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Prognostic Value of SYNTAX Score in Patients with Infarct-related Cardiogenic Shock: Insights from the CULPRIT-SHOCK Trial

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ABSTRACT

Objective: To evaluate the prognostic value of the SYNTAX scores (SS) in patients undergoing percutaneous coronary intervention (PCI) for multivessel coronary disease with infarct-related cardiogenic shock (CS).

Background: The prognostic value of the SYNTAX scores (SS) in this high-risk setting remains unclear.

Methods: The CULPRIT-SHOCK trial was an international, open-label trial, where patients presenting with infarct-related CS and multivessel disease were randomized to a culprit-lesion-only or an immediate multivessel PCI strategy. Baseline SS was assessed by a central core laboratory and categorized as low SS ($SS \leq 22$), intermediate SS ($22 < SS \leq 32$) and high SS ($SS > 32$). Adjudicated endpoints of interest were the 30-day risk of death or renal replacement therapy (RRT) and 1-year death. Associations between baseline SS and outcomes were assessed using multivariate logistic regression.

Results: Pre-PCI SS was available in 624 patients, of whom 263 (42.1%), 207 (33.2%) and 154 (24.7%) presented with low, intermediate and high SS, respectively. A stepwise increase in the incidence of adverse events was observed from low to intermediate and high SS for the 30-day risk of death or RRT and the 1-year risk of death ($p < 0.001$, for all). After multiple adjustments, intermediate and high SS remained strongly associated with 30-day risk of death or renal replacement therapy and 1-year risk of all-cause death. There was no significant interaction between SYNTAX score and the coronary revascularization strategy for any outcomes.

Conclusion: In patients presenting with multivessel disease and infarct-related CS, the SYNTAX score was strongly associated with 30-day death or RRT and 1-year mortality.

KEY WORDS: cardiogenic shock; percutaneous coronary intervention; SYNTAX score

CONDENSED ABSTRACT

We evaluated the prognosis value of angiographic core laboratory calculated baseline SYNTAX score (SS) in patients undergoing percutaneous coronary intervention (PCI) for multivessel coronary disease with infarct-related cardiogenic shock (CS) in the CULPRIT SHOCK trial. Of the 624 included patients, a low, intermediate and high SS was present in 263 (42.1%), 207 (33.2%) and 154 (24.7%) patients, respectively. After multiple adjustments, intermediate and high SS remained strongly associated with 30-day risk of death or renal replacement therapy and 1-year risk of all-cause death. There was no significant interaction between SS and the coronary revascularization strategy for any outcomes.

ABBREVIATIONS AND ACRONYMS

CI: Confidence interval

CS: Cardiogenic shock

CULPRIT-SHOCK: Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock

MI: Myocardial infarction

OR: Odds Ratio

PCI: Percutaneous coronary intervention

SS: SYnergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) score

INTRODUCTION

The SYnergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) score was created, more than a decade ago, to provide an angiographic tool grading the complexity of coronary artery disease in patient with left main (LM) or multivessel disease (1). In such patients, the value of SYNTAX score has become an essential element for the decision between revascularization options by the heart team (2). Moreover, in patients undergoing percutaneous coronary intervention (PCI), the SYNTAX score has been found to be an independent predictor of long-term major adverse cardiac and cerebrovascular events and death, in all-comers as in higher-risk patients presenting with acute coronary syndrome (3–9). Cardiogenic shock (CS) is a dreaded complication of acute myocardial infarction (MI) burdened with a high morbidity and mortality (10–12). The vast majority of patients presenting with infarct-related CS have multivessel coronary artery disease (13). There is, however, limited evidence on the prognostic impact of the SYNTAX score in this setting (14). Therefore, the purpose of this prespecified analysis was to investigate the association between baseline SYNTAX score and outcomes in patients randomized in the Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial.

METHODS

Study design and study population. The design of the CULPRIT-SHOCK trial has been previously described (15–17). Briefly, the CULPRIT-SHOCK trial was an investigator-initiated, international, multicenter, open-label trial where patients presenting with acute infarct-related CS and multivessel coronary artery disease were randomized, in a 1:1 ratio, to a strategy of culprit-lesion-only PCI (with optional staged revascularization) or immediate multivessel PCI. In all patients, the culprit lesion was treated first with the use of standard PCI techniques and with recommended use of drug-eluting stents. In the culprit-lesion-only group, staged revascularization was performed according to the patient clinical status and the presence of residual ischemia. In the multivessel PCI group, any >70% stenosis of major coronary arteries (i.e. ≥ 2 mm diameter), including chronic total occlusion, were recommended to be treated with immediate PCI following the treatment of the culprit lesion with a recommended maximum dose of contrast material of 300 mL. For the purpose of the prespecified analysis, all angiographic analyses were performed by a central angiographic core laboratory (ACTION-Coeur, Pitié-Salpêtrière Hospital, Paris, France) (13). Baseline SYNTAX score was calculated by consensus of two trained readers and categorized as previously described as low (≤ 22), intermediate ($22 < \text{SYNTAX score} < 32$) or high (≥ 33) (2, 13). In case of disagreement, the opinion of a third reviewer, and if necessary, a fourth reviewer was obtained and the final decision was achieved by consensus. The investigation was approved by the ethic committee or institutional review board of each participating center and written informed consent was obtained with the use of a prespecified process that varied slightly according to the country (15).

Study endpoints. The endpoints of interest were the composite of all-cause death or severe renal failure leading to renal-replacement therapy within 30 days after randomization, all-cause mortality and the composite of all-cause mortality, MI or stroke within 30 days and

1 year after randomization. Events were defined as previously reported and adjudicated by an independent clinical event committee (13, 15, 16). Specific follow-up was performed at 30 days, 6 months and 1 year by means of structured telephone interview, with any potential endpoint events verified by review of original records. Death registries were searched to identify or confirm all deaths.

Statistical analysis

Categorical variables were described as proportion and compared with Chi-square test or Fisher's exact test. Continuous variables were described as median (Q1-Q3) and compared using the Kruskal-Wallis test. As previously published, event rates were compared using Chi-square testing (15, 16). Kaplan-Meier curves were also used to show event rates over time with classification according to the baseline SYNTAX score and compared using long-rank test. Patients without event were censored at 30 days or 1 year according to the endpoint. Multivariate logistic regression models were used to evaluate the independent association between SYNTAX score (low SYNTAX score was used as the reference group) and outcomes. In each model, SYNTAX score was adjusted on baseline clinical and procedural characteristics possibly associated with outcomes in univariate analysis ($p < 0.2$) and are detailed in **Online Table 1** and **2**. Sensitivity analyses were performed for each outcome, adjusting baseline SYNTAX score on consistent covariates as well as the effective revascularization strategy undergone by the patients to account for crossover among the groups of randomization. Results are interpreted in term of adjusted Odd Ratio (aOR) with their 95% confidence interval (95%CI). Interaction between baseline SYNTAX score, and revascularization strategy (randomization group) was evaluated for each outcome using logistic regression. 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

Baseline and procedural characteristics. A central core-laboratory evaluation of the baseline SYNTAX score was available in 624 (91.0%) of the 686 randomized patients with available informed consent. Baseline and procedural characteristics of patients with and without available SYNTAX score are detailed in **Online Table 3 and 4**. A low, intermediate and high SYNTAX score was present in 263 (42.1%; 95% CI [38.3-46.1]), 207 (33.2%; 95% CI [29.6-37.0]) and 154 (24.7%; 95% CI [21.5-28.2]) patients respectively. Baseline and procedural characteristics are detailed in **Table 1 and 2**. Patients with higher SYNTAX score were older, with more frequent peripheral artery disease and higher use of catecholamine or need for mechanical support. There were no differences between the groups in regard to discharge medication.

