adjudicated by ACTION Core Laboratory

Table 3: Clinical outcomes at 30-days and 1-year according to residual SYNTAX score

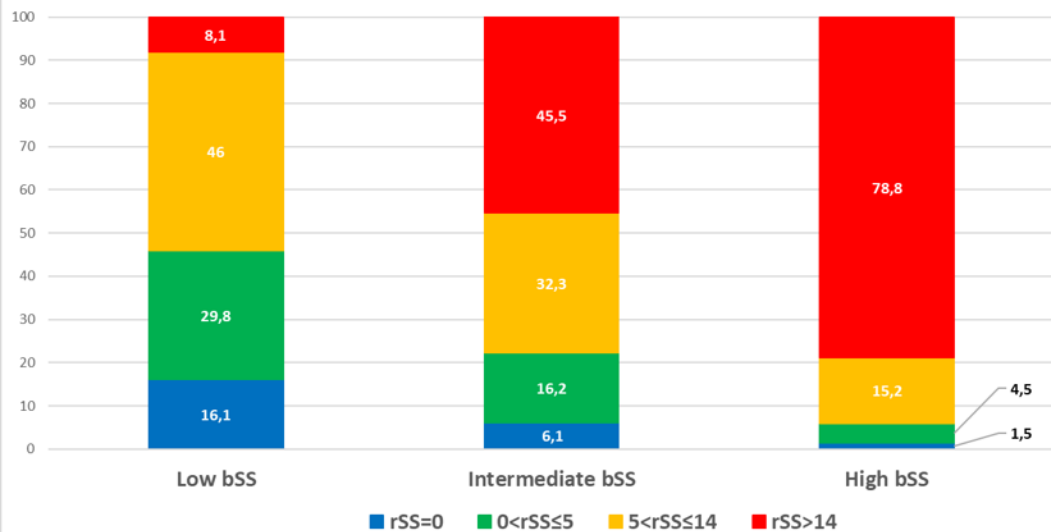
	rSS = 0 (N=102)	0 < rSS ≤ 5 (N=100)	5 < rSS ≤ 14 (N=196)	rSS > 14 (N=189)	P-value
30-days					
Death or Renal Replacement Therapy	37 (36.3%)	39 (39.0%)	102 (52.0%)	116 (61.4%)	< 0.001
Death	32 (31.4%)	35 (35.0%)	94 (48.0%)	113 (59.8%)	< 0.001
Renal Replacement Therapy	16 (15.7%)	14 (14.0%)	27 (13.8%)	26 (13.8%)	0.970
Recurrent Myocardial Infarction	3 (2.9%)	2 (2.0%)	2 (1.0%)	1 (0.5%)	0.252
Rehospitalization for congestive heart failure	0 (0.0%)	1 (1.0%)	1 (0.5%)	0 (0.0%)	0.668
Death, recurrent MI or rehospitalization for congestive HF	34 (33.3%)	38 (38.0%)	97 (49.5%)	113 (59.8%)	< 0.001
Staged or urgent repeat revascularization	13 (12.7%)	12 (12.0%)	24 (12.2%)	18 (9.5%)	0.798
Stroke	1 (1.0%)	4 (4.0%)	7 (3.6%)	5 (2.6%)	0.554
BARC type 2-3-5 bleeding	18 (17.6%)	18 (18.0%)	40 (20.4%)	40 (21.2%)	0.857
1-year					
Death	35 (34.3%)	42 (42.0%)	105 (53.6%)	121 (64.0%)	< 0.001

