

Correlates of One-Year Survival in Patients With Cardiogenic Shock Complicating Acute Myocardial Infarction

Angiographic Findings From the SHOCK Trial

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OBJECTIVES	The goal of this study was to describe the core laboratory angiographic findings of “SHould we emergently revascularize Occluded Coronaries for cardiogenic shock” (SHOCK) trial participants and to determine the relationship of angiographic parameters to one-year survival.
BACKGROUND	In the SHOCK trial, emergency revascularization improved one-year survival of patients with cardiogenic shock compared with initial medical stabilization including thrombolysis and intraaortic balloon counterpulsation.
METHODS	Coronary angiography was performed by protocol in 147 of 152 (97%) patients in the emergency revascularization (ERV) group and by clinical selection in 100 of 150 (67%) patients in the initial medical stabilization (IMS) group. Of the other 50 IMS patients, 45 of 50 (90%) died rapidly and did not undergo angiography.
RESULTS	Left ventricular ejection fraction was correlated with one-year survival in both treatment groups ($p < 0.001$). In the IMS group, the hazard ratio for death was 2.59 (95% confidence interval 1.47 to 4.58, $p = 0.001$) per diseased vessel (0/1 vs. 2 vs. 3). In the ERV group, the hazard ratio for death per diseased vessel was 1.11 (95% confidence interval 0.79 to 1.56, $p = 0.559$). Multivariate analysis of the angiography cohort (without regard for left ventriculogram measurements) identified initial Thrombolysis in Myocardial Infarction flow grade ($p = 0.032$), number of diseased vessels (for IMS patients only, $p = 0.024$), and culprit vessel ($p = 0.004$) as independent correlates of one-year survival, even after adjustment for key clinical factors. In the smaller cohort with left ventricular ejection fraction measured ($n = 97$), ejection fraction and culprit vessel remained independently correlated with survival.
CONCLUSIONS	For patients in cardiogenic shock, left ventricular function and culprit vessel were independent correlates of one-year survival. (J Am Coll Cardiol 2003;42:1373–9) © 2003 by the American College of Cardiology Foundation

Important predictors of survival in patients with coronary artery disease include age, severity of angina or ischemia,

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extent of coronary artery disease, patency of the infarct-related artery, and left ventricular function (1–11). In

patients with cardiogenic shock complicating acute myocardial infarction, the multicenter randomized trial entitled “SHould we emergently revascularize Occluded Coronaries for cardiogenic shock” (SHOCK) trial has demonstrated that emergency revascularization by percutaneous coronary intervention (PCI) or coronary artery bypass surgery (CABG) improves one-year survival in patients with cardiogenic shock due to left ventricular failure as compared with patients treated with initial medical stabilization (12,13), with 13 lives saved per 100 patients treated. Core laboratory angiographic findings from the SHOCK trial were examined in order to describe the angiographic profile of patients in cardiogenic shock and to determine the correlates of one-year survival using multivariate analysis.

METHODS

Trial design. The study design was a randomized trial at 36 international centers comparing the two treatment strat-

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
ERV	= emergency revascularization
IMS	= initial medical stabilization
LAD	= left anterior descending artery
LCX	= left circumflex artery
LM	= left main coronary artery
LVEF	= left ventricular ejection fraction
MR	= mitral regurgitation
PCI	= percutaneous coronary intervention
RCA	= right coronary artery
SHOCK	= "SHould we emergently revascularize Occluded Coronaries for cardiogenic shock" trial
SVG	= saphenous vein graft
TIMI	= Thrombolysis In Myocardial Infarction

egies of emergency revascularization (ERV) and initial medical stabilization (IMS). Each center obtained institutional review committee approval (12,14). By protocol, enrolled patients had shock onset within 36 h of myocardial infarction and were randomized within 12 h of shock onset. Patients assigned to the ERV group had to have angioplasty or bypass surgery as soon as possible and within 6 h of randomization; intraaortic balloon counterpulsation was recommended for both groups. For patients assigned to the IMS group, thrombolytic therapy was strongly recommended. In the latter group, delayed revascularization a minimum of 54 h after randomization was encouraged if clinically indicated, although coronary angiography was allowed at any time. Complete details of study design and eligibility criteria are previously described (14). The angiographic analysis reported in this study is based on studies performed before revascularization.