Associations of baseline SYNTAX score with outcomes. Median duration of follow-up for outcomes was 136.5 [2.0-365.0] days and one patient was lost to follow-up at one year. The 30-day and 1-year outcomes according to the baseline SYNTAX score are detailed in **Table 3 and Figure 1 and 2**. In univariate analysis, a stepwise increase in the incidence of adverse events transitioning from low to intermediate and high SYNTAX score was observed with the 30-day rates of death, death or renal replacement therapy and death, MI or stroke. A consistent stepwise increase with higher baseline SYNTAX score was observed with 1-year rates of death and death, MI or stroke. After adjustment, results remained consistent with a stepwise increase of the risk of death, death or renal replacement therapy and the composite of death, MI or stroke at 30 days, as well as the 1-year risk of death and 1-year risk of death or MI or stroke with increasing SYNTAX score categories (**Figure 3**).

Sensitivity analysis and interaction test. Results remained consistent when adjusted for the effective revascularization strategy (**Online Figure 1**). No significant interaction were

observed between the baseline SYNTAX score value and the coronary revascularization strategy for all-cause death or renal replacement therapy at 30 days ($p=0.61$), renal replacement therapy at 30 days ($p=0.47$), all-cause death at 30 days and 1 year ($p=0.72$ and $p=0.34$, respectively), and the composite of all-cause death, MI or stroke at 30 days and 1-year ($p=0.76$ and $p=0.39$, respectively), as detailed in the Online Figure 2.

DISCUSSION

The main results of the present study are as follows: in patients with infarct-related MI and multivessel disease undergoing PCI, baseline SYNTAX score is strongly associated with 30-day and 1-year all-cause death, all-cause death or renal replacement therapy and all-cause death, MI or stroke. There was no significant interaction between the baseline SYNTAX score and the coronary revascularization strategy for any of these outcomes.

Initially designed prospectively as an angiographic scoring system to evaluate the complexity of coronary artery disease, the SYNTAX score has also been validated as a prognosis tool for the risk of ischemic outcomes following PCI. In fact, the baseline SYNTAX score has been found to predict mortality in patient undergoing PCI in the setting of both chronic and acute coronary syndromes (5, 8, 18). The present study extends this finding to CS patients as the baseline SYNTAX score is strongly associated with all ischemic outcomes at both 30 days and 1 year (19, 20). There is only limited available data regarding the evaluation of the SYNTAX score in patients undergoing PCI in the setting of acute MI-related CS. Previous to our study, a prospective European observational study also reported baseline SYNTAX score to be independently associated with 90-day mortality (14). However, the study was limited by a small sample size and the relatively short duration of follow-up of 90 days.

Another interesting finding of our study is the strong association between the baseline SYNTAX score and renal replacement therapy. In a post-hoc analysis of the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial, baseline SYNTAX score was reported to be independently associated with the risk of acute kidney injury following PCI (21). Higher baseline SYNTAX score is equivalent to more complex coronary artery disease, which may require longer procedure time, resulting in higher dose of contrast media or increased risk of periprocedural complications, thus potentially increasing the risk of acute kidney injury with or without the need for renal replacement therapy (22). In the present analysis, the duration of fluoroscopy and the total dose of contrast media were, in fact, increased in patients with the highest SYNTAX scores. However, we did not find an incremental risk of renal replacement therapy associated with increased SYNTAX score, conversely to other ischemic endpoints, suggesting that the dose of contrast media may only be one of several factors involved in this association. There is an association between the complexity of coronary artery disease, as estimated by the SYNTAX score, and the extent of atherosclerosis of other arterial beds (22–25). Thus, it is plausible that patients presenting with higher baseline SYNTAX scores may also present with more severe atherosclerosis of the aorta or renal arteries, resulting in higher rates of acute kidney injury, particularly in the setting of CS (26, 27).

The CULPRIT-SHOCK trial reported that a strategy of culprit-lesion-only PCI, compared to a multivessel PCI strategy, was associated with a reduction of the composite of death or renal replacement therapy at 30 days. In the present analysis, no significant interaction was present between baseline SYNTAX score and the revascularization strategy for any adverse outcomes. These results suggest that the choice of coronary revascularization strategy in patients with multivessel disease and infarct-related CS undergoing PCI should not

depend on the complexity of coronary artery disease, as evaluated by the SYNTAX score and that a culprit-lesion-only PCI should remain the preferred strategy.

We acknowledge several limitations to our study. First, baseline SYNTAX score was not available for all the patients randomized in the CULPRIT-SHOCK trial. Second, the present substudy was limited to the prognostic value of baseline SYNTAX score and did not include more updated and complete version of the score such as the logistic clinical SYNTAX score or SYNTAX score II, nor did it evaluate the prognosis value of the residual SYNTAX score, which would warrant further studies on these associated scores (28–31).

CONCLUSION

In patients with multivessel coronary artery disease and infarct-related CS undergoing PCI, baseline SYNTAX score is strongly associated with early and late adverse outcomes. The coronary revascularization strategy in this setting should not depend on the complexity or extent of the baseline coronary artery disease.

PERSPECTIVES

WHAT IS KNOWN?

SYNTAX score has been found to be an independent predictor of long-term major adverse cardiac and cerebrovascular events and death in patients undergoing percutaneous coronary intervention (PCI).

WHAT IS NEW?

In this prespecified subanalysis of the CULPRIT SHOCK trial, higher baseline SYNTAX score was strongly associated with early and late adverse outcomes in patients undergoing PCI for infarct-related cardiogenic shock with multivessel disease. The absence of significant interaction between baseline SYNTAX score, the revascularization strategy and any adverse outcomes suggests that a culprit lesion PCI only should remained the preferred strategy in this setting.

WHAT IS NEXT?

Future study evaluating the prognosis impact of more complete version of the score such as logistic clinical SYNTAX score or SYNTAX score II are warranted.

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FIGURE LEGENDS

Figure 1. Kaplan-Meier curves of survival without adverse events within 30-days of randomization according to baseline SYNTAX score category: all-cause death or renal replacement therapy (A), all-cause death, myocardial infarction or stroke (B) and all-cause death (C).

No: number

Figure 2. Kaplan-Meier curves of survival without adverse event within 1-year of randomization according to the baseline SYNTAX score: all-cause death, myocardial infarction or stroke (A), all-cause death (B).

No: Number

Central Illustration. Association of SYNTAX score with 30-day and one-year outcomes after multivariable adjustment

RRT: renal replacement therapy; MI: myocardial infarction; aOR: Adjusted odd ratio; CI: confidence interval;. Covariables of adjustment for each outcome are detailed in Online Table 1 and 2