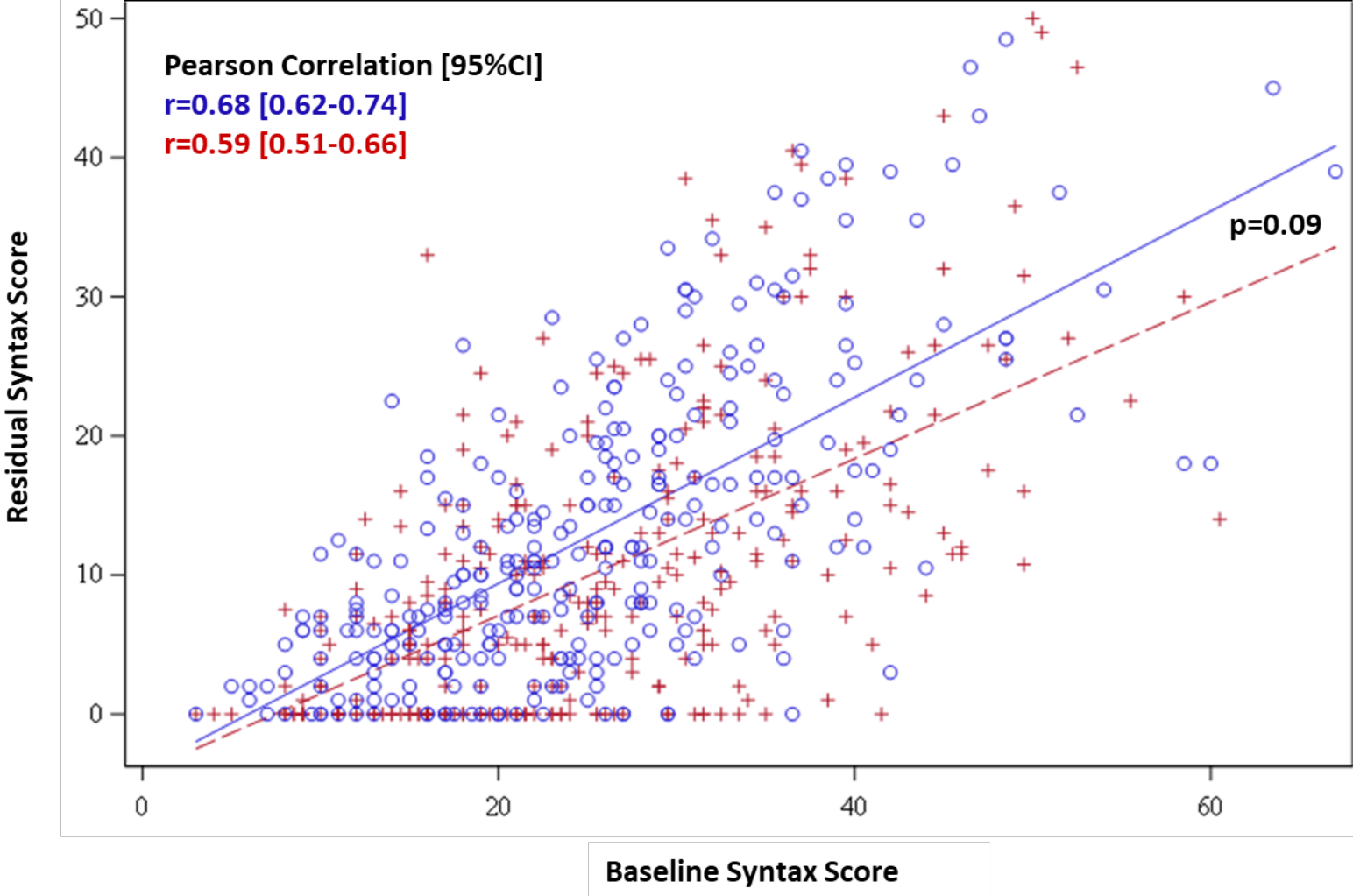
BARC: bleeding academic research consortium