Angiographic core laboratory protocol. All coronary and left ventricular cineangiograms were reviewed at the core laboratory (New York Hospital) using the Thrombolysis In Myocardial Infarction (TIMI) criteria (15), the Rentrop coronary collateral circulation classification (16), and an estimate of the amount of myocardium at risk based on the coronary artery jeopardy score (17). The angiographic parameters that were examined included: location, severity, and morphology of all coronary lesions; TIMI flow; identification of ischemia related artery (culprit vessel) by electrocardiogram and lesion morphology; modified American Heart Association/American College of Cardiology culprit lesion type (18,19); quantification of left ventricular function (20); amount of mitral regurgitation (MR) (0 to 4 scale); and presence of ventricular septal defect, flail mitral leaflet, and left ventricular thrombus. Significant coronary artery disease was defined as $\geq 50\%$ diameter stenosis. Patients with significant left main stenosis and left dominant coronary anatomy were classified as having both left main and three-vessel coronary artery disease. Each angiogram was read by two independent readers using standardized data forms, with discrepancies resolved by a third

reader. All readers were blinded to treatment group and enrolling center.

Statistical analysis. Categorical angiographic findings of patients classified by treatment assignment were compared using a Fisher exact test. Treatment group differences in continuous variables were compared by Student's *t* test for age, systolic blood pressure, and heart rate and using the Wilcoxon rank sum test for all other variables. For all analyses of one-year survival, six patients who were trial ineligible (five assigned to emergency revascularization and one assigned to initial medical stabilization) due to severe MR, aortic dissection, or left ventricular free wall rupture identified after randomization were excluded. The Kaplan-Meier method (21) was used to estimate survival curves by coronary anatomy. Multivariate modeling of one-year survival was conducted using Cox proportional hazards regression. One patient with unknown one-year vital status was excluded from survival curves and Cox modeling due to informative censoring (patient not found in the Social Security Death Index but not documented to be alive at one year). Descriptive statistics are presented as means \pm SD, medians and interquartile range, or as percentages. All analyses were conducted with the Statistical Analysis System (SAS Institute, Inc., Cary, North Carolina) and S-Plus software (Statistical Sciences, Inc., Seattle, Washington).

RESULTS

Baseline angiographic findings. A total of 302 patients were randomized to emergency revascularization ($n = 152$) or initial medical stabilization ($n = 150$). Coronary angiography was performed, by protocol, on 147 of 152 (97%) patients in the ERV group and 100 of 150 (67%) patients selected from the IMS group. Five patients randomized to emergency revascularization died before coronary angiography could be performed. Of the 50 IMS patients who did not undergo angiography, 45 (90%) died rapidly despite having a similar mean age (67 ± 11 vs. 66 ± 11 years) as the IMS patients who underwent angiography. The cardiac index, however, was somewhat lower in these IMS patients compared with those who underwent angiography (1.6 ± 0.5 vs. 1.8 ± 0.5 , $p = 0.093$) and they were more likely to have a history of peripheral vascular disease (25.8% vs. 8.3%, $p = 0.027$), and a history of bypass graft surgery (16.0% vs. 7.0%, $p = 0.092$). Of a total of 247 coronary angiograms performed, 243 could be interpreted, as three films were not obtained, and one was of poor quality. In this angiographic cohort of 243 patients, 90% of patients assigned to a strategy of emergency revascularization and 37% of patients assigned to initial medical stabilization with possible delayed revascularization underwent revascularization (62% PCI, 38% CABG for IMS and ERV). This cohort was 66 ± 10 years old and 33% female, with mean systolic blood pressure and cardiac index on support measures of 89 ± 21 mm Hg and 1.8 ± 0.6 l/min/m², respectively.