Table 1. Baseline characteristics

	Total (n=624)	Low SS (n=263)	Intermediate SS (n=207)	High SS (n=154)	p-value
Age, years	69.0 (60.0-78.0)	67.0 (58.0-76.0)	69.0 (60.0-78.0)	71.0 (63.0-79.0)	0.01
Male sex	475/624 (76.1%)	195/263 (74.1%)	158/207 (76.3%)	122/154 (79.2%)	0.50
Body mass index	26.6 (24.5-29.4)	26.3 (24.5-29.4)	27.1 (24.5-29.4)	26.8 (24.6-29.4)	0.83
<i>Cardiovascular risk factors</i>					
Current smoking	163/600 (27.2%)	80/256 (31.3%)	54/196 (27.6%)	29/148 (19.6%)	0.04
Hypertension	363/613 (59.2%)	144/260 (55.4%)	128/203 (63.1%)	91/150 (60.7%)	0.23
Hypercholesterolemia	197/610 (32.3%)	76/260 (29.2%)	71/200 (35.5%)	50/150 (33.3%)	0.35
Diabetes mellitus	189/611 (30.9%)	71/260 (27.3%)	63/200 (31.5%)	55/151 (36.4%)	0.15
Previous myocardial infarction	93/614 (15.1%)	33/259 (12.7%)	28/204 (13.7%)	32/151 (21.2%)	0.06
Previous stroke	40/615 (6.5%)	13/261 (5.0%)	11/203 (5.4%)	16/151 (10.6%)	0.06
Known peripheral artery disease	70/616 (11.4%)	23/261 (8.8%)	22/204 (10.8%)	25/151 (16.6%)	0.06
Known renal insufficiency	40/615 (6.5%)	19/261 (7.3%)	11/204 (5.4%)	10/150 (6.7%)	0.71
Previous percutaneous coronary intervention	101/614 (16.4%)	39/259 (15.1%)	35/204 (17.2%)	27/151 (17.9%)	0.72
Resuscitation before randomization	330/623 (53.0%)	152/263 (57.8%)	105/207 (50.7%)	73/153 (47.7%)	0.10
Fibrinolysis before randomization	32/622 (5.1%)	15/262 (5.7%)	10/207 (4.8%)	7/153 (4.6%)	0.85
Arterial lactate > 2 mmol/L	400/607 (65.9%)	162/259 (62.5%)	134/198 (67.7%)	104/150 (69.3%)	0.31
Anterior ST-segment elevation myocardial infarction	207/601 (34.4%)	70/253 (27.7%)	81/200 (40.5%)	56/148 (37.8%)	0.01
Systolic blood pressure, mmHg	100.0 (85.0-125.0)	100.5 (86.0-125.5)	100.0 (85.0-126.0)	100.0 (80.0-120.0)	0.70
Diastolic blood pressure, mmHg	60.0 (50.0-80.0)	60.0 (50.0-80.0)	60.0 (50.5-80.0)	62.0 (50.0-80.0)	0.73
Mean blood pressure, mmHg	76.0 (63.3-93.3)	76.7 (63.3-92.3)	73.8 (63.3-95.0)	76.2 (62.3-93.3)	0.69
Use of catecholamine	558/621 (89.9%)	230/262 (87.8%)	183/206 (88.8%)	145/153 (94.8%)	0.06
Duration of catecholamine, days	2.0 (1.0-5.0)	2.0 (1.0-4.5)	2.0 (1.0-6.0)	2.0 (1.0-5.0)	0.36
Number of affected vessels					<0.001
1	5/624 (0.8%)	4/263 (1.5%)	1/207 (0.5%)	0	
2	231/624 (37.0%)	141/263 (53.6%)	69/207 (33.3%)	21/154 (13.6%)	
3	388/624 (62.2%)	118/263 (44.9%)	137/207 (66.2%)	133/154 (86.4%)	
Vessel related to the infarction*					<0.001

Left anterior descending artery	270/624 (43.3%)	92/263 (35.0%)	109/207 (52.7%)	69/154 (44.8%)	
Left circumflex artery	129/624 (20.7%)	58/263 (22.1%)	42/207 (20.3%)	29/154 (18.8%)	
Right coronary artery	173/624 (27.7%)	104/263 (39.5%)	40/207 (19.3%)	29/154 (18.8%)	
Left main artery	52/624 (8.3%)	9/263 (3.4%)	16/207 (7.7%)	27/154 (17.5%)	
≥1 Chronic total occlusion*	134/624 (21.5%)	21/263 (8.0%)	39/207 (18.8%)	74/154 (51.9%)	<0.001
SS*	25.0 (17.5-32.0)	16.0 (12.5-19.0)	26.5 (25.0-29.5)	38.8 (35.5-44.5)	<0.001
Left ventricular ejection fraction	n=236	n=96	n=77	n=63	
	32.5 (25.0-40.0)	38.0 (29.0-45.0)	30.0 (25.0-40.0)	30.0 (20.0-39.0)	<0.001

* Core Laboratory data; SS: SYNTAX score

Table 2. Procedural characteristics

	Total (n=624)	Low SS (n=263)	Intermediate SS (n=207)	High SS (n=154)	p-value
Arterial access					
Femoral	510/624 (81.7%)	216/263 (82.1%)	166/207 (80.2%)	128/154 (83.1%)	0.76
Radial	119/624 (19.1%)	49/263 (18.6%)	43/207 (20.8%)	27/154 (17.5%)	0.72
Brachial	3/624 (0.5%)	2/263 (0.8%)	1/207 (0.5%)	0	0.79
Stent in culprit lesion					
Any	596/624 (95.5%)	259/263 (98.5%)	196/207 (94.7%)	141/154 (91.6%)	0.003
Bare-metal stent	34/596 (5.7%)	16/259 (6.2%)	9/196 (4.6%)	9/141 (6.4%)	0.71
Drug-eluting stent	561/596 (94.1%)	241/259 (93.1%)	186/196 (94.9%)	134/141 (95.0%)	0.62
Bioresorbable scaffold in culprit lesion	5/596 (0.8%)	3/259 (1.2%)	1/196 (0.5%)	1/141 (0.7%)	0.85
Aspiration thrombectomy of culprit lesion	90/624 (14.4%)	32/263 (12.2%)	31/207 (15.0%)	27/154 (17.5%)	0.31
TIMI grade for blood flow					
Before PCI of culprit lesion*					<0.001
0	285/620 (46.0%)	83/261 (31.8%)	115/207 (55.6%)	87/152 (57.2%)	
I	57/620 (9.2%)	22/261 (8.4%)	25/207 (12.1%)	10/152 (6.6%)	
II	75/620 (12.1%)	40/261 (15.3%)	22/207 (10.6%)	13/152 (8.6%)	
III	203/620 (32.7%)	116/261 (44.4%)	45/207 (21.7%)	42/152 (27.6%)	
After PCI of culprit lesion					<0.001
0	43/600 (7.2%)	7/256 (2.7%)	18/202 (8.9%)	18/142 (12.7%)	
I	26/600 (4.3%)	5/256 (2.0%)	10/202 (5.0%)	11/142 (7.7%)	
II	60/600 (10.0%)	20/256 (7.8%)	32/202 (15.8%)	8/142 (5.6%)	
III	471/600 (78.5%)	224/256 (87.5%)	142/202 (70.3%)	105/142 (73.9%)	
Immediate PCI of non-culprit lesions	328/624 (52.6%)	142/263 (54.0%)	101/207 (48.8%)	85/154 (55.2%)	0.40
Total dose of contrast material, mL	220.0 (155.0-300.0)	200.0 (150.0-271.0)	202.5 (154.0-280.0)	260.0 (200.0-350.0)	<0.001
Total duration fluoroscopy, min	15.1 (9.2-24.0)	13.0 (8.0-19.3)	14.3 (9.2-23.0)	21.7 (14.6-32.0)	<0.001
Staged PCI of non-culprit lesions	60/624 (9.6%)	27/263 (10.3%)	23/207 (11.1%)	10/154 (6.5%)	0.30
Mechanical circulatory support	172/624 (27.6%)	44/263 (16.7%)	67/207 (32.4%)	61/154 (39.6%)	<0.001
Mild hypothermia	209/622 (33.6%)	102/262 (38.9%)	67/206 (32.5%)	40/154 (26.0%)	0.02
Mechanical ventilation	504/621 (81.2%)	205/262 (78.2%)	168/206 (81.6%)	131/153 (85.6%)	0.18

