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One-Year Outcomes after PCI Strategies in Cardiogenic Shock

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ABSTRACT

BACKGROUND

Among patients with acute myocardial infarction, cardiogenic shock, and multivessel coronary artery disease, the risk of a composite of death from any cause or severe renal failure leading to renal-replacement therapy at 30 days was found to be lower with percutaneous coronary intervention (PCI) of the culprit lesion only than with immediate multivessel PCI. We evaluated clinical outcomes at 1 year.

METHODS

We randomly assigned 706 patients to either culprit-lesion-only PCI or immediate multivessel PCI. The results for the primary end point of death or renal-replacement therapy at 30 days have been reported previously. Prespecified secondary end points at 1 year included death from any cause, recurrent myocardial infarction, repeat revascularization, rehospitalization for congestive heart failure, the composite of death or recurrent infarction, and the composite of death, recurrent infarction, or rehospitalization for heart failure.

RESULTS

As reported previously, at 30 days, the primary end point had occurred in 45.9% of the patients in the culprit-lesion-only PCI group and in 55.4% in the multivessel PCI group (P=0.01). At 1 year, death had occurred in 172 of 344 patients (50.0%) in the culprit-lesion-only PCI group and in 194 of 341 patients (56.9%) in the multivessel PCI group (relative risk, 0.88; 95% confidence interval [CI], 0.76 to 1.01). The rate of recurrent infarction was 1.7% with culprit-lesion-only PCI and 2.1% with multivessel PCI (relative risk, 0.85; 95% CI, 0.29 to 2.50), and the rate of a composite of death or recurrent infarction was 50.9% and 58.4%, respectively (relative risk, 0.87; 95% CI, 0.76 to 1.00). Repeat revascularization occurred more frequently with culprit-lesion-only PCI than with multivessel PCI (in 32.3% of the patients vs. 9.4%; relative risk, 3.44; 95% CI, 2.39 to 4.95), as did rehospitalization for heart failure (5.2% vs. 1.2%; relative risk, 4.46; 95% CI, 1.53 to 13.04).

CONCLUSIONS

Among patients with acute myocardial infarction and cardiogenic shock, the risk of death or renal-replacement therapy at 30 days was lower with culprit-lesion-only PCI than with immediate multivessel PCI, and mortality did not differ significantly between the two groups at 1 year of follow-up. (Funded by the European Union Seventh Framework Program and others; CULPRIT-SHOCK ClinicalTrials.gov number, NCT01927549.)

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*A complete list of the investigators in the CULPRIT-SHOCK trial is provided in the Supplementary Appendix, available at NEJM.org.

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Early revascularization has been shown to reduce mortality among patients with acute myocardial infarction that is complicated by cardiogenic shock.[1-3] Most patients with cardiogenic shock present with multivessel coronary artery disease,[4] which is associated with higher mortality than single-vessel disease.[5-7] For the treatment of patients with multivessel disease, current European guidelines for the management of acute ST-segment elevation myocardial infarction recommend immediate percutaneous coronary intervention (PCI) of both culprit and nonculprit lesions,[8] and U.S. appropriate-use criteria consider immediate revascularization of both culprit and nonculprit arteries during the same procedure to be highly appropriate.[9] However, the 30-day results of the Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial[10] showed that the risk of a composite of death from any cause or severe renal failure leading to renal-replacement therapy was lower with culprit-lesion-only PCI than with immediate multivessel PCI, thus challenging the guideline recommendations. On the basis of these results, the European revascularization guidelines have now downgraded immediate multivessel PCI in cardiogenic shock to a class III B recommendation (i.e., a recommendation that the procedure is not useful and may be harmful, according to evidence from a single randomized trial).[11]

In light of the short-term results of the CULPRIT-SHOCK trial, the use of multivessel PCI in patients with cardiogenic shock is now controversial.[12,13] Although immediate multivessel PCI is associated with initial harm, the resulting complete revascularization could lead to a benefit over the long term. This possibility is supported by pooled evidence from nonrandomized trials showing that the higher short-term mortality with multivessel PCI than with culprit-lesion-only PCI was not sustained after longer-term follow-up.[14,15] Furthermore, a recent registry study suggested that there was lower mortality at 1 year with multivessel PCI than with culprit-lesion-only PCI.[16] Further data obtained during longer observation periods in randomized trials have been limited. Here, we report the 1-year results of the CULPRIT-SHOCK trial.

