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Cardiogenic Shock Complicating Acute Myocardial Infarction—Etiologies, Management and Outcome: A Report from the SHOCK Trial Registry

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OBJECTIVES This SHOCK Study report seeks to provide an overview of patients with cardiogenic shock (CS) complicating acute myocardial infarction (MI) and the outcome with various treatments. The outcome of patients undergoing revascularization in the SHOCK Trial Registry and SHOCK Trial are compared.

BACKGROUND Cardiogenic shock is the leading cause of death in patients hospitalized for acute MI. The randomized SHOCK Trial reported improved six-month survival with early revascularization.

METHODS Patients with CS complicating acute MI who were not enrolled in the concurrent randomized trial were registered. Patient characteristics were recorded as were procedures and vital status at hospital discharge.

RESULTS Between April 1993 and August 1997, 1,190 patients with CS were registered and 232 were randomized in the SHOCK Trial. Predominant left ventricular failure (78.5%) was most common, with isolated right ventricular shock in 2.8%, severe mitral regurgitation in 6.9%, ventricular septal rupture in 3.9% and tamponade in 1.4%. In-hospital Registry mortality was 60%, with ventricular septal rupture associated with a significantly higher mortality (87.3%) than all other categories ($p < 0.01$). The risk profile and mortality were lower for Registry patients who were managed with thrombolytic therapy and/or intra-aortic balloon counterpulsation, coronary angiography, angioplasty and/or coronary artery bypass surgery. After adjusting for these differences, the extent to which survival was improved with early revascularization was similar to that observed in the randomized SHOCK Trial.

CONCLUSIONS In this prospective Registry the etiology of CS was a mechanical complication in 12%. The similarity of the beneficial treatment effect in patients undergoing early revascularization in the SHOCK Trial Registry and SHOCK Trial provides strong support for the generalizability of the SHOCK Trial results. (J Am Coll Cardiol 2000;36:1063–70) © 2000 by the American College of Cardiology

Over the past 15 years, 30-day mortality and overall complications of acute myocardial infarction (MI) have been substantially reduced by the use of reperfusion therapy (1–3). However, cardiogenic shock (CS) remains the leading cause of death in patients hospitalized with acute MI (4). Thrombolytic therapy alone has had a limited effect on the outcome of patients presenting with pump failure (1,3). Further insights into the mechanisms of shock and the outcomes of various treatment modalities currently in use are needed to substantially alter the high mortality rate of CS.

Nonrandomized studies have reported a reduced mortality rate for patients with CS undergoing revascularization (5–10). A recently reported international randomized trial, SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK? (the SHOCK Trial), was supported by the National Heart, Lung, and Blood Institute. The SHOCK Trial assessed the effects on 30-day mortality of a direct invasive strategy (emergency early coronary angiography and revascularization), compared with a strategy of initial medical stabilization (including thrombolysis and intra-aortic balloon counterpulsion [IABP]) followed by delayed mechanical revascularization as clinically determined (11). Concurrent with this randomized trial, data have also been collected on patients with suspected CS complicating acute MI who were not randomized at the 36 participating institutions. This Registry of the SHOCK Trial offers a unique opportunity to: 1) further define the mechanisms responsible for CS in patients with acute MI, 2) review the utilization rates of therapeutic modalities and their impact on mortality, and 3) compare the effect of early revascularization on mortality in both the Registry and Trial

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Abbreviations and Acronyms

CK	=	creatine kinase
CS	=	cardiogenic shock
LBBB	=	left bundle branch block
LV	=	left ventricular, left ventricle
MI	=	myocardial infarction
MR	=	mitral regurgitation
PCWP	=	pulmonary capillary wedge pressure
RV	=	right ventricular, right ventricle
SHOCK	=	SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK?
VSR	=	ventricular septal rupture

cohorts. This report provides an overview of the entire SHOCK study. In-depth analyses of the major etiologies of shock, and the various treatment modalities, are presented in other reports in this supplementary issue of the *Journal*. Enrollment in the SHOCK Trial Registry and SHOCK Trial started in April 1993 and was completed for the Registry on August 31, 1997, and for the Trial on November 30, 1998. Eleven hundred and ninety patients were enrolled in the SHOCK Trial Registry, and 232 patients were enrolled in the SHOCK Trial as of August 31, 1997. This is the largest body of experience prospectively collected to date relating to unselected patients with CS complicating acute MI.