Coronary angiography revealed extensive, severe coronary

Table 1. SHOCK Trial Core Laboratory Angiographic Findings by Treatment Group Assignment

Characteristics	n	Initial Medical Stabilization	n	Emergency Revascularization	p Value
Number randomized		150		152	—
Coronary angiography performed, n (%)		100 (67%)		147 (97%)	< 0.001
Number of angiograms reviewed		99		144	
Median hours from shock onset to angiography*	100	12.8 [2.0, 108.4]	147	5.0 [2.6, 8.8]	< 0.001
Number of diseased vessels (%)	96		143		0.918
0		3.1		1.4	
1		8.3		12.6	
2		24.0		21.7	
3		64.6		64.3	
Left main coronary artery disease (%)	97	17.5	141	23.4	0.332
Jeopardy score	96	7.4 ± 3.6	143	7.7 ± 3.5	0.462
Left ventriculogram performed, n (%)	99	55 (55.6)	144	52 (36.4)	0.004
Left ventricular ejection fraction (%)	49	32.5 ± 13.9	46	29.1 ± 10.6	0.184
Mitral regurgitation (%)	54	1.2 ± 1.3	47	1.2 ± 1.6	0.756
0		44.4		55.3	0.871
1		18.5		6.4	
2		20.4		17.0	
3		9.3		4.3	
4†		7.4		17.0	
Ventricular septal defect (%)	54	0	50	0	
Flail mitral leaflet (%)	43	2.3	43	0	1.00
Left ventricular thrombus (%)	55	1.8	48	0	1.00

*Eleven initial medical stabilization (IMS) and four emergency revascularization (ERV) patients underwent coronary angiography before shock onset. Values in brackets represent 25th to 75th percentiles. Times are presented for all 247 patients in the trial who underwent coronary angiography, although only 243 were reviewed. There was a bimodal distribution of IMS angiography: half underwent angiography within 2 h of randomization and half 21 or more h postrandomization. Two patients had significant left main stenosis with left dominant coronary anatomy without additional coronary artery disease and were, therefore, classified as having both left main and three vessel coronary artery disease. †Four IMS and eight ERV patients had 4+ mitral regurgitation (mean left ventricular ejection fraction 29.7%) observed on left ventriculogram. Two of these patients were declared ineligible post-randomization and are excluded from survival analyses.

SHOCK = "SHould we emergently revascularize Occluded Coronaries for cardiogenic shock" trial.

artery disease in both groups with almost two-thirds of the patients having three-vessel disease and 21% having left main disease (Table 1). By protocol design, angiography was performed later after shock onset for IMS compared with ERV patients (median 12.8 vs. 5.0 h), and the rate of thrombolytic therapy use was higher in IMS patients (63.3% vs. 49.3%). There were no significant differences in the distribution of the number of diseased vessels or the rate of left main coronary artery (LM) disease between groups. The extent of coronary artery disease as measured by the coronary artery jeopardy score was also similar in the IMS and ERV groups (7.4 ± 3.6 vs. 7.7 ± 3.5, p = 0.462). Almost one-third (32%) had TIMI flow 3 in the culprit lesion at the time of angiography. The distribution of initial flow differed by treatment assignment with IMS patients more likely to have a patent vessel (p = 0.045) (Table 2). This finding was expected due to the association between thrombolytic therapy and TIMI flow (56% TIMI 2/3 flow in patients who received thrombolytic therapy vs. 40% TIMI 2/3 flow in those who did not). In addition, IMS patients were studied later and, therefore, had a longer period of time for thrombolysis to establish reperfusion.

Analysis of the left ventriculograms performed revealed that the left ventricular ejection fraction (LVEF) (31 ± 12%, n = 97) and the degree of MR (1.2 ± 1.4, n = 101) were similar in the two groups. No ventricular septal defects were noted in either group. There was a 2.3% incidence of

flail mitral leaflet and a 1.8% incidence left ventricular thrombus noted in the IMS group.

Culprit lesion characteristics. The distribution of culprit vessel location was similar for the two treatment groups (p = 0.298). The left anterior descending artery (LAD) was the culprit vessel in 49% of patients, and the right coronary artery (RCA) was the culprit vessel in 29% of patients (Table 2). The left circumflex (LCX), LM, and saphenous vein grafts (SVG) were less often culprit vessels. There was no significant difference in the distribution of culprit lesion types between the IMS and the ERV patients (p = 0.188).