Methods

Trial Design and Oversight

The trial design and the short-term results have been published previously.[4,10] In summary, the CULPRIT-SHOCK trial was an investigator-initiated, multicenter, randomized, open-label, multicenter trial that compared culprit-lesion-only PCI (with optional staged revascularization) with immediate multivessel PCI in patients who had acute myocardial infarction that was complicated by cardiogenic shock. The protocol (available with the full text of this article at NEJM.org) was designed by the principal investigator and was modified and approved by the steering committee[4]; it was also approved by regional and national ethics review boards. The trial was registered at ClinicalTrials.gov 4 months after the enrollment of the first patient, as discussed in the Supplementary Appendix (available at NEJM.org).

Trial funding was provided by the European Union Seventh Framework Program, the German Heart Research Foundation, and the German Cardiac Society. Additional support was provided by the German Center for Cardiovascular Research. These institutions had no involvement in the conduct of the trial, as reported previously. Data were maintained and independent statistical analysis was performed by a coordinating research organization, Institut für Herzinfarktforschung (Institute for Myocardial Infarction Research). The steering committee vouches for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. The statistician vouches for the accuracy of the data analysis. The patient-level data, analytic methods, and trial materials cannot be made available to other researchers, because the European Union contract and the consortium agreement of the trial do not allow data sharing.

Patients

Patients who had acute myocardial infarction that was complicated by cardiogenic shock, as described previously,[10] were eligible for the trial if they met the following criteria: planned early revascularization by means of PCI, multivessel coronary artery disease (defined as at least two major vessels [≥2 mm diameter] with >70% stenosis of the diameter), and an identifiable culprit lesion. Exclusion criteria were resuscitation for longer than 30 minutes, no intrinsic heart action, an assumed severe deficit in cerebral function with fixed dilated pupils, an indication for primary coronary-artery bypass grafting, single-vessel coronary artery disease, a mechanical cause of cardiogenic shock, the onset of shock more than 12 hours before randomization, an age of more than

90 years, shock with a noncardiogenic cause, massive pulmonary embolism, known severe renal insufficiency (creatinine clearance, <30 ml per minute), and other severe concomitant disease associated with a life expectancy of less than 6 months. Written informed consent was obtained with the use of a prespecified process (see the Supplementary Appendix).[4]

RANDOMIZATION, TREATMENT, AND FOLLOW-UP

Patients underwent randomization immediately after diagnostic angiography. Randomization was performed centrally with the use of an Internet-based program with randomly changing blocks of 4 or 6 and stratification according to center.

Patients were randomly assigned, in a 1:1 ratio, to undergo either culprit-lesion-only PCI or immediate multivessel PCI. In all patients, the culprit lesion was treated first, with the use of standard PCI techniques and with the recommended use of drug-eluting stents. In patients in the culprit-lesion-only PCI group, all other lesions were to be left untreated at the time of the initial procedure. Staged revascularization was recommended on the basis of the patient's clinical status and the presence of residual ischemia on objective testing. In patients in the multivessel PCI group, all additional lesions (major coronary arteries with >70% stenosis of the diameter), including chronic total occlusions, were recommended to be treated with PCI immediately after treatment of the culprit lesion. In each group, the advised maximum dose of contrast material was 300 ml.

The use of mechanical circulatory support was left to the discretion of the operator. If renal-replacement therapy was deemed to be necessary, the method, duration, and reason for initiation were documented.

Trial-specific follow-up assessments were performed at 6 months and at 1 year by means of a structured telephone interview. Any potential end-point event was verified in a review of original records. In addition, death registries were searched to identify or confirm all deaths.

END POINTS

The primary end point was a composite of death from any cause or severe renal failure leading to renal-replacement therapy within 30 days after randomization; results for this outcome have been reported previously.[10] For the 1-year analysis, results are reported for the following prespecified secondary end points: death from any cause, renal-replacement therapy, recurrent myocardial infarction, repeat revascularization, and rehospitalization for congestive heart failure. In addition, results are reported for the composite of death or recurrent infarction and for the composite of death, recurrent infarction, or rehospitalization for heart failure.

Safety end points included stroke and bleeding, which was defined as bleeding of type 2, 3, or 5 on the Bleeding Academic Research Consortium (BARC) scale (with type 2 indicating any overt, actionable sign of bleeding; type 3, bleeding with a decrease in the hemoglobin level of >3 g per deciliter, any transfusion, cardiac tamponade, or intracranial or ocular involvement; and type 5, fatal bleeding).[4,17] Quality of life was assessed with the European Quality of Life–5 Dimensions (EQ-5D) questionnaire (www.euroqol.org), including a visual-analogue scale, at 6 months and at 1 year. As a post hoc exploratory analysis, the primary end point of a composite of death or renal-replacement therapy was assessed at 1 year. Definitions of all end points are provided in the Supplementary Appendix. All end-point events were adjudicated by a clinical end-points committee whose members were unaware of the group assignments.