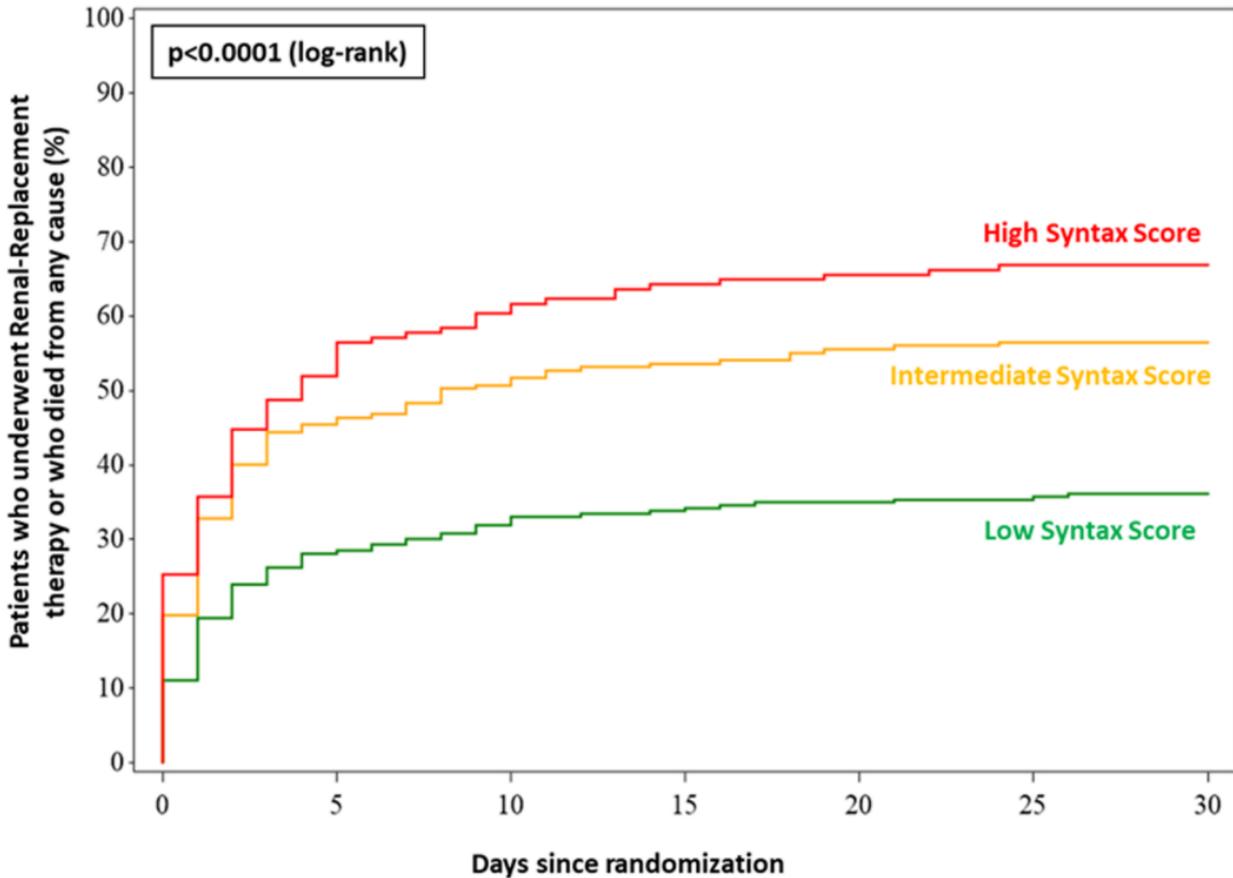
Duration of mechanical ventilation, days	3.0 (1.0-8.0)	3.0 (1.0-7.0)	3.0 (1.0-8.0)	2.5 (1.0-7.0)	0.62
Subsequent medications in patients who survived until hospital discharged					
Statin	307/330 (93.0%)	165/176 (93.8%)	88/97 (90.7%)	54/57 (94.7%)	0.64
Beta-blocker	301/330 (91.2%)	160/176 (90.9%)	89/97 (91.8%)	52/57 (91.2%)	0.97
ACE inhibitors or ARB	288/330 (87.3%)	148/176 (84.1%)	89/97 (91.8%)	51/57 (89.5%)	0.17
Aspirin	325/330 (98.5%)	173/176 (98.3%)	95/97 (97.9%)	57/57 (100%)	0.84
Clopidogrel	143/330 (43.3%)	74/176 (42.0%)	46/97 (47.4%)	23/57 (40.4%)	0.61
Prasugrel	117/330 (35.5%)	69/176 (39.2%)	27/97 (27.8%)	21/57 (36.8%)	0.17
Ticagrelor	132/330 (40.0%)	65/176 (36.9%)	43/97 (44.3%)	24/57 (42.1%)	0.46

* Core Laboratory data; SS: Syntax score; PCI: percutaneous coronary intervention; ACE: angiotensin converting enzyme ARB: Angiotensin II receptor blockers

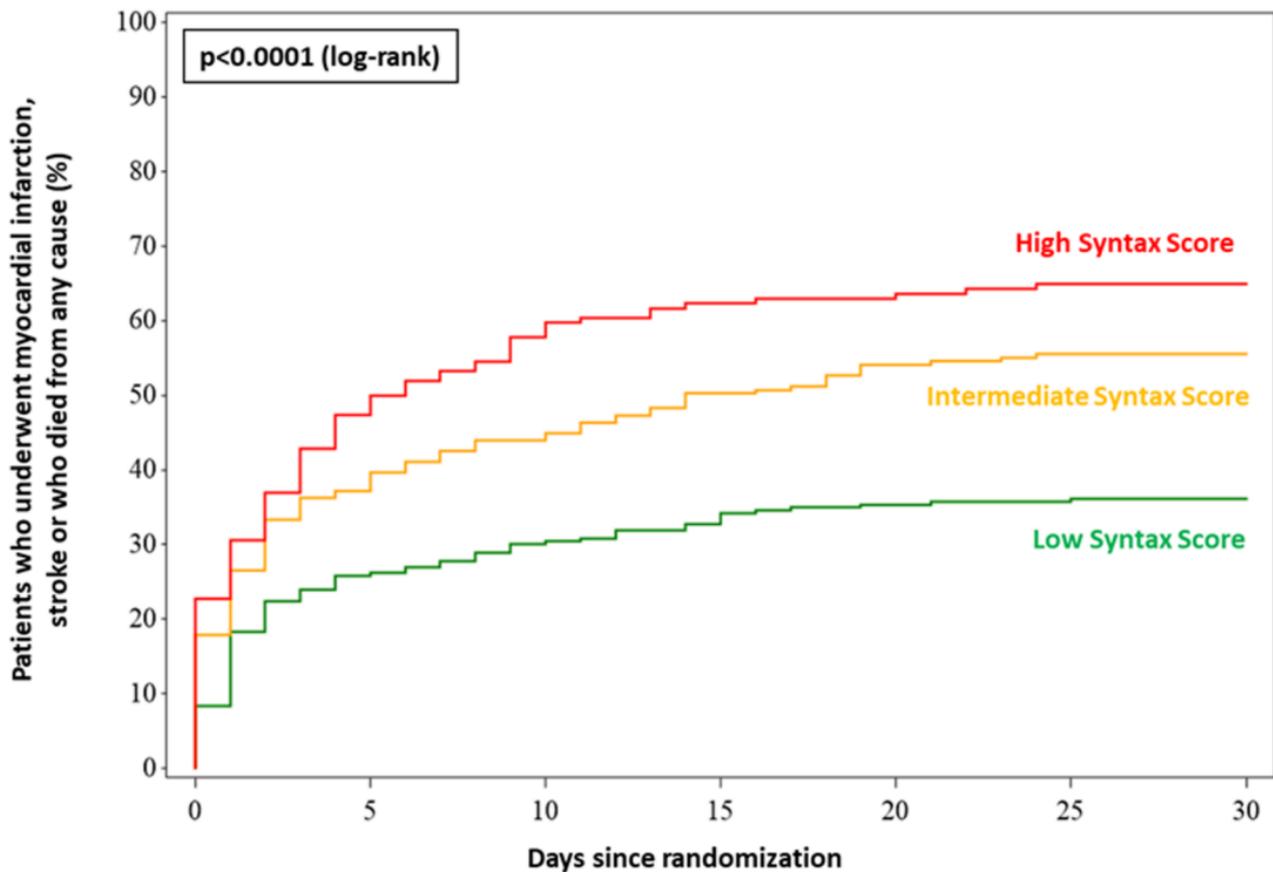
Table 3. Early and late outcomes according to the baseline syntax score