METHODS

Patient sample. One thousand one hundred ninety patients with suspected CS complicating acute MI were prospectively registered. A local discharge diagnosis of acute MI and CS (DRG's 410 and 785.51) or a suspected diagnosis of CS complicating acute MI, regardless of the final discharge diagnosis, constituted the criteria for registry enrollment.

Thirty-six centers were initiated in a staggered fashion, with the first patient enrolled in April 1993. Seven hundred and thirty patients (61%) were registered in 24 U.S. centers, 256 (22%) in five Canadian centers, 76 (6%) in four Belgian centers and 128 (11%) in Australia, New Zealand and Brazil. All centers obtained Institutional Review Board or Ethics Committee approval for the abstraction of medical records.

Enrollment in the SHOCK Trial Registry rather than the randomized SHOCK Trial occurred if a patient with suspected CS failed to meet all trial inclusion criteria or specified time windows, met a trial exclusion criterion, or was unable or refused to give consent. As previously reported (12), the criteria for CS for the randomized SHOCK Trial consisted of: 1) hypotension (systolic blood pressure $<$90 mm Hg for at least 30 min, need for vasopressors, or IABP support); 2) clinical evidence of end organ hypoperfusion; and 3) confirmatory hemodynamic or radiographic features: pulmonary capillary wedge pressure (PCWP) $\geq$15 mm Hg and cardiac index $\leq$2.2 l/min/m^2 (for non-anterior MI) or pulmonary congestion on a chest X-ray, with subsequent hemodynamic confirmation (for anterior MI). Moreover, only patients with CS due to predominant LV failure with ECG evidence of recent total coronary occlusion, e.g., ST elevation, Q waves, new left bundle branch block (LBBB) or posterior MI with anterior ST depression, were eligible for the trial.

Enrollment in the SHOCK Trial Registry, however, which forms the basis for the current report, required only that CS be suspected on clinical grounds. Etiologies of CS other than predominant LV failure (e.g., acute severe mitral regurgitation [MR], ventricular septal rupture [VSR], isolated right ventricular [RV] failure, cardiac tamponade or rupture, prior severe valvular heart disease, excess beta or calcium channel blockade, dilated cardiomyopathy, and CS associated with recent hemorrhage or cardiac catheterization laboratory complication) constituted clinical exclusion criteria in the SHOCK Trial, and patients with such etiologies were entered into the SHOCK Trial Registry. Patients with VSR or acute severe MR without CS were not registered, because the diagnosis of suspected CS was required. Patients with any etiology of CS whose course was outside the time windows of CS $\leq$36 h after MI and randomization $\leq$12 h after shock diagnosis were also included in the SHOCK Trial Registry.

Data from the 302 patients enrolled in the randomized SHOCK Trial between April 1993 and November 1998 (11) are presented: 1) to assess the effect of revascularization on mortality in the SHOCK Trial Registry, compared to the SHOCK Trial, and 2) to assess the incidence of major etiologies of shock for all screened (Registry and Trial) patients. For the latter analysis, we included only the 232 predominant LV failure patients enrolled in the Trial as of August 31, 1997, the time period concurrent with Registry enrollment. Mortality rates for the major shock etiologies are presented for: 1) all Registry patients, 2) the predominant LV failure cohort within the Registry and 3) the Registry and concurrent Trial patients combined.

Data collection. Data were abstracted from the medical record by the SHOCK study coordinators, who were centrally trained to complete standardized study report forms. Patient characteristics, MI characteristics, hemodynamics, medication and procedure utilization, and vital status at hospital discharge were recorded.

Definitions. Predominant LV failure was designated as the etiology of CS when none of the other following major shock categories was indicated as present: isolated RV shock, mechanical cause (acute severe MR, VSR, or tamponade/LV rupture), prior severe valvular heart disease, excess beta or calcium channel blockade, or shock resulting from a cardiac catheterization laboratory complication. ECG locations were defined as follows (GUSTO I) (13):

$V_1 - V_4$ Anterior; II, III, AVF Inferior;

$V_5 - V_6$ Apical; I, AVL Lateral; $V_1 - V_2$ Posterior.

Reinfarction was defined as follows: 1) recurrent chest pain or ischemic symptoms ≥30 min and recurrent ST-segment elevation, new Q waves, or new LBBB; 2) total creatine kinase (CK) at least twice the upper limit of normal and >25% or 200 U/mL over the previous value, with an elevated CK-MB level; or 3) a rise in CK-MB above the upper limit of normal after it had reverted to the normal range.