Relationship of angiographic findings to survival. Overall one-year survival for all patients in the ERV group was 47% and 34% for IMS (p = 0.025) (13). The association between the number of diseased coronary arteries and one-year survival depended on treatment group (interaction p = 0.018). Disease severity was significantly correlated (p = 0.002) with one-year survival for the IMS group. However, in the ERV group the number of diseased coronary arteries was not associated with survival. In the IMS group, the hazard ratio for death was 2.59 (95% confidence interval 1.47 to 4.58, p = 0.001) per diseased vessel (0/1 vs. 2 vs. 3). In the ERV group, the hazard ratio for death per diseased vessel was 1.11 (95% confidence interval 0.79 to 1.56, p = 0.559). Similarly, while coronary artery jeopardy score was inversely correlated with one-year survival in the IMS group (p < .001), this correlation was not observed (p = 0.404) in

Table 2. Culprit Lesion Characteristics of SHOCK Trial Patients

Characteristics	n	Initial Medical Stabilization (%)	n	Emergency Revascularization (%)	p Value
Culprit vessel	90		137		0.298
LAD	48	53.3	64	46.7	
RCA	26	28.9	40	29.2	
LCX	10	11.1	19	13.9	
SVG	4	4.4	3	2.2	
LM	2	2.2	11	8.0	
Culprit lesion type	85		130		0.188
A	0	0.0	0	0.0	
B ₁	34	40.0	42	32.3	
B ₂	38	44.7	61	46.9	
C	13	15.3	27	20.8	
Culprit lesion TIMI flow	88		134		0.045
0	28	31.8	65	48.5	
1	9	10.2	9	6.7	
2	20	22.7	21	15.7	
3	31	35.2	39	29.1	

The vascular distribution supplied by the seven SVG culprit vessels were as follows: LAD (three), LCX (two), RCA (two). LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main; RCA = right coronary artery; SHOCK = "SHould we emergently revascularize Occluded Coronaries for cardiogenic shock" trial; SVG = saphenous vein graft; TIMI = Thrombolysis In Myocardial Infarction.

patients who were assigned to ERV (treatment group by jeopardy score interaction, $p = 0.036$). Of the IMS patients who underwent angiography, those who underwent early angiography (less than 2 h after randomization) had more extensive coronary artery disease (72% three-vessel disease) compared with those who underwent angiography several days later, on average (more than 2 h after randomization) (56% three-vessel disease). Thus, disease severity could explain the high (90%) mortality in IMS patients who did not undergo angiography.

Left ventricular ejection fraction was strongly correlated with one-year survival in all patients (Fig. 1), with an odds

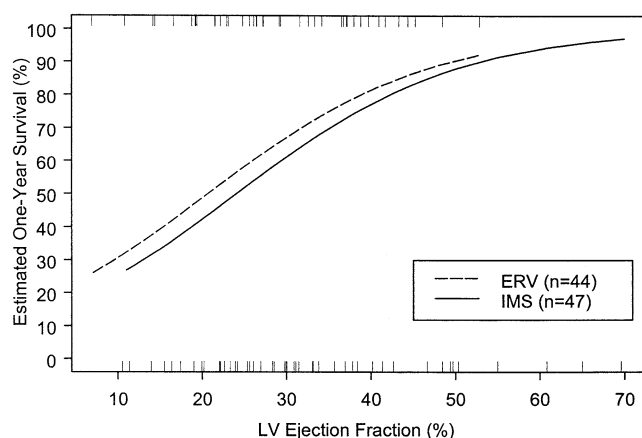


Figure 1. One-year survival estimates of "SHould we emergently revascularize Occluded Coronaries for cardiogenic shock" (SHOCK) trial patients by left ventricular (LV) ejection fraction. Survival rates increase with increasing ejection fraction ($p = 0.001$), and this relationship is independent of treatment assignment (interaction $p = 0.778$). For each level of ejection fraction, survival is better for emergency revascularization (ERV) patients. Data frequency for ERV and initial medical stabilization (IMS) patients is shown by fringe on top and bottom of the plot, respectively. Three patients identified as ineligible after randomization due to severe mitral regurgitation or LV free rupture were excluded.

ratio for death of 0.68 per 5-unit increase in ejection fraction (95% confidence interval 0.54 to 0.86, $p = 0.001$). Thus, for every 5-unit increase in baseline ejection fraction, the odds of dying in one year were reduced by one-third. This effect was independent of treatment group assignment (interaction $p = 0.778$). An increase in the amount of MR was inversely associated with one-year survival in the IMS group ($p = 0.017$). This was not observed in the ERV group ($p = 0.604$) although the number of patients in some of these categories was small (Table 3), and the treatment group by MR grade interaction was not significant.