STATISTICAL ANALYSIS

The sample-size calculation and the design for the 30-day analysis have been described previously and are summarized in the Supplementary Appendix.[4,10] For the 1-year analysis, data were included for all the patients who had at least 30 days of follow-up. All analyses were performed according to the intention-to-treat principle. The 1-year event rates were the percentages of patients who had an event within 365 days after randomization. Event rates were compared by chi-square tests. Robustness of results was evaluated in sensitivity analyses performed in the per-protocol and as-treated populations. End points that did not include death from any cause as a component were analyzed in all patients as well as in patients who survived. Kaplan–Meier curves are used to show event rates over time with classification according to group assignment. We also performed a post hoc landmark analysis using a cutoff point of 30 days after randomization, with hazard ratios calculated separately for events that occurred within 30 days and those that occurred between 30 days and 1 year.

Data from the quality-of-life assessment were analyzed, with chi-square tests, in patients who survived. Values on the visual-analogue scale were compared with Mann–Whitney U tests. Predefined subgroup analyses for 1-year mortality were performed, as described previously.[10] The resulting relative risks and 95% confidence intervals are presented in a forest plot. The Breslow–Day test was used to analyze the interaction between group assignment and subgroup.

No adjustment for multiple comparisons was performed for any of the analyses. P values are not reported, since all analyses presented here are for secondary end points. All analyses were conducted with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

PATIENTS

In total, 1075 patients with cardiogenic shock were screened at 83 centers, and 706 patients (65.7%) were randomly assigned to undergo culprit-lesion-only PCI (351 patients) or immediate multivessel PCI (355 patients) (Fig. 1). Full informed consent was obtained for 344 and 342 patients, respectively. One patient was lost to follow-up within 30 days, and one additional patient was lost to follow-up between 30 days and 1 year. Data on vital status were available at 1 year for 343 patients in the culprit-lesion-only PCI group and for 341 patients in the multivessel PCI group, exactly meeting the prespecified sample-size requirement of 684 patients after withdrawals.

The characteristics of the patients at baseline and procedural characteristics, including medications at discharge, are shown in Table 1 and Table 2, respectively. Immediate crossover occurred in 43 patients (12.5%) in the culprit-lesion-only PCI group and in 32 patients (9.4%) in the multivessel PCI group. Among patients who received stents, drug-eluting stents were used in 93.6% of the patients in the culprit-lesion-only PCI group and in 95.1% in the multivessel PCI group. There was no significant difference between the two groups in the Thrombolysis in Myocardial Infarction grade for epicardial perfusion before or after PCI of the culprit artery. The overall dose of contrast material was significantly greater and the duration of fluoroscopy was significantly longer in the multivessel PCI group than the culprit-lesion-only PCI group.

CLINICAL END POINTS

As reported previously, at 30 days, the primary end point of a composite of death or renal-replacement therapy had occurred in 158 of 344 patients (45.9%) in the culprit-lesion-only PCI group and in 189 of 341 patients (55.4%) in the multivessel PCI group (relative risk, 0.83; 95% confidence interval [CI], 0.71 to 0.96; P=0.01). At 1 year, mortality did not differ significantly between the culprit-lesion-only PCI group and the multivessel PCI group; death from any cause had occurred in 172 of 344 patients (50.0%) and 194 of 341 patients (56.9%), respectively (relative risk, 0.88; 95% CI, 0.76 to 1.01) (Table 3 and Fig. 2A). Death from cardiovascular causes had occurred in 159 patients (46.2%) in the culprit-lesion-only PCI group and in 180 patients (52.8%) in the multivessel PCI group (relative risk, 0.88; 95% CI, 0.75 to 1.02). (For details on causes of death at 1 year, see Table S1 in the Supplementary Appendix.)

A post hoc landmark analysis revealed a difference between the two groups in mortality within the first 30 days (relative risk, 0.84; 95% CI, 0.72 to 0.98), but mortality was similar in the two groups thereafter (relative risk, 1.08; 95% CI, 0.60 to 1.93) (Fig. 2B). Between 30 days and 1 year, 23 patients (6.7%) died in the culprit-lesion-only PCI group and 18 patients (5.3%) died in the multivessel PCI group. Results for mortality between baseline and 1 year in the intention-to-treat population were similar to results in the per-protocol population (relative risk, 0.87; 95% CI, 0.75 to 1.02) and the as-treated population (relative risk, 0.90; 95% CI, 0.78 to 1.03). Predefined subgroup analyses revealed consistency of the results across all subgroups (Fig. S1 in the Supplementary Appendix).