	Low SS (n=263)	Intermediate SS (n=207)	High SS (n=154)	p-value
30-day outcomes				
All-cause death or renal replacement therapy	36.1% (95)	56.5% (117)	66.9% (103)	<0.001
All-cause death	33.1% (87)	53.1% (110)	63.0% (97)	<0.001
Renal replacement therapy	9.1% (24)	17.4% (36)	16.9% (26)	0.016
All-cause death, myocardial infarction or stroke	36.1% (95)	55.6% (115)	64.9% (100)	<0.001
1-year outcomes				
All-cause death, myocardial infarction or stroke	41.8% (110)	60.9% (126)	72.7% (112)	<0.001
All-cause death	38.4% (101)	57.5% (119)	68.8% (106)	<0.001

Results are provided as number (observed incidence); SS: SYNTAX score

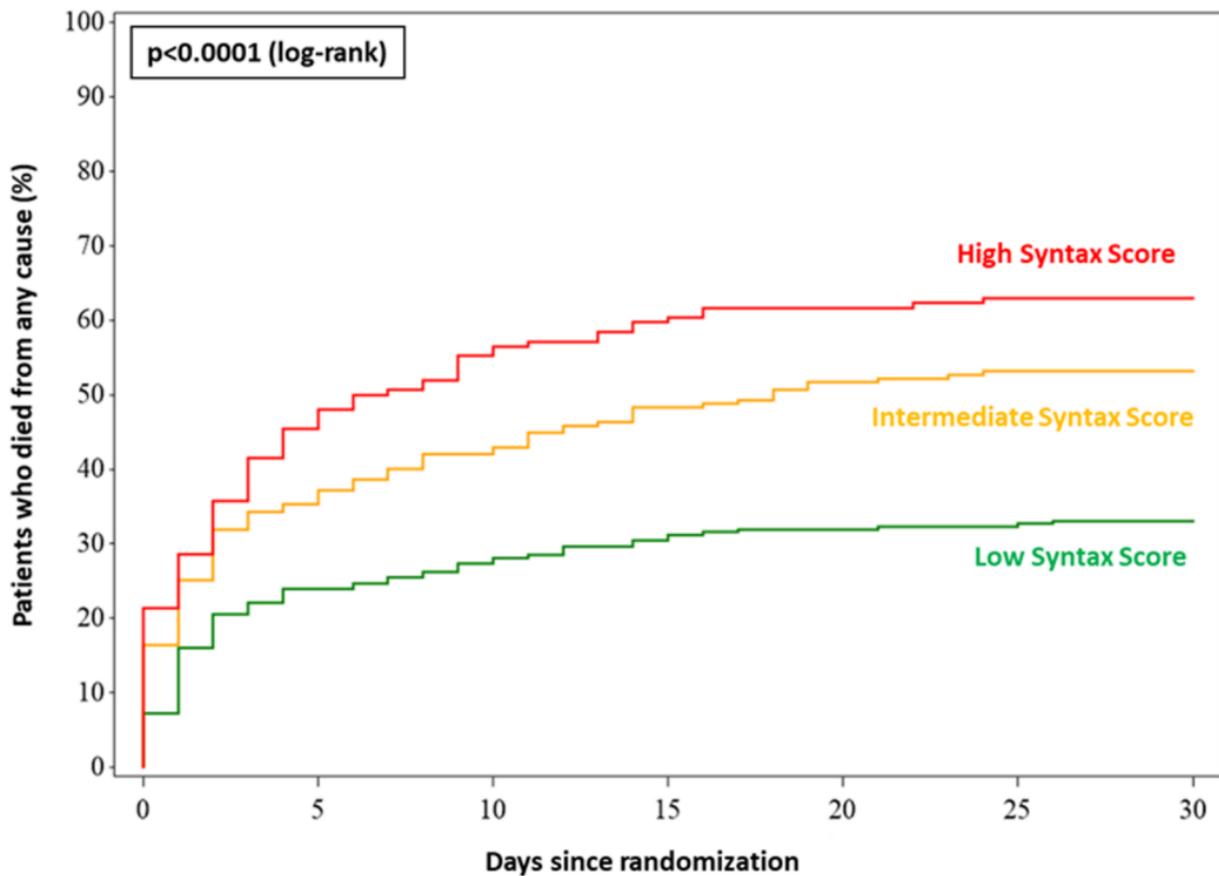


No. at risk							
High Syntax Score	154	74	61	55	53	51	51
Intermediate Syntax Score	207	113	102	96	92	90	90
Low Syntax Score	263	189	179	174	171	170	168