In ERV patients and those selected to undergo angiography in the IMS group, the greatest one-year survival was seen when the RCA was the culprit vessel (Table 3). Mean LVEF was highest ($39.1 \pm 14.1\%$) in patients with the RCA as the culprit vessel. After adjustment for LVEF ($n = 85$), the survival of patients with a right coronary culprit artery was similar to that of patients with a LAD culprit artery but still higher than patients with either an LM, LCX, or SVG culprit. In the IMS group, there was 100% mortality at one year when the culprit vessel was the LM or a SVG (six patients). Severity of culprit lesion type and culprit lesion thrombus score did not have a significant association with survival in either group. The majority of patients (78%) had grade 0-1 collaterals to the culprit vessel. Collateral score did not correlate with one-year survival in either treatment group. In this study, a composite measure of initial TIMI 2/3 flow or Rentrop 2/3 collateral score was not associated with improved one-year survival compared with low-flow states (TIMI 0/1 flow and Rentrop 0/1 collateral score).

Multivariate analysis. Cox proportional hazards regression models for one-year survival were constructed, which considered all of the angiographic variables analyzed as well as

Table 3. Relationship of SHOCK Trial Core Laboratory Angiographic Findings to One-Year Survival

Characteristics	One-Year Survival Rate		
	n	%	p Value*
Number of diseased vessels†			0.013/0.005
0/1	31	64.5	
2	50	60.0	
3	151	41.7	
Mitral regurgitation			0.321/0.039
0	48	68.8	
1+	13	53.9	
2+	19	52.6	
3+	7	42.9	
4+	10	40.0	
Culprit vessel			< 0.001
RCA	63	68.3	
LAD	111	46.0	
LCX	27	33.3	
LM	12	25.0	
SVG	7	14.3	
Initial TIMI flow			0.846/0.498
0	90	45.6	
1	18	50.0	
2	41	53.7	
3	66	50.0	
Culprit lesion type (%)			0.052/0.065
B ₁	75	52.0	
B ₂	95	52.6	
C	39	30.8	
Culprit vessel collateral score (Rentrop)			0.874/0.961
0	128	50.0	
1	30	50.0	
2	37	46.0	
3	8	62.5	
Culprit lesion thrombus score			0.018/0.077
0	42	50.0	
1	116	41.4	
2	13	53.9	
3	24	79.2	
4	20	50.0	
TIMI 2/3 flow or Rentrop 2/3			0.451/NA
"Low flow"	63	44.4	
Patent artery	145	51.0	

n represents the total number of patients in each angiographic subgroup. One-year survival was unavailable for one patient. Six patients with severe mitral regurgitation, left ventricular free wall rupture, or aortic dissection identified post-randomization are excluded. *Fisher exact test p value/Mantel-Haenszel test for linear trend p value. †Treatment assignment by characteristic interaction p = 0.020 by logistic regression and p = 0.018 by Cox regression.

LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main coronary artery; NA = not applicable; RCA = right coronary artery; SHOCK = "SHould we emergently revascularize Occluded Coronaries for cardiogenic shock" trial; SVG = saphenous vein graft; TIMI = Thrombolysis In Myocardial Infarction.

the following six clinical variables often found to be risk factors in acute myocardial infarction or shock populations: age, gender, systolic blood pressure, anterior myocardial infarction, cardiac index, and pulmonary capillary wedge pressure. Two final models were composed: one using left ventriculogram data (44% of SHOCK angiography patients) and one without incorporating left ventriculogram data. Table 4 summarizes the model that does not incorporate left ventriculogram measures (n = 214). This model

includes increasing age, increasing number of diseased vessels (in the IMS group, only a twofold increase in risk of death with each additional diseased artery was found; interaction p = 0.084), decreasing initial TIMI flow grade, and non-RCA culprit lesions as independent risk factors for death at one year. Table 5 summarizes the left ventriculogram model (n = 73), which includes increasing age, female gender, decreasing cardiac index and LVEF, decreasing initial TIMI flow grade (in the ERV group only), and non-RCA/non-LAD culprit lesions as independent risk factors. The number of diseased coronary arteries is not an independent predictor of survival in the IMS group in this multivariate model because coronary anatomy correlated with LVEF. Among patients with left ventriculograms, mean LVEF was 46% for patients with 0 or 1 diseased arteries, 33% for two-vessel disease, and 29% for three-vessel disease.