Events leading to renal-replacement therapy occurred only within the first 30 days, with no further events recorded between 30 days and 1 year of follow-up. Such an event occurred in 11.6% of the patients in the culprit-lesion-only PCI group and in 16.4% in the multivessel PCI group (relative risk, 0.71; 95% CI, 0.49 to 1.03) (Table 3). Recurrent myocardial infarction occurred in 1.7% of the patients in the culprit-lesion-only PCI group and in 2.1% in the multivessel PCI group (relative risk, 0.85; 95% CI, 0.29 to 2.50), and the composite of death or recurrent infarction was observed in 50.9% and 58.4%, respectively (relative risk, 0.87; 95% CI, 0.76 to 1.00)

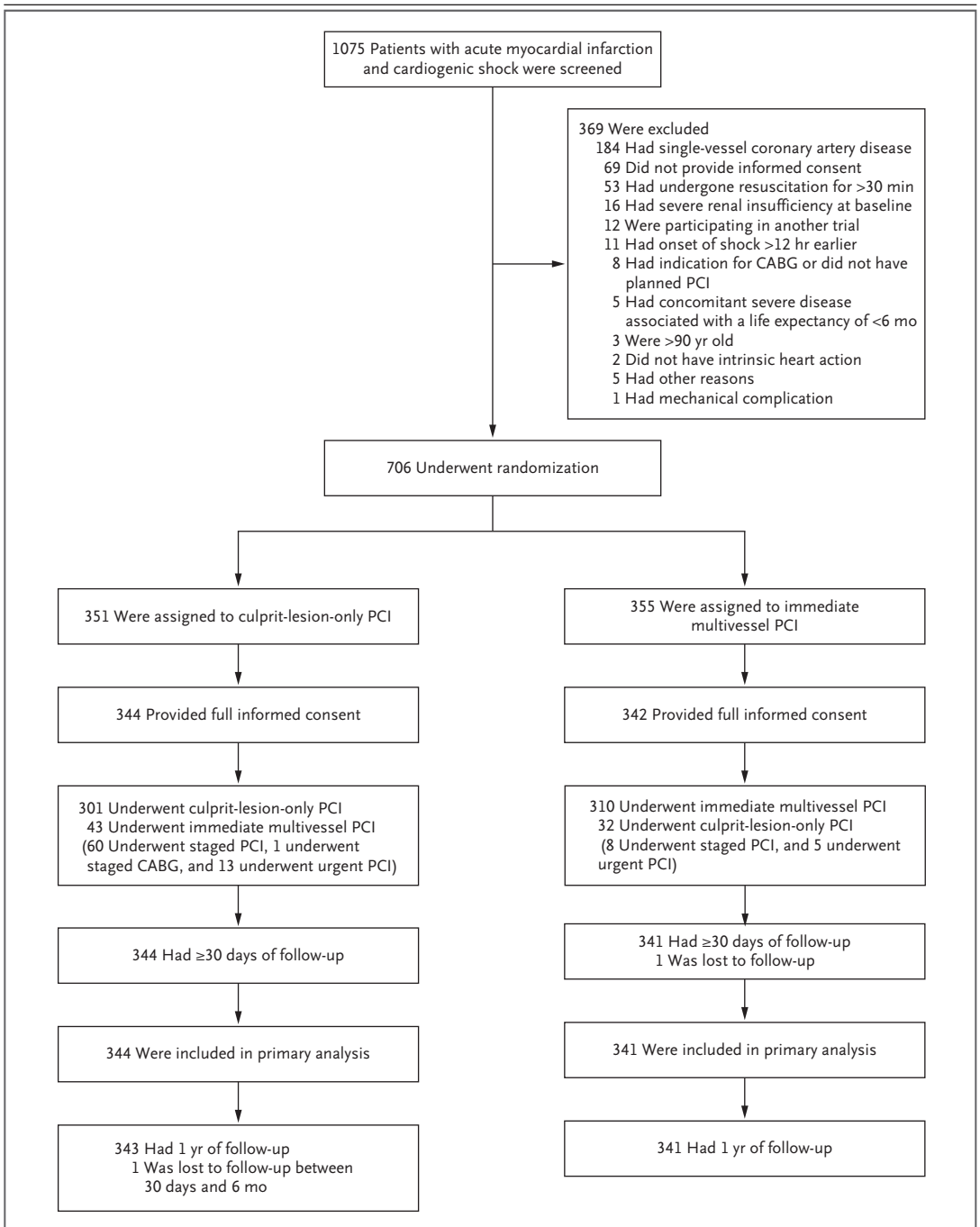

Figure 1. Screening, Randomization, Treatment, and Follow-up at 30 Days and at 1 Year in the Intention-to-Treat Population.

CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

(Table 3, and Fig. S2 in the Supplementary Appendix).

Repeat revascularization was performed more often with the culprit-lesion-only PCI strategy than with the multivessel PCI strategy (in 32.3% of the patients vs. 9.4%; relative risk, 3.44; 95% CI, 2.39 to 4.95) (Table 3, and Fig. S3 in the Supplementary Appendix). Although there were

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=342)
Age — yr		
Median	70	70
Interquartile range	60–78	60–77
Male sex — no./total no. (%)	257/343 (74.9)	267/342 (78.1)
Body-mass index†		
Median	26.6	26.7
Interquartile range	24.2–29.4	24.7–29.4
Cardiovascular risk factors — no./total no. (%)		
Current smoking	85/334 (25.4)	89/325 (27.4)
Hypertension	200/339 (59.0)	206/335 (61.5)
Hypercholesterolemia	112/338 (33.1)	116/333 (34.8)
Diabetes mellitus	102/337 (30.3)	116/335 (34.6)
Previous myocardial infarction — no./total no. (%)	60/339 (17.7)	53/335 (15.8)
Previous stroke — no./total no. (%)	29/341 (8.5)	20/336 (6.0)
Known peripheral artery disease — no./total no. (%)	43/341 (12.6)	37/337 (11.0)
Previous PCI — no./total no. (%)	64/339 (18.9)	63/335 (18.8)
Previous coronary-artery bypass grafting — no./total no. (%)	20/341 (5.9)	13/337 (3.9)
Resuscitation before randomization — no./total no. (%)	177/341 (51.9)	189/342 (55.3)
ST-segment elevation myocardial infarction — no./total no. (%)	206/335 (61.5)	209/330 (63.3)
Systolic blood pressure — mm Hg		
Median	100	100
Interquartile range	83–120	85–130
Diastolic blood pressure — mm Hg		
Median	60	61
Interquartile range	50–80	50–80
Mean blood pressure — mm Hg		
Median	76	76
Interquartile range	63–92	63–93
Use of catecholamine — no./total no. (%)	304/344 (88.4)	309/339 (91.2)
Creatinine — mg/dl‡		
Median	1.17	1.20
Interquartile range	0.90–1.66	0.90–1.68
Creatinine clearance — ml/min		
Median	64	66
Interquartile range	42–95	43–93
No. of affected vessels — no./total no. (%)		
1	3/343 (0.9)	2/342 (0.6)
2	122/343 (35.6)	124/342 (36.3)
3	218/343 (63.6)	216/342 (63.2)

Table 1. (Continued.)

Characteristic	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=342)
Vessel related to the infarction — no./total no. (%)		
Left anterior descending artery	132/343 (38.5)	156/342 (45.6)
Left circumflex artery	76/343 (22.2)	70/342 (20.5)
Right coronary artery	102/343 (29.7)	89/342 (26.0)
Left main artery	31/343 (9.0)	22/342 (6.4)
Bypass graft	2/343 (0.6)	5/342 (1.5)
≥1 Chronic total occlusion — no./total no. (%)	77/344 (22.4)	82/342 (24.0)
Left ventricular ejection fraction — %		
Median	33	30
Interquartile range	25–40	21–40

* There were no significant differences between the two groups in baseline characteristics. PCI denotes percutaneous coronary intervention.
† Body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ To convert the values for creatinine to micromoles per liter, multiply by 88.4.

few cases of rehospitalization for congestive heart failure, the rate was higher in the culprit-lesion-only PCI group than in the multivessel PCI group (5.2% vs. 1.2%; relative risk, 4.46; 95% CI, 1.53 to 13.04) (Table 3, and Fig. S4 in the Supplementary Appendix).

The rate of the composite of death, recurrent infarction, or rehospitalization for heart failure did not differ significantly between the two groups (Table 3, and Fig. S5 in the Supplementary Appendix). In addition, the rates for safety end points did not differ significantly between the two groups (Table 3). The original primary end point of a composite of death or renal-replacement therapy was evaluated in a post hoc analysis at 1 year; an end-point event occurred in 52.0% of the patients in the culprit-lesion-only PCI group and in 59.5% in the multivessel PCI group (relative risk, 0.87; 95% CI, 0.76 to 0.99) (Table 3, and Fig. S6 in the Supplementary Appendix).