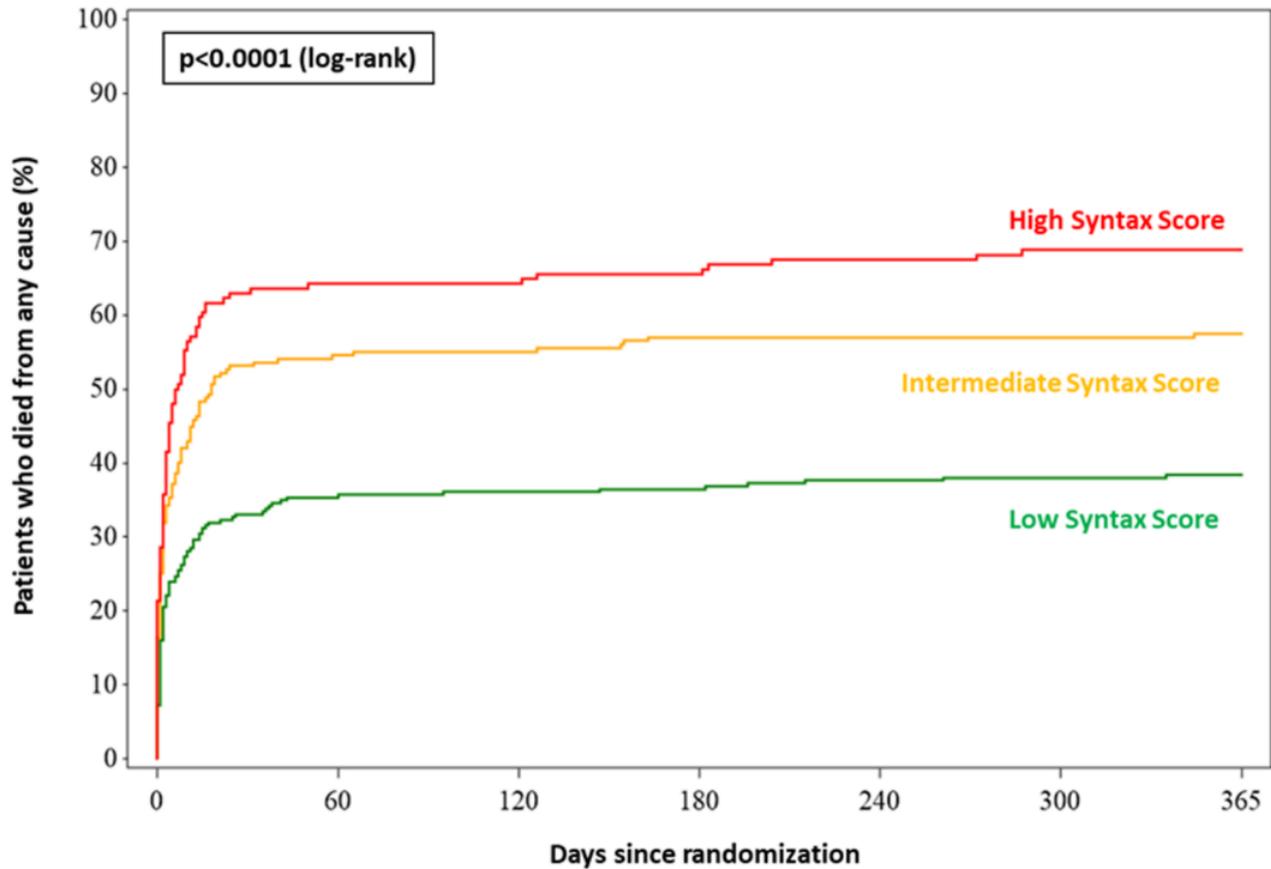


No. at risk

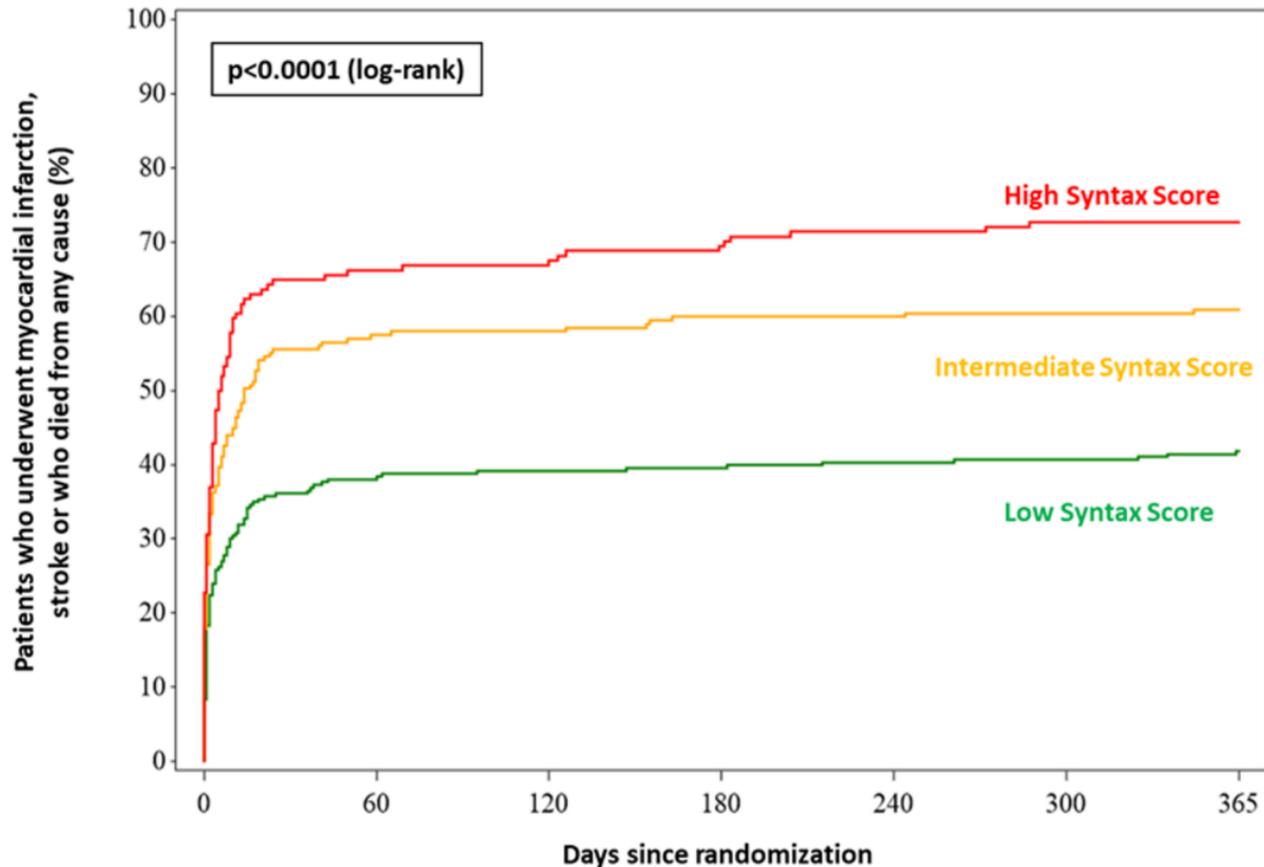
High Syntax Score	154	81	65	58	57	54	54
Intermediate Syntax Score	207	130	116	103	95	92	92
Low Syntax Score	263	195	184	177	170	169	168



No. at risk	0	5	10	15	20	25	30
High Syntax Score	154	84	69	62	59	57	57
Intermediate Syntax Score	207	134	120	107	100	97	97
Low Syntax Score	263	200	191	183	179	178	176



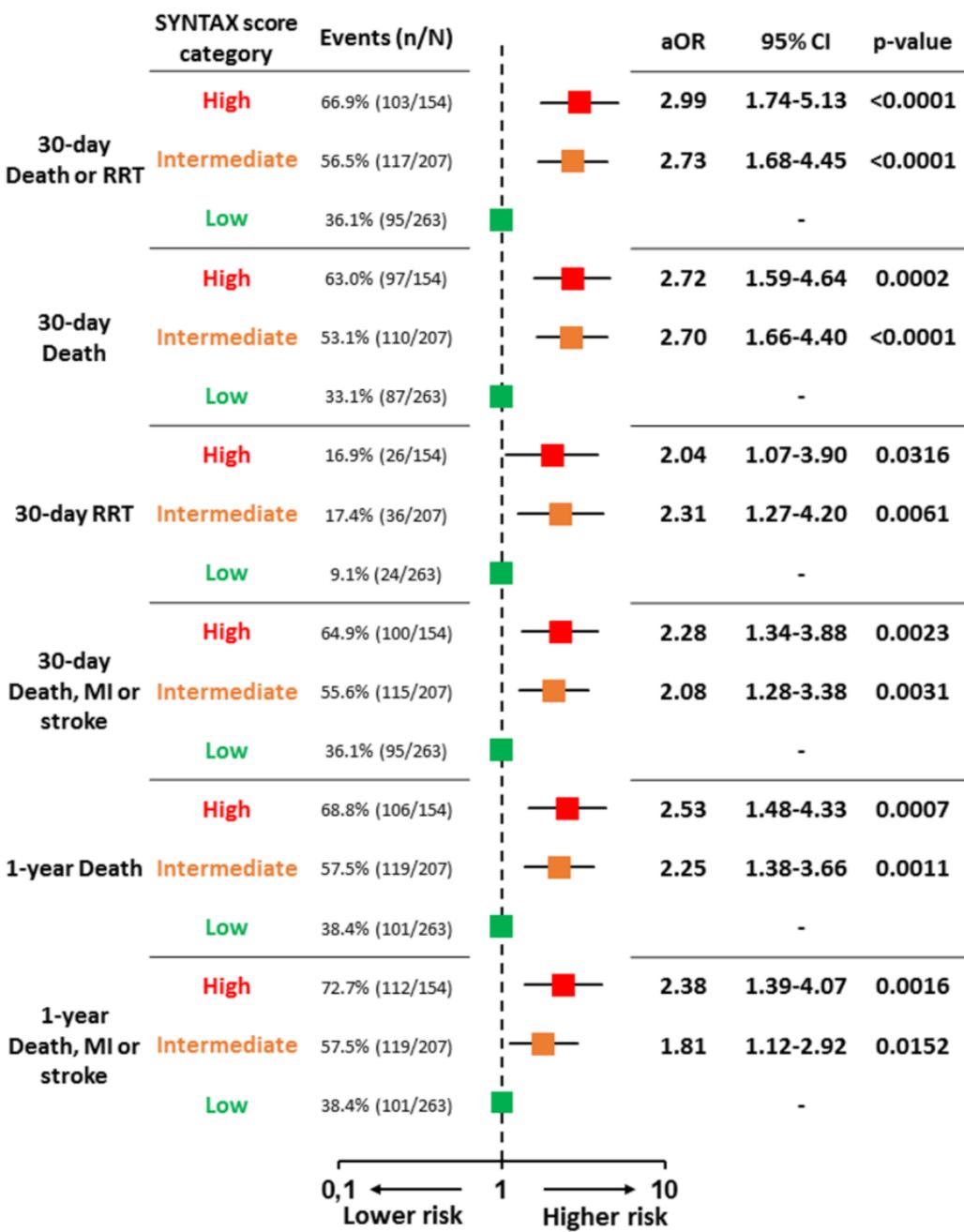
No. at risk	0	60	120	180	240	300	365
High Syntax Score	154	55	55	53	50	48	43
Intermediate Syntax Score	207	93	92	88	88	88	74
Low Syntax Score	263	170	168	167	164	163	142