DISCUSSION

Angiographic findings in the SHOCK trial revealed high rates of LM and three-vessel coronary artery disease with a predominance of LAD culprit arteries, initial TIMI 0, 1 flow, and complex lesion types. These findings suggest an important role for further innovations in pharmacologic (22) and catheter-based interventional approaches as well as for urgent coronary artery bypass surgery, despite high risk. Coronary artery bypass grafting was urgently performed in 39% of the SHOCK trial patients assigned to early revascularization and was an important factor in the overall improved one-year survival for this treatment group (12,13). Nevertheless, in the National Registry of Myocardial Infarction, the low rate of 2% to 5% early CABG for shock patients has not changed between 1994 and 2001 (23). This is in contrast to significantly increasing rates of PCI for shock. The rapid death of 90% of IMS patients who did not undergo angiography is a further indication for urgent angiography and early revascularization.

In the presence of cardiogenic shock, LVEF, initial TIMI flow, and culprit vessel were found to be independent correlates of one-year survival. Interestingly, left ventricular function measured with intraaortic balloon pump and inotropic support was moderately, but not severely, depressed. Similar levels of left ventricular dysfunction (LVEF, 29%) are seen in patients with chronic congestive heart failure due to ischemic heart disease with New York Heart Association functional class II and III (24) and in early post-myocardial infarction patients, with mild or no congestive heart failure (LVEF, 33%) (25). This suggests a complex interplay of acute changes in left ventricular performance and systemic vascular resistance in the genesis of shock (26,27).

Normal TIMI 3 flow before mechanical reperfusion has been found to be an independent determinant of survival in an analysis from the Primary Angioplasty in Myocardial Infarction (PAMI) trials; however, patients with cardiogenic shock were excluded from those studies (28). Thus,

Table 4. Multivariate Model for One-Year Survival (n = 214): All Angiography Patients

Variables	Hazard Ratio for Death	95% CI	p Value
Age (yrs)	1.36 per 10 year increase	(1.12, 1.65)	0.002
Initial TIMI flow grade	0.85 per 1 grade increase	(0.73, 0.99)	0.032
Number of diseased vessels			0.084*
ERV	1.08 per vessel	(0.74, 1.57)	0.708
IMS	2.01 per vessel	(1.10, 3.69)	0.024
Culprit vessel			0.0004
Right coronary	0.32†	(0.18, 0.57)	
Left anterior descending	0.78†	(0.50, 1.23)	
Right coronary vs. left anterior descending	0.41	(0.32, 0.52)	

*p value for treatment group × number of diseased vessels interaction term; †Compared with left circumflex, left main, and saphenous vein graft.

CI = confidence interval; ERV = emergency revascularization; IMS = initial medical stabilization; TIMI = Thrombolysis In Myocardial Infarction.

this is the first report to suggest the importance of early reperfusion before revascularization in patients with cardiogenic shock. In the IMS patients who underwent angiography, for whom the revascularization rate was low (37%), extent of coronary artery disease correlated with survival. However, for the ERV group, which had a high rate of revascularization (87%), there was no association of extent of coronary artery disease at baseline and survival in the shock cohort. The latter observation is not surprising as revascularization with bypass surgery is known to “neutralize” the impact of the number of diseased coronary arteries on survival (29,30).

Although inferior myocardial infarction results in fewer deaths than anterior myocardial infarction for all patients having myocardial infarction, differential outcome based on culprit vessel has not been previously reported for patients with confirmed shock due to predominant left ventricular failure. In the current study, RCA culprit was associated with superior survival. The limited subset with complete data available for the multivariate model and the selective performance of left ventricular angiography, likely based on patient stability, preclude a full understanding of the reason for this observation. Infarction in the distribution of the RCA can cause shock due to combined right ventricular and

left ventricular dysfunction. Right ventricular dysfunction may resolve more completely than left ventricular dysfunction after reperfusion and, therefore, be associated with improved outcome. The observation that outcome may vary by culprit vessel should be considered in risk models and in assuring balanced groups in small randomized trials.