EQ-5D values were obtained for 286 of the 317 patients who survived. Results on the quality-of-life assessment, including the visual-analogue scale, at 6 months and at 1 year did not differ significantly between the two groups (Figs. S7 and S8 in the Supplementary Appendix).

DISCUSSION

This multicenter, randomized trial compared culprit-lesion-only PCI (with the option of staged revascularization) with immediate multivessel PCI in patients with acute myocardial infarction, cardiogenic shock, and multivessel coronary artery disease. We previously reported that the risk of a composite of death from any cause or renal-replacement therapy was lower with culprit-lesion-only PCI than with multivessel PCI in the 30-day analysis of this trial. In the analysis reported here, we found that mortality did not differ significantly between the two groups at 1 year. However, the rates of rehospitalization for heart failure and repeat revascularization were higher in the culprit-lesion-only PCI group than the multivessel PCI group at 1 year.

The major randomized trials for cardiogenic shock showed that death in patients with cardiogenic shock was mainly confined to the first 30 days, with mortality during that period ranging from 39.7 to 46.7%, depending on the cohorts of patients included in the trial, the revascularization strategy, and the standard method for revascularization during that time.[2,18,19] Mortality between 30 days and 1 year was 6.6% in the Should We Emergently Revascularize Occluded

Table 2. Procedural Characteristics.

Variable	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=342)	P Value
Arterial access — no./total no. (%)			
Femoral	287/343 (83.7)	277/342 (81.0)	0.36
Radial	61/343 (17.8)	66/342 (19.3)	0.61
Brachial	2/343 (0.6)	1/342 (0.3)	>0.99
Stent in culprit lesion — no./total no. (%)			
Any	326/343 (95.0)	324/342 (94.7)	0.86
Bare metal	20/326 (6.1)	17/324 (5.2)	0.63
Drug eluting	305/326 (93.6)	308/324 (95.1)	0.41
Bioresorbable scaffold in culprit lesion — no./total no. (%)	2/326 (0.6)	3/324 (0.9)	0.69
TIMI grade for blood flow — no./total no. (%)*			
Before PCI of culprit lesion			0.49
0	189/339 (55.8)	178/337 (52.8)	
I	37/339 (10.9)	45/337 (13.4)	
II	56/339 (16.5)	50/337 (14.8)	
III	57/339 (16.8)	64/337 (19.0)	
After PCI of culprit lesion			0.46
0	13/342 (3.8)	16/338 (4.7)	
I	12/342 (3.5)	8/338 (2.4)	
II	28/342 (8.2)	21/338 (6.2)	
III	289/342 (84.5)	293/338 (86.7)	
Immediate PCI of nonculprit lesions — no./total no. (%)	43/344 (12.5)	310/342 (90.6)	<0.001
Immediate complete revascularization achieved — no./total no. (%)	26/344 (7.6)	277/342 (81.0)	<0.001
Total dose of contrast material — ml			<0.001
Median	190	250	
Interquartile range	140–25	200–350	
Total duration of fluoroscopy — min			<0.001
Median	13	19	
Interquartile range	7–20	12–29	
Staged PCI of nonculprit lesions within 30 days — no./total no. (%)	60/344 (17.4)	8/341 (2.3)	<0.001
Staged coronary-artery bypass grafting within 30 days — no./total no. (%)	1/344 (0.3)	0/341 (0)	>0.99
Mechanical circulatory support — no./total no. (%)	99/344 (28.8)	95/342 (27.8)	0.77
Mechanical ventilation — no./total no. (%)	273/344 (79.4)	282/339 (83.2)	0.20
Subsequent medications in patients who survived until hospital discharge — no./total no. (%)			
Statin	184/195 (94.4)	152/165 (92.1)	0.40
Beta-blocker	181/195 (92.8)	148/165 (89.7)	0.29
Angiotensin-converting–enzyme inhibitor or angiotensin II type 1 receptor antagonist	176/195 (90.3)	140/165 (84.8)	0.12
Aspirin	191/195 (97.9)	163/165 (98.8)	0.54
Clopidogrel	89/195 (45.6)	73/165 (44.2)	0.79
Prasugrel	67/195 (34.4)	56/165 (33.9)	0.93
Ticagrelor	78/195 (40.0)	65/165 (39.4)	0.91

* Thrombolysis in Myocardial Infarction (TIMI) grades for blood flow range from 0 to III, with higher grades indicating better flow. TIMI grades were reported by the investigator.