Multivessel PCI

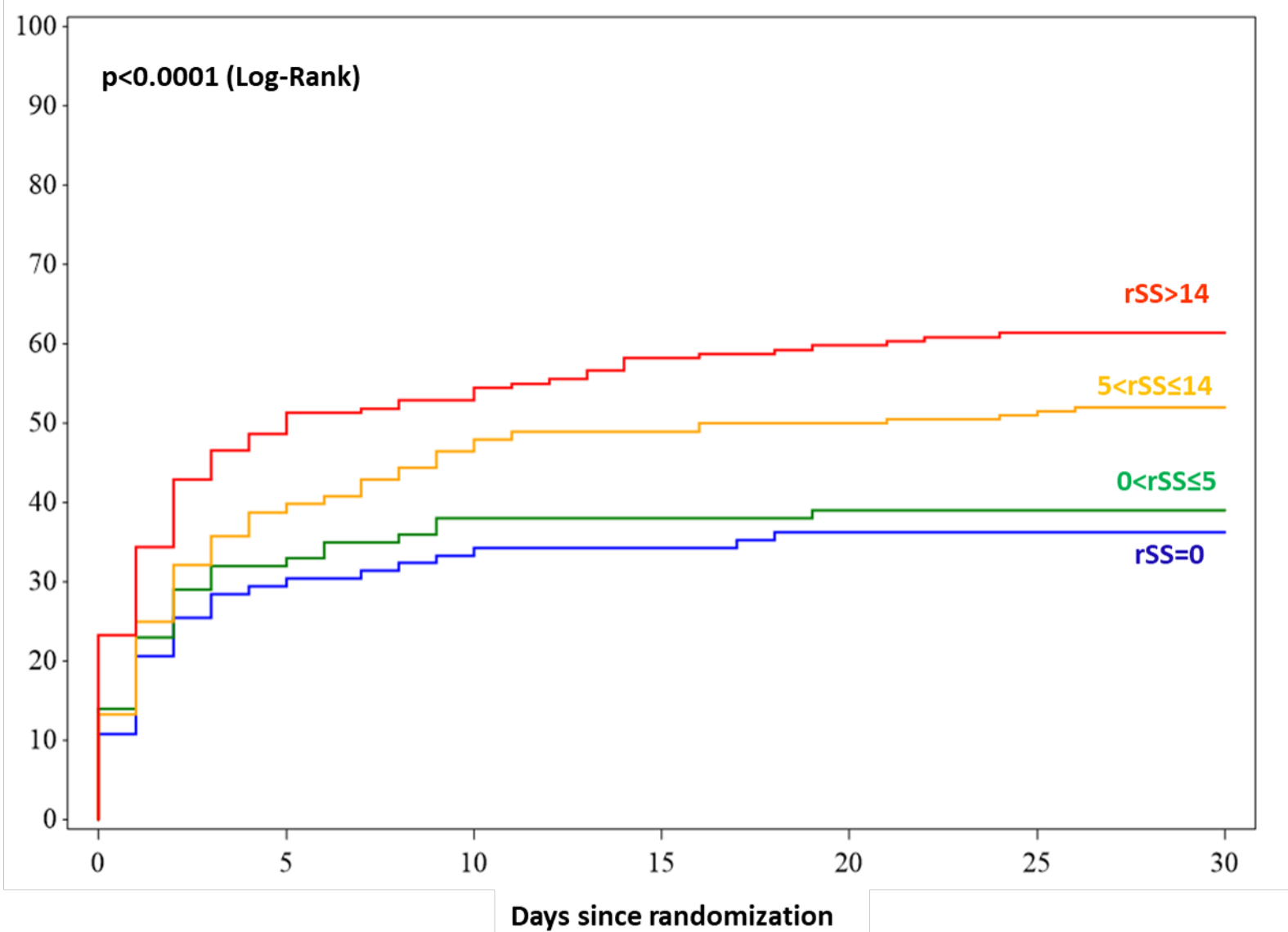


Culprit Only PCI