Hemodynamic data. Right heart catheterization was performed in 790 Registry patients, with PCWP recorded in 739 patients and cardiac index in 562 patients. Left ventricular (LV) ejection fraction was measured at any time during the hospitalization in 468 patients, by LV angiography (37%), gated blood pool scan (4%) or echocardiography (59%). Hemodynamic measurements included those recorded while the patient was receiving supportive therapy.

Statistical methods. The characteristics of patients with predominant LV failure versus other causes of shock were compared using the Fisher exact test for categorical variables, the Wilcoxon rank-sum test for ordinal and non-normally distributed continuous variables, and Student *t*-test for normally distributed continuous variables. Median values are presented with 25th and 75th percentiles, and means with standard deviation. In six patients there were multiple causes of shock, and for the purposes of comparison of mortality rates these patients were categorized as having one cause based on the following hierarchical ranking: 1) predominant LV failure, 2) VSR, 3) severe MR, 4) isolated RV failure, 5) cardiac tamponade and 6) other cause of shock. The p values reported for the comparisons of these groups are unadjusted for multiple comparisons. Four patients are included in the overall mortality analysis; but the etiology of shock was unknown, and these patients are not included in any shock subgroup. Logistic regression was used to model mortality (dead vs. alive) of patients with predominant LV failure by revascularization status, with adjustment for factors associated with selection for revascularization. Forty-one patients were excluded from modeling, because the revascularization attempt occurred before shock onset. Models, including cardiac index as a covariate, were restricted (by definition) to patients undergoing right heart catheterization, approximately half of all predominant LV failure patients. All analyses were conducted using the Statistical Analysis System (SAS Institute; Cary, North Carolina).

Results. Eleven hundred and ninety patients were registered as of August 31, 1997, the closing date of the SHOCK Trial Registry database. The SHOCK Trial randomized 232 patients with predominant LV failure during the concurrent period of April 1993 through August 1997 and an additional 70 patients as of the completion of Trial enrollment on November 30, 1998. Characteristics of the patients in the Registry are shown in Table 1. The mean age was 68.7 ± 11.8 years, and 40.3% were women. There were high rates of history of MI, hypertension, diabetes and smoking.

Table 1. Registry Patient Characteristics

	All Patients	Predominant LV Failure	Other Categories
n	1,190	884	306
Age (yrs)	68.7 ± 11.8	68.5 ± 12.1	69.5 ± 11.1
Male (%)	59.7	63.6	48.3*
White, non-Hispanic (%)	82.0	83.6	77.4**
History of MI (%)	37.4	40.1	29.5***
History of hypertension (%)	53.1	51.7	57.2
Diabetes (%)	32.6	32.8	32.0
Smoker (%)	50.1	51.5	45.9
History of elevated lipids (%)	41.8	40.2	46.4
History of renal insufficiency (%)	10.9	10.7	11.6
History of PTCA (%)	6.2	6.7	4.8
History of CABG (%)	9.6	10.1	8.1
Other severe illness (%)	18.1	17.7	19.4
History of peripheral vascular disease (%)	17.9	18.8	15.4

*$p < 0.0001$ vs. LV failure; **$p = 0.019$ vs. LV failure; ***$p = 0.001$ vs. LV failure.

Major shock categories. The incidences of the major categories of shock were assessed. Predominant LV failure caused CS in 78.5% of all (Registry and Trial, n = 1,422) cases. Acute severe MR was diagnosed in 98 (6.9%), VSR in 55 (3.9%), isolated RV shock in 40 (2.8%), tamponade/rupture in 20 (1.4%) and other causes (as defined in the Methods section) in 95 (6.7%) (Fig. 1). Six patients fell into more than one category (see the Methods section), and four patients could not be categorized.

MI characteristics of Registry patients. Multiple-site infarct locations were often noted on ECG (50%). Anterior MI was diagnosed in 55%, inferior in 46%, posterior in 19%, lateral in 32%, apical in 11% and unknown in 10%. Electrocardiographic evidence of ST elevation and/or Q waves or new LBBB MI was present in 79.1%. Median time from MI to shock was 7.0 h (25th to 75th percentile, 1.8 to 22.0). The highest creatine phosphokinase was elevated a median of 8.4 times (25th to 75th percentile, 2.9 to 18.6) above the upper limit of normal. Recurrent MI and recurrent ischemia occurred between the initial MI associated with hospital admission and shock in 9.3% and 19.7% of patients, respectively, and were associated with hypotension in 86.1% and 69.5%, respectively.