Table 3. Clinical and Safety Outcomes at 1 Year.*

Outcome	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=341)	Relative Risk (95% CI)
	no. (%)		
Death from any cause†	172 (50.0)	194 (56.9)	0.88 (0.76–1.01)
Renal-replacement therapy‡	40 (11.6)	56 (16.4)	0.71 (0.49–1.03)
Recurrent myocardial infarction	6 (1.7)	7 (2.1)	0.85 (0.29–2.50)
Death or recurrent infarction	175 (50.9)	199 (58.4)	0.87 (0.76–1.00)
Rehospitalization for congestive heart failure	18 (5.2)	4 (1.2)	4.46 (1.53–13.04)
Death, recurrent infarction, or rehospitalization for heart failure	190 (55.2)	203 (59.5)	0.87 (0.93–1.06)
Repeat revascularization			
Any	111 (32.3)	32 (9.4)	3.44 (2.39–4.95)
PCI	107 (31.1)	29 (8.5)	3.66 (2.50–5.36)
Coronary-artery bypass grafting	4 (1.2)	3 (0.9)	1.32 (0.30–5.86)
Death or renal-replacement therapy	179 (52.0)	203 (59.5)	0.87 (0.76–0.99)
Stroke	15 (4.4)	14 (4.1)	1.06 (0.52–2.17)
Bleeding			
Any	75 (21.8)	86 (25.2)	0.86 (0.66–1.13)
BARC type 2, 3, or 5§	65 (18.9)	79 (23.2)	0.82 (0.61–1.09)

* Confidence intervals were not adjusted for multiple comparisons, and clinical inferences may not be reproducible. Results for clinical end points that were analyzed only for patients who survived are shown in Table S2 in the Supplementary Appendix.
† Causes of death are shown in Table S1 in the Supplementary Appendix.
‡ Renal-replacement therapy was defined as any treatment that included dialysis, hemofiltration, or hemodiafiltration.
§ On the Bleeding Academic Research Consortium (BARC) scale, type 2 indicates any overt, actionable sign of bleeding; type 3, bleeding with a decrease in the hemoglobin level of more than 3 g per deciliter, any transfusion, cardiac tamponade, or intracranial or ocular involvement; and type 5, fatal bleeding.

Coronaries for Cardiogenic Shock (SHOCK) trial and 12.3% in the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial.[20,21] These rates are similar to the 6.6% mortality between 30 days and 1 year that was reported in this trial. The results of the landmark analysis showed a benefit of culprit-lesion-only PCI over multivessel PCI with respect to short-term mortality, and there was no statistical difference between the two groups in mortality thereafter. These findings do not support the hypothesis that immediate multivessel PCI is associated with a higher short-term risk of death than culprit-lesion-only PCI but with a diminished risk during the longer-term course.[22]

The rate of rehospitalization for heart failure was higher in the culprit-lesion-only PCI group than in the multivessel PCI group, although the rates were low in both groups and the absolute difference in risk between the two groups was small. It is possible that this finding could be related to the higher rate of complete revascularization in the multivessel PCI group than in the culprit-lesion-only PCI group, with complete revascularization leading to subsequent improved ventricular function and a lower subsequent incidence of heart failure. However, this interpretation is only speculative, since, to our knowledge, no randomized trials have addressed this issue and data on ventricular function were not obtained in this trial. The higher rate of rehospitalization for heart failure in the culprit-lesion-only PCI group could also be a consequence of competing risks. Patients with cardiogenic shock are at an extreme risk for death, and if they die early, they therefore do not survive long enough for heart failure to develop in the longer-term course. Accordingly, because culprit-lesion-only PCI has shown a benefit over multivessel PCI with respect to short-term survival, the risk of