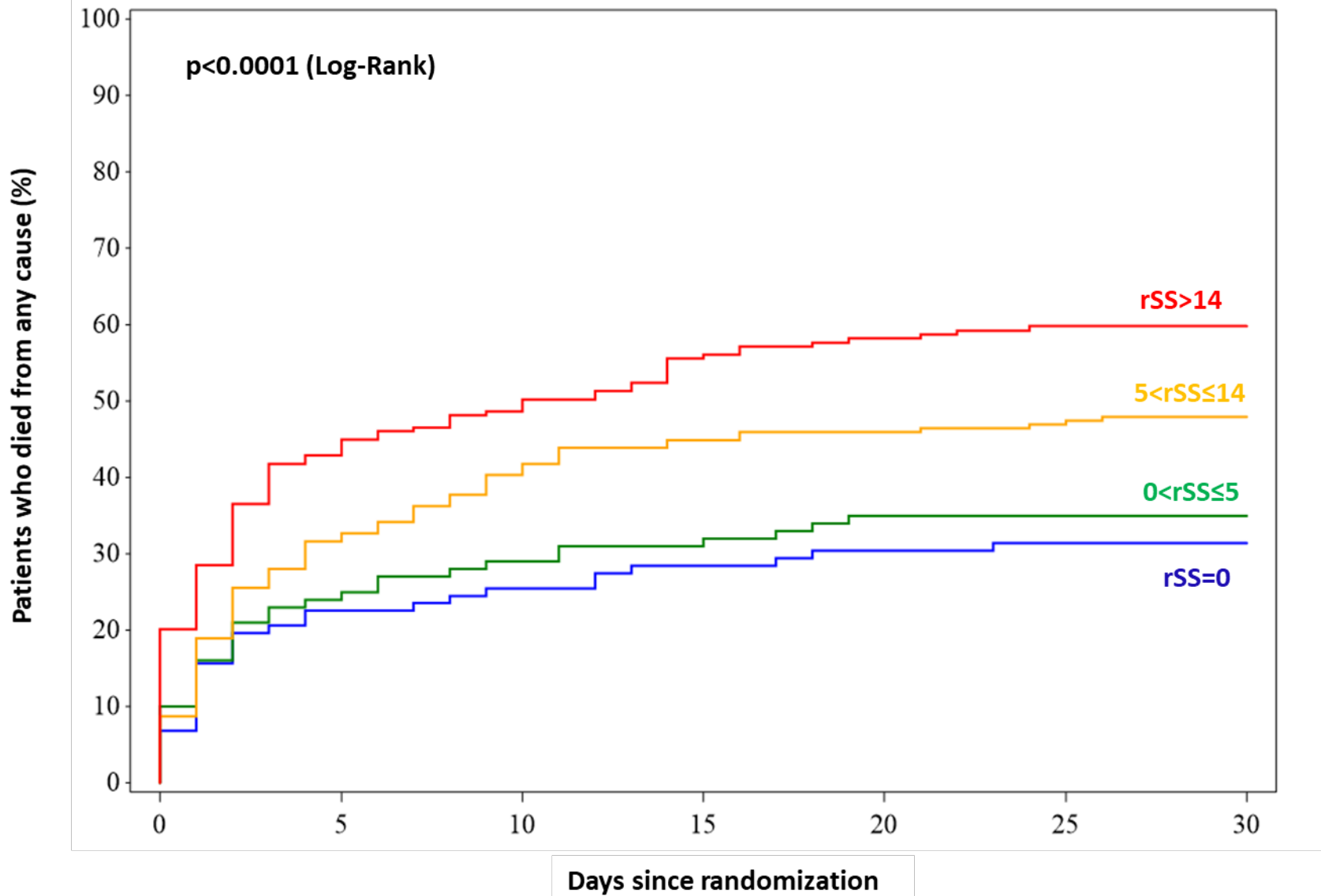


Patients underwent Renal-Replacement therapy or who died from any cause (%)