Study limitations. Although 95% of patients assigned to emergency revascularization had undergone angiography and had core laboratory review, only two-thirds of patients assigned to initial medical stabilization were selected to undergo angiography. Of the remaining third, 45/50 (90%) died rapidly and were not studied. Therefore, the association of anatomic findings and survival in the IMS group is representative only of survivors of the early phase of shock. Angiographic findings from the ERV group are most representative of those that could be expected in patients with shock similar to those enrolled in this trial because selection bias is minimized. Furthermore, only 44% of angiography patients had a left ventriculogram completed (36% in ERV, 56% in IMS). The difference in percentage of patients from each group having a left ventriculogram performed is most likely related to a concern for giving a contrast load during an acute myocardial infarction complicated by cardiogenic shock. It should also be noted that

Table 5. Multivariate Model for One-Year Survival (n = 73): Left Ventriculogram Cohort

Variables	Hazard Ratio for Death	95% CI	p Value
Age (yrs)	1.56 per 10 year increase	(0.94, 2.28)	0.022
Female	6.35 vs. male	(2.33, 17.28)	< 0.001
Cardiac index	0.51 per 0.5 unit increase	(0.30, 0.86)	0.011
LV ejection fraction	0.47 per 10 unit increase	(0.28, 0.79)	0.004
Initial TIMI flow grade			0.004*
ERV	0.37 per 1 grade increase	(0.21, 0.65)	< 0.001
IMS	1.36 per 1 grade increase	(0.79, 2.36)	0.266
Culprit vessel			0.034
Right coronary	0.27†	(0.06, 1.15)	
Left anterior descending	0.23†	(0.08, 0.73)	
Right coronary vs. left anterior descending	1.15	(0.29, 4.59)	

*p value for treatment group × initial TIMI flow grade interaction term; †Compared with left circumflex, left main, and saphenous vein graft.

CI = confidence interval; ERV = emergency revascularization; IMS = initial medical stabilization; LV = left ventricular; TIMI = Thrombolysis In Myocardial Infarction.

LVEF was often measured on inotropic and intraaortic balloon pump support. Estimates of LVEF and MR presented here may not be representative of unsupported cardiogenic shock.

Conclusions. Cardiogenic shock is associated with extensive coronary artery disease and only moderately severe depression of left ventricular function. Left ventricular function and the culprit vessel are independently correlated with one-year survival. Emergency revascularization by angioplasty or bypass surgery improves survival in cardiogenic shock by neutralizing the impact of the extent of coronary artery disease on survival.