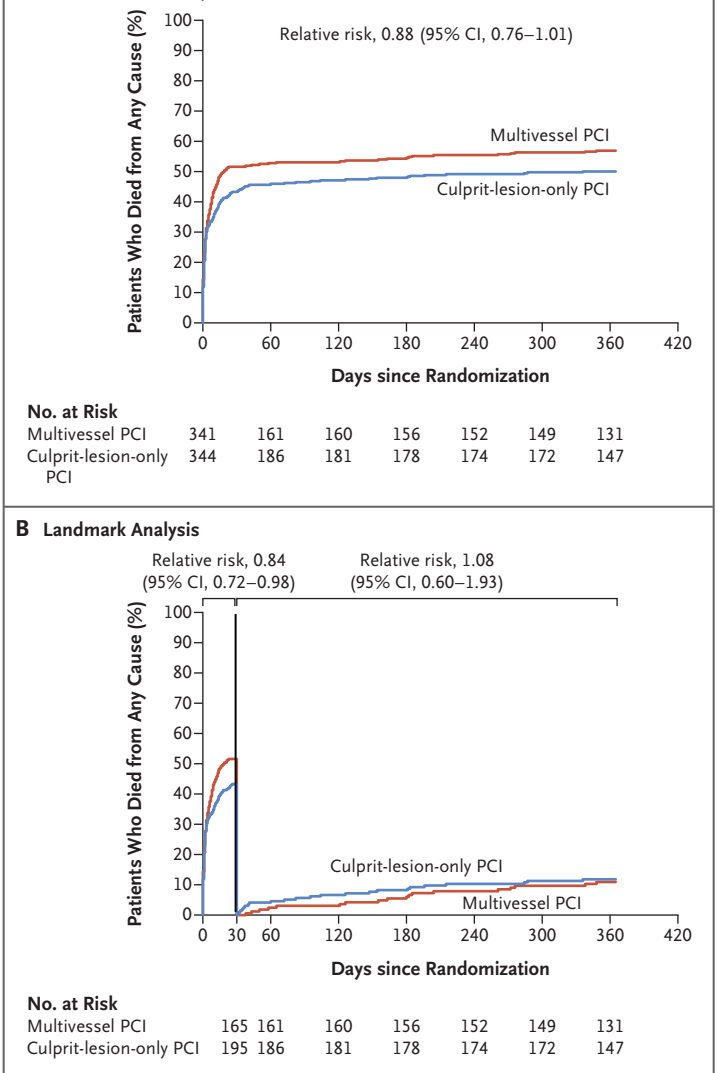

Figure 2. Time-to-Event and Landmark Analyses for Death from Any Cause through 1 Year.

Panel A shows Kaplan–Meier estimates of the rate of death from any cause through 1 year. Panel B shows the results of a landmark analysis of the rate of death from any cause through 30 days, as well as the rate between 30 days and 1 year.

heart failure within the first year may be higher with culprit-lesion-only PCI than with multivessel PCI.

In previous studies involving patients with acute myocardial infarction who did not have cardiogenic shock, the differences in outcomes between those who underwent culprit-lesion-only PCI and those who underwent immediate multivessel or early staged PCI were driven mainly by a difference in the rate of repeat revascularization and not by differences in rates of hard end points, such as death or recurrent infarction. Among patients who have cardiogenic shock, the short-term risks that are associated with longer procedure times, more complex initial interventions, and higher doses of contrast material seem to outweigh any potential benefits associated with reducing the subsequent risk of repeat revascularization. In this trial, after 1 year, 32.3% of the patients in the culprit-lesion-only PCI group had undergone staged or urgent repeat revascularization. This rate is higher than rates seen in trials of revascularization strategies in patients who did not have cardiogenic shock, which range from 8.2 to 17.4% at 1 year of follow-up.[23-26] The higher rate of repeat revascularization in the culprit-lesion-only PCI group in this trial may be related to the extent of coronary artery disease, the presence of impaired left ventricular function, and the severity of illness in patients with cardiogenic shock, as well as to the trial design. It is unclear whether an even higher rate of revascularization of nonculprit lesions could have prevented rehospitalizations for heart failure.

This trial has several limitations. First, all the end points in the 1-year analysis are exploratory because the trial was powered for the 30-day analysis of the primary composite end point. Second, blinding was not possible owing to the nature of the intervention performed. Management of cardiogenic shock involves a complex series of clinical decisions, and residual bias in the course of such management cannot be ruled out. Third, the results of serial echocardiography to assess cardiac function were not available, and such results would have allowed us to explore potential underlying causes of the initial higher mortality with multivessel PCI and the subsequent higher rate of rehospitalization for heart failure with culprit-lesion-only PCI.

In conclusion, this multicenter, randomized trial compared culprit-lesion-only PCI (with the option of staged revascularization) with immediate multivessel PCI in patients with acute myocardial infarction, cardiogenic shock, and multivessel coronary artery disease. At 30 days, the risk of a composite of death from any cause or renal-replacement therapy was significantly lower with culprit-lesion-only PCI than with multivessel PCI. At 1 year, mortality did not differ significantly between the two groups. However,

the incidence of rehospitalization for heart failure was higher and repeat revascularization was more frequent with culprit-lesion-only PCI than with multivessel PCI at 1 year.

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APPENDIX

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