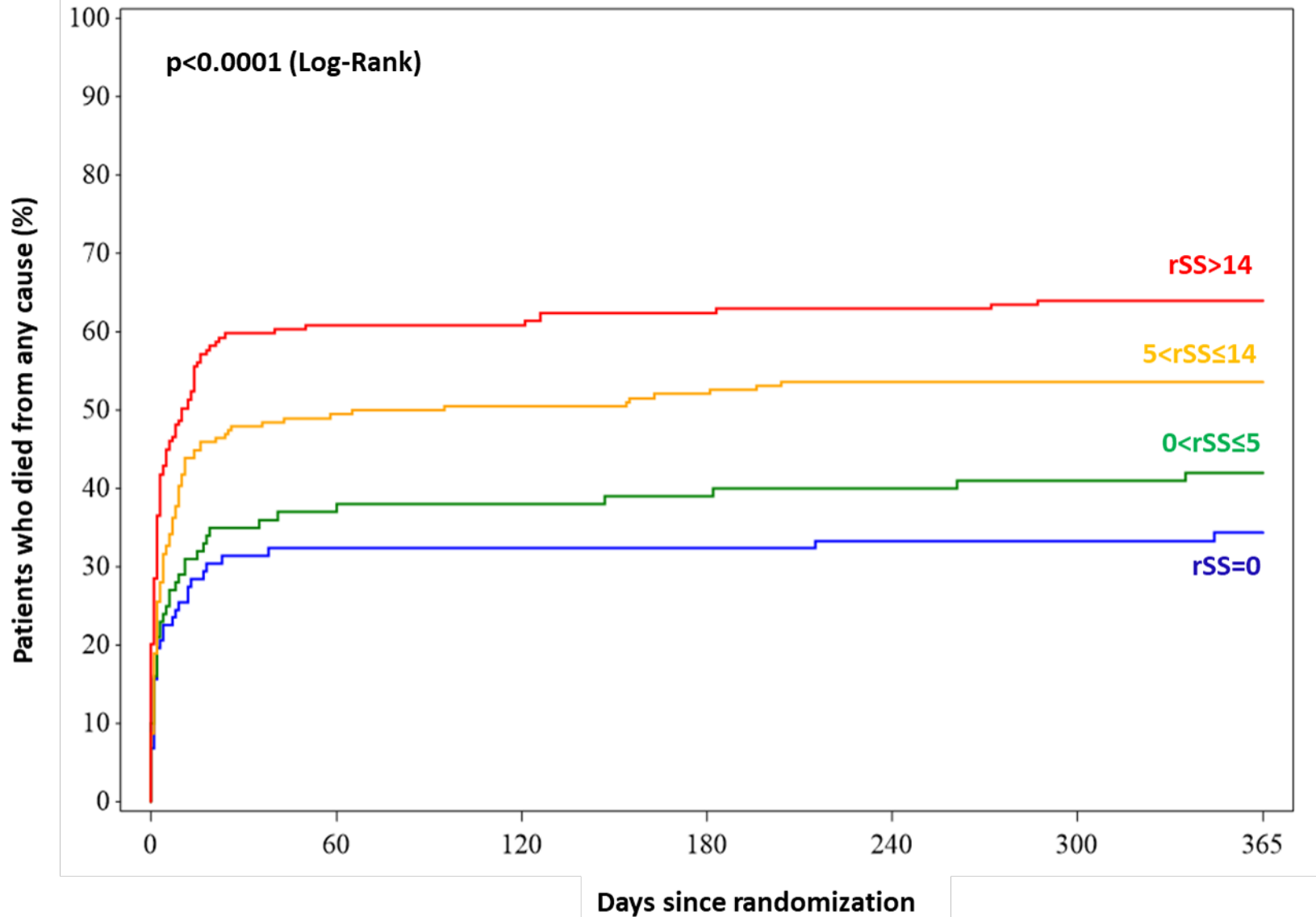


No. at risk

rSS=0	102	72	68	67	65	65	65
0<rSS≤5	100	68	62	62	61	61	61
5<rSS≤14	196	120	105	100	98	96	94
rSS>14	189	97	89	79	76	73	73



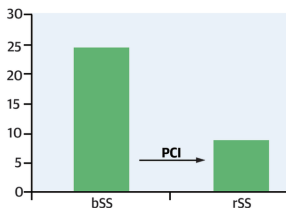
No. at risk							
rSS=0	102	79	76	73	71	70	70
0 < rSS ≤ 5	100	76	71	69	65	65	65
5 < rSS ≤ 14	196	134	117	108	106	104	102
rSS > 14	189	108	97	84	79	76	76



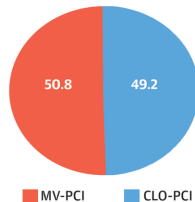
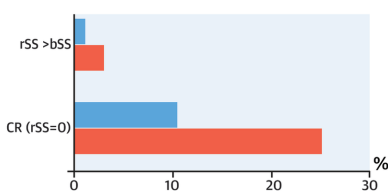
No. at risk

rSS=0	102	69	69	69	68	68	59
0<rSS≤5	100	63	62	61	60	59	51
5<rSS≤14	196	98	96	93	90	90	74
rSS>14	189	74	74	71	70	68	63

Baseline and Residual SYNTAX Score



bSS/rSS Correlation and Rates of Complete Revascularization

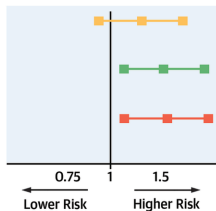


Association of rSS with CV Outcomes

30-Day Death or RRT

30-Day Death

1-Year Death



aOR 95% CI p-value

1.25 0.93-1.69 0.140

1.49 1.11-2.01 0.008

1.52 1.11-2.07 0.008