Hemodynamics and pharmacologic support. The hemodynamic values for all Registry patients, including those with predominant LV failure causing CS (Table 2), were most often recorded after support measures (IABP and/or vasopressors) were instituted. For the 790 who underwent right heart catheterization, the range of cardiac index and PCWP was broad. Pharmacologic support included vasopressors in 95.1% (dopamine 89.3%, norepinephrine 31.6%, epinephrine 41.9%) and/or dobutamine in 70.1%.

Predominant LV failure. In the Registry group with predominant LV failure (n = 884), patients were more likely to have had prior MI (40.1% vs. 29.5%, p = 0.001)

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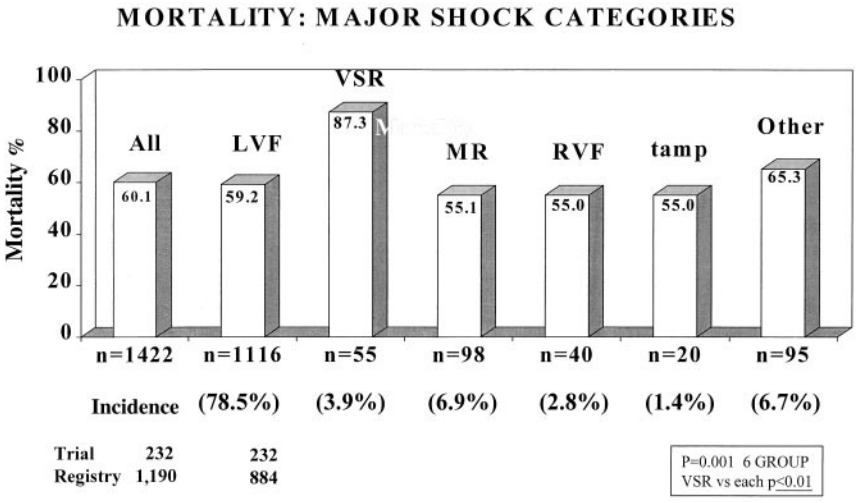

Figure 1. The complete population of all shock patients screened, including 1,190 Registered patients and 232 Trial patients randomized concurrent with the Registry from 4/93 – 8/97, is represented in the figure. Of the 1,116 patients with LVF, 844 were Registry and 232 were Trial. The mortality rates for the 1,190 Registry patients and 884 LVF Registry patients are 61.4% and 60.8%, respectively. The incidence (%, below each bar) and mortality for the major shock categories is shown. LVF = predominant LV failure (see Methods section), RVF = isolated RV shock, MR = acute severe mitral regurgitation, VSR = ventricular septal rupture, Tamp = cardiac tamponade/rupture. Other causes are described in the methods section. The categorization of cardiogenic shock was unknown in four patients who had a 75% mortality rate. Between group comparisons are based on hierarchical groups in order from left to right. Six patients fell into more than one category (see text).

and to be white (83.6% vs. 77.4%, $p = 0.019$), compared with patients in the other shock categories (Table 1). Women represented a smaller proportion of the Registry patients with predominant LV failure, compared with the other shock categories (36.4% vs. 51.7%, $p < 0.0001$). Otherwise, there were no significant differences in the patient characteristics of those with predominant LV failure compared to those in the other shock categories. Among LV failure patients, anterior MI location on ECG was most common (58.8%), although 34.4% had inferior MI without anterior involvement. Of the latter, 100 (38.3%) had a prior MI. Therefore, 21.2% of those with predominant LV failure had a first inferior MI with no anterior involvement. Over half of this subgroup (53.4%) had lateral, posterior and/or apical involvement on ECG.

Mortality. In-hospital mortality for the major shock categories is shown in Figure 1, with an overall (Registry and concurrent Trial combined) rate of 60.1%. The rates were significantly different among the six etiologies. Ventricular septal rupture patients had higher mortality (87.3%) than those with predominant LV failure ($p = 0.0002$), RV shock ($p = 0.002$), MR ($p = 0.0001$), as well as every other category ($p < 0.01$). The mean in-hospital LV ejection fraction of 257 Registry survivors was significantly higher than that of 211 nonsurvivors (34.3 ± 13.7% vs. 30.4 ± 13.7%, $p < 0.002$). Within the predominant LV failure subgroup, the mean LV ejection fraction for 196 survivors was higher than that of 143 nonsurvivors (32.9 ± 12.8 % vs. 27.4 ± 11.7%, $p < 0.0001$). Registry patients who were transferred (44%) to the SHOCK Trial tertiary care center had a markedly lower mortality than direct admissions (56%) to those centers (54% vs. 67%, $p = 0.001$).