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REFERENCES

1. Diver DJ, Gersh BJ. Efficacy of percutaneous transluminal coronary angioplasty: randomized trials of myocardial revascularization. In: Topol EJ, editor. *Textbook of Interventional Cardiology*. 3rd edition. Philadelphia, PA: WB Saunders, 1999:209-37.
2. Hammermeister KE, De Rouen TA, Dodge HT. Variables predictive of survival in patients with coronary artery disease: selection by univariate and multivariate analysis from the clinical, electrocardiographic, exercise, arteriographic, and quantitative angiographic evaluation. *Circulation* 1979;59:421-30.
3. Weiner DA, Ryan T, McCabe CH, et al. Prognostic importance of a clinical profile and exercise test in medically treated patients with coronary artery disease. *J Am Coll Cardiol* 1984;3:772-9.
4. Califf RM, Mark DB, Harrell FE, et al. Importance of clinical measures of ischemia in the prognosis of patients with documented coronary artery disease. *J Am Coll Cardiol* 1988;11:20-6.
5. Detre K, Peduzzi P, Murphy M, et al. Effect of bypass surgery survival in patients with low- and high-risk subgroups delineated by use of simple clinical variables. *Circulation* 1981;63:1329-8.
6. CASS Principal Investigators. Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery: survival data. *Circulation* 1983;68:939-50.
7. Passamani E, Davis KB, Gillispie MJ, Killip T, for the CASS Principle Investigators and Associates. A randomized trial of coronary bypass surgery: survival of patients with a low ejection fraction. *N Engl J Med* 1985;312:1665-71.
8. European Coronary Surgery Study Group. Long term results of prospective randomized trial of coronary artery bypass surgery in stable angina pectoris. *Lancet* 1982;2:1173-80.
9. Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Eleven-year survival in the Veterans Administration Randomized Trial of Coronary Bypass Surgery for Stable Angina. *N Engl J Med* 1984;311:1333-9.
10. White HD, Norris RM, Brown MA, et al. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. *Circulation* 1987;76:44-51.
11. White HD, Cross DB, Elliott JM, et al. Long-term prognostic importance of patency of the infarct-related coronary artery after thrombolytic therapy for acute myocardial infarction. *Circulation* 1994;89:61-7.
12. Hochman JS, Sleeper LA, Webb JG, et al., for the SHOCK Investigators. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *N Engl J Med* 1999;341:625-34.
13. Hochman JS, Sleeper LA, Webb JG, et al. Effect of early revascularization for cardiogenic shock on 1 year mortality: the SHOCK trial results. *JAMA* 2001;285:190-2.
14. Hochman JS, Sleeper LA, Godfrey E, et al., for the SHOCK Trial Study Group. Should we emergency revascularize occluded coronaries for cardiogenic shock: an international randomized trial of emergency PTCA/CABG-trial design. *Am Heart J* 1999;137:313-21.
15. The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction: results of the Thrombolysis in Myocardial Infarction (TIMI) phase II trial. *N Engl J Med* 1989;320:618-27.
16. Rentrop P, Cohen M, Blanke H, et al. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. *J Am Coll Cardiol* 1982;5:587-92.
17. Califf RM, Phillips HR, Hindman MC, et al. Prognostic value of a coronary artery jeopardy score. *J Am Coll Cardiol* 1985;5:1055-63.
18. Ryan TJ, Faxon DP, Gunnary RM, et al. Guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Coronary Angioplasty). *J Am Coll Cardiol* 1998;12:529-45.
19. Ellis SG, Vandormael MG, Cowley MJ, et al., and the Multivessel Angioplasty Prognosis Study Group. Coronary morphologic and clinical determinants of procedural outcome with angioplasty for multivessel coronary disease: implications for patient selection. *Circulation* 1990;82:1193-202.
20. Sheehan FH. Cardiac angiography. In: Marcus ML, Schelbert HR, Skorton DJ, Wolf GL, editors. *Cardiac Imaging—A Companion to Braunwald's Heart Disease*. Philadelphia, PA: WB Saunders Company, 1991:109-48.
21. Kalbfleisch JD, Prentice RL. *The Statistical Analysis of Failure Time Data*. New York, NY: Wiley, 1980:12-5.
22. Cotter G, Kaluski E, Blatt A, et al. L-NMMA (a nitric oxide synthase inhibitor) is effective in the treatment of cardiogenic shock. *Circulation* 2000;101:1358-61.
23. Babaev A, Every N, Frederick P, et al. Trends in revascularization and mortality in patients with cardiogenic shock complicating acute myocardial infarction: observations from the National Registry of Myocardial Infarction. *Circulation* 2002;106:II364.
24. Australia/New Zealand Heart Failure Research Collaborative Group. Randomized, placebo-controlled trial of carvedilol in patients with congestive heart failure due to ischemic heart failure. *Lancet* 1997;349:375-80.
25. Dargie HJ. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. *Lancet* 2001;357:1385-90.
26. Cotter G, Moshkovitz Y, Milovanov O, et al. Acute heart failure: a novel approach to its pathogenesis and treatment. *Eur J Heart Fail* 2002;4:457-61.
27. Hochman JS. Cardiogenic shock complicating acute myocardial infarction: expanding the paradigm. *Circulation* 2003;107:2998-3002.
28. Stone G, Cox D, Garcia E, et al. Normal flow (TIMI-3) before mechanical reperfusion therapy is an independent determinant of survival in acute myocardial infarction: analysis from the Primary Angioplasty in Myocardial Infarction trials. *Circulation* 2001;104:636-41.
29. Califf RM, Harrell FE Jr., Lee KL, et al. The evolution of medical and surgical therapy for coronary artery disease: a 15-year perspective. *JAMA* 1989;261:2077-86.
30. Kirklin JW, Akins CW, Blackstone EH, et al. ACC/AHA task force report: guidelines and indications for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association task force on assessment of diagnostic and therapeutic cardiovascular procedures (subcommittee on coronary artery bypass surgery). *J Am Coll Cardiol* 1991;17:543-89.

APPENDIX

For a list of committee members, principal investigators, and study coordinators in the SHOCK trial, please see the October 15, 2003, issue of *JACC* at www.cardiosource.com/jacc.html.