No. at risk	0	60	120	180	240	300	365
High Syntax Score	154	52	51	47	44	42	38
Intermediate Syntax Score	207	87	86	82	82	81	69
Low Syntax Score	263	163	160	159	157	156	133

Prognostic Value of SYNTAX Score in Patients with Infarct-related Cardiogenic Shock

a predefined analysis of the CULPRIT SHOCK trial



**Prognostic Value of SYNTAX Score in Patients with Multivessel Coronary Artery
Disease and Infarct-related Cardiogenic Shock:
Insight from the CULPRIT-SHOCK Trial
Online documents**

Online Figures legend and title

Online Figure 1. Associations of SYNTAX score with 30-day and 1-year outcomes after multivariable adjustment including the effective revascularization strategy.

RRT: renal replacement therapy; MI: myocardial infarction; aOR: Adjusted odd ratio; CI: confidence interval. Number of included patients for each outcomes are: 30-day death or RRT, N=567; 30-day death, N=567; 30-day RRT, N=585; 30-day death, MI or stroke, N=568; 1 year Death, N=567; 1 year death, MI or stroke, N=569. Covariables of adjustment for each outcome are detailed in Online Table 1 and 2.

Online Figure 2. Clinical outcomes according to the baseline SYNTAX score and the revascularization strategy

PCI: percutaneous coronary intervention; OR: odds ratio; CI: confidence interval; RRT : renal replacement therapy

Online Table 1. Variables associated with 30-day outcomes - univariate analysis

	All-cause death or renal replacement therapy	All-cause death	Renal replacement therapy	All-cause death or Myocardial infarction or Stroke
Age (years)	<.0001	<.0001	0.3361	<.0001
Sex	0.2778	0.0985	0.6759	0.1347
Body Mass Index (kg/m ²)	0.0905	0.1822	0.1048	0.2319
Smoking status	<.0001	<.0001	0.3467	<.0001
Hypertension	0.6243	0.8155	0.1793	0.9923
Hypercholesterolemia	0.0005	0.0002	0.5403	0.0002
Diabetes mellitus	0.0077	0.0392	0.0911	0.0389
Prior myocardial infarction	0.9646	0.8188	0.4890	0.7460
Prior stroke	0.1901	0.2674	0.2404	0.2651
Known peripheral artery disease	0.5920	0.7021	0.8084	0.9356
Known renal insufficiency	0.0496	0.0372	0.0384	0.0076
Prior percutaneous coronary intervention	0.1195	0.0582	0.3425	0.0251
Arterial lactate >2mmol/l	0.0044	0.0047	0.2200	0.0026
Fibrinolysis before randomization	0.7593	0.7359	0.7623	0.9702
Resuscitation before randomization	0.6675	0.7723	0.5525	0.4877
Anterior ST-segment elevation	0.2527	0.3388	0.4180	0.1676
Femoral access	0.0054	0.0088	0.0118	0.0468
Mechanical circulatory support	<.0001	<.0001	0.0003	<.0001
Mild hypothermia	0.4461	0.9388	0.0006	0.9767
Mechanical ventilation	<.0001	<.0001	0.0361	<.0001
Catecholamine therapy	<.0001	<.0001	0.0205	<.0001
Post-PCI TIMI flow at 3 in culprit lesion	0.0006	0.0002	0.8554	0.0005
Randomized coronary revascularization strategy	0.0253*	0.0633*-	0.0271*	0.1285*
Effective coronary revascularization strategy	0.0136**	0.0659*	0.0067**	0.1474**

Gray cell are covariates of adjustment (p<0.2)

* Covariate of adjustment for primary analysis

** Covariate of adjustment for sensitivity analysis

Online Table 2. Variables associated with 1-year outcomes - univariate analysis

	All-cause death	All-cause death or Myocardial infarction or Stroke
Age (years)	<.0001	<.0001
Sex	0.2475	0.1924
Body Mass Index (kg/m ²)	0.1816	0.3388
Smoking status	<.0001	<.0001
Hypertension	0.5687	0.4635
Hypercholesterolemia	0.0022	0.0255
Diabetes mellitus	0.0008	0.0007
Prior myocardial infarction	0.3520	0.3897
Prior stroke	0.0856	0.1074
Known peripheral artery disease	0.6368	0.5465
Known renal insufficiency	0.0402	0.0113
Prior percutaneous coronary intervention	0.3863	0.3147
Arterial lactate>2mmol/l	0.0042	0.0167
Fibrinolysis before randomization	0.1245	0.2532
Resuscitation before randomization	0.7664	0.6055
Anterior ST-segment elevation	0.3700	0.0961
Femoral access	0.0172	0.1149
Mechanical circulatory support	<.0001	<.0001
Mild hypothermia	0.8924	0.7848
Mechanical ventilation	<.0001	<.0001
Catecholamine therapy	<.0001	<.0001
Post-PCI TIMI flow at 3 in culprit lesion	0.0006	0.0033
Randomized coronary revascularization strategy	0.0947*	0.0471*
Effective coronary revascularization strategy	0.0879**	0.0740**

Gray cell are covariates of adjustment (p<0.2)

* Covariate of adjustment for primary analysis

** Covariate of adjustment for sensitivity analysis

Online Table 3. Baseline characteristics of patients with and without available baseline SYNTAX score

	Available baseline SYNTAX score (n=624)	No available baseline SYNTAX score (n=62)	p-value
Age, years	69.0 (60.0-78.0)	75.0 (68.0-78.0)	0.01
Male sex	475/624 (76.1%)	49/61 (80.3%)	0.46
Body mass index	26.6 (24.5-29.4)	27.1 (24.7-30.0)	0.55
<i>Cardiovascular risk factors</i>			
Current smoking	163/600 (27.2%)	11/59 (18.6%)	0.16
Hypertension	363/613 (59.2%)	43/61 (70.5%)	0.09
Hypercholesterolemia	197/610 (32.3%)	31/61 (50.8%)	0.004
Diabetes mellitus	189/611 (30.9%)	29/61 (47.5%)	0.008
Previous myocardial infarction	93/614 (15.1%)	20/60 (33.3%)	<0.001
Previous stroke	40/615 (6.5%)	9/62 (14.5%)	0.03
Known peripheral artery disease	70/616 (11.4%)	10/62 (16.1%)	0.27
Known renal insufficiency	40/615 (6.5%)	6/61 (9.8%)	0.29
Previous percutaneous coronary intervention	101/614 (16.4%)	26/60 (43.3%)	<0.001
Resuscitation before randomization	330/623 (53.0%)	36/60 (60.0%)	0.30
Fibrinolysis before randomization	32/622 (5.1%)	2/60 (3.3%)	0.76
Arterial lactate > 2 mmol/L	400/607 (65.9%)	40/57 (70.2%)	0.51
Anterior ST-segment elevation myocardial infarction	207/601 (34.4%)	15/60 (25.0%)	0.14
Systolic blood pressure, mmHg	100.0 (85.0-125.0)	99.0 (82.0-123.0)	0.44
Diastolic blood pressure, mmHg	60.0 (50.0-80.0)	60.0 (50.0-77.0)	0.51
Mean blood pressure, mmHg	76.0 (63.3-93.3)	73.3 (61.2-87.8)	0.45
Use of catecholamine	558/621 (89.9%)	55/62 (88.7%)	0.78
Duration of catecholamine, days	2.0 (1.0-5.0)	2.0 (1.0-5.0)	0.61
Number of affected vessels			0.14
1	5/624 (0.8%)	0	
2	231/624 (37.0%)	15/61 (24.6%)	
3	388/624 (62.2%)	46/61 (75.4%)	
Left ventricular ejection fraction	n=236 32.5 (25.0-40.0)	n=19 28.0 (20.0-40.0)	0.09