Table 2. Hemodynamic Profile of Registry Patients*

	All Registry Patients (n = 1,190)		Predominant LV Failure (n = 884)	
	n	Mean ± SD	N	Mean ± SD
Systolic BP (mm Hg)	1,124	87.7 ± 22.3	833	88.4 ± 23.0
Diastolic BP (mm Hg)	976	52.3 ± 17.0	729	52.7 ± 17.2
Heart rate (mm Hg)	1,121	95.7 ± 26.2	832	95.2 ± 25.8
PCWP (mm Hg)	739	23.4 ± 8.4	534	23.7 ± 8.6
Cardiac index (1/min/m^2)	562	2.08 ± 0.77	408	2.06 ± 0.78
PA systolic (mm Hg)	482	41.2 ± 12.8	341	41.1 ± 12.8
PA diastolic (mm Hg)	484	23.6 ± 7.8	343	23.8 ± 8.0
LV ejection fraction (%)	468	32.6 ± 13.8	339	30.6 ± 12.6

*Measurements were most often obtained on support measures; sympathomimetic amines and/or intra-aortic balloon counterpulsation

BP = Blood pressure; LV = Left ventricular; PA = Pulmonary artery; PCWP = Pulmonary capillary wedge pressure.

Procedure utilization and outcome for Registry patients with predominant LV failure. Registry patients were clinically selected (not randomized) to undergo different treatments, which were not mutually exclusive. Thrombolytic therapy was administered in 36%, while IABP was placed in 53%. Thrombolytic therapy alone (15%), IABP use alone (33%), and thrombolytic therapy with IABP use (20%) were each associated with lower mortality than no IABP or no thrombolytic therapy use (32%) (62.9%, 52.6%, 46.5% vs. 76.5% in-hospital mortality, respectively, $p < 0.005$).

Left heart cardiac catheterization with coronary angiography and revascularization performed at any time during the hospitalization are shown in Figure 2. Also shown are in-hospital mortality rates for patients undergoing early percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft surgery (CABG) within 18 h of shock diagnosis. This timing of revascularization corre-

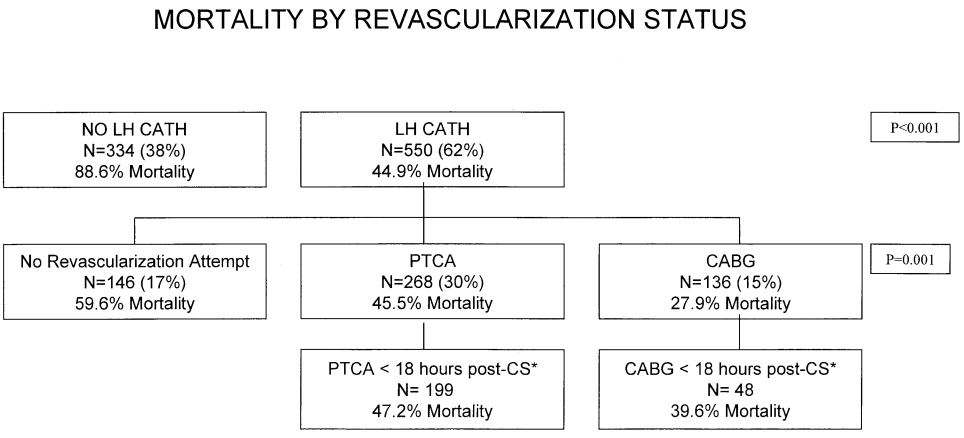

Figure 2. Patients with predominant LV failure clinically selected to undergo left heart catheterization and coronary angiography (LH cath) had a lower mortality than those with no LH cath. Patients with no revascularization attempt had higher mortality, with the lowest mortality observed in patients selected to undergo CABG. The CABG group includes 18 patients who underwent CABG post-PTCA; these patients are not included in the PTCA group. The mortality rates for those undergoing early revascularization (within 18 h of shock diagnosis), at a time comparable to the randomized SHOCK Trial, are shown. The median times to PTCA and CABG are 2.8 and 3.9 h, respectively, for those revascularized <18 h post-shock.
*Patients with PTCA