Online Table 4. Procedural characteristics of patients with and without available baseline SYNTAX score

	Available baseline SYNTAX score (n=624)	No available baseline SYNTAX score (n=62)	p-value
Arterial access			
Femoral	510/624 (81.7%)	54/61 (88.5%)	0.18
Radial	119/624 (19.1%)	8/61 (13.1%)	0.25
Brachial	3/624 (0.5%)	0	1.00
Stent in culprit lesion			
Any	596/624 (95.5%)	54/61 (88.5%)	0.03
Bare-metal stent	34/596 (5.7%)	3/54 (5.6%)	1.00
Drug-eluting stent	561/596 (94.1%)	52/54 (96.3%)	0.76
Bioresorbable scaffold in culprit lesion	5/596 (0.8%)	0	1.00
Aspiration thrombectomy of culprit lesion	90/624 (14.4%)	9/62 (14.8%)	0.94
Randomized to culprit lesion only PCI	309/624 (49.5%)	35/62 (56.5%)	0.30
Immediate PCI of non-culprit lesions	328/624 (52.6%)	25/62 (40.3%)	0.07
Total dose of contrast material, mL	220.0 (155.0-300.0)	235.0 (150.0-350.0)	0.37
Total duration fluoroscopy, min	15.1 (9.2-24.0)	19.4 (11.4-27.6)	0.24
Staged PCI of non-culprit lesions	60/624 (9.6%)	8/61 (13.1%)	0.38
Mechanical circulatory support	172/624 (27.6%)	22/62 (35.5%)	0.19
Mild hypothermia	209/622 (33.6%)	20/62 (32.3%)	0.83
Mechanical ventilation	504/621 (81.2%)	51/62 (82.3%)	0.83
Duration of mechanical ventilation, days	3.0 (1.0-8.0)	2.0 (1.0-5.0)	0.15
Subsequent medications in patients who survived until hospital discharged			
Statin	307/330 (93.0%)	29/30 (96.7%)	0.71
Beta-blocker	301/330 (91.2%)	28/30 (93.3%)	1.00
ACE inhibitors or ARB	288/330 (87.3%)	28/30 (93.3%)	0.56
Aspirin	325/330 (98.5%)	29/30 (96.7%)	0.41
Clopidogrel	143/330 (43.3%)	19/30 (63.3%)	0.04
Prasugrel	117/330 (35.5%)	6/30 (20.0%)	0.09
Ticagrelor	132/330 (40.0%)	11/30 (36.7%)	0.72

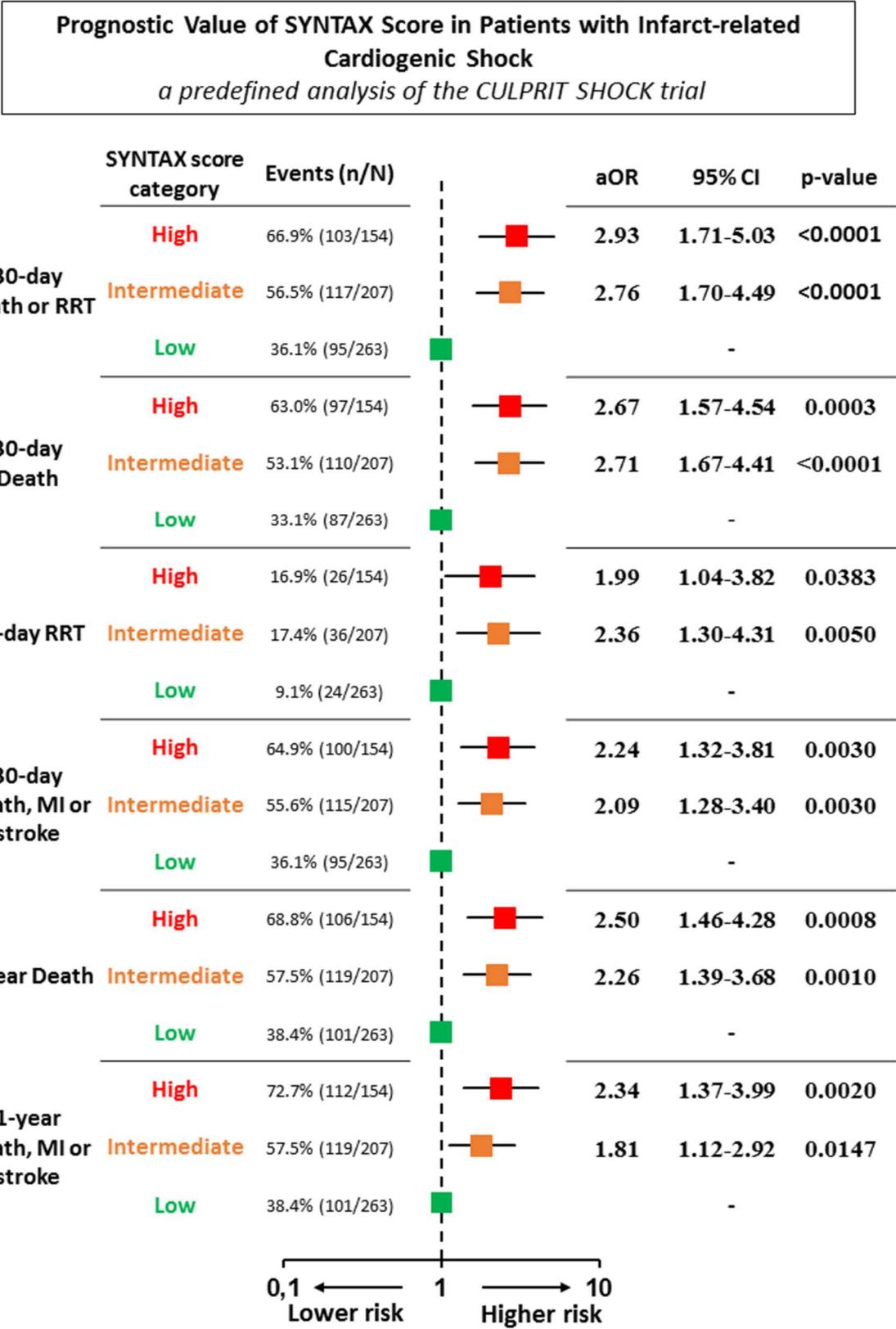
PCI: percutaneous coronary intervention, ACE: angiotensin converting enzyme, ARB: Angiotensin II receptor blockers

Online Table 5. Early and late outcomes in patients with and without available baseline SYNTAX score

	Available baseline SYNTAX score (n=624)	No available baseline SYNTAX score (n=61*)	p-value
30-day outcomes			
All-cause death or renal replacement therapy	50.5% (315)	52.5% (32)	0.768
All-cause death	47.1% (294)	50.8% (31)	0.580
Renal replacement therapy	13.8% (86)	16.4% (10)	0.575
All-cause death, myocardial infarction or stroke	49.7% (310)	55.7% (34)	0.366
1-year outcomes			
All-cause death, myocardial infarction or stroke	52.2% (326)	65.6% (40)	0.046
All-cause death	55.8% (348)	68.9% (42)	0.049

*One patient was lost to follow within 30 days of randomization and was excluded of the original analysis

Online Figure 1. Associations of SYNTAX score with 30-day and 1-year outcomes after multivariable adjustment including the effective revascularization strategy.



Online Figure 2. Clinical outcomes according to the baseline SYNTAX score and the revascularization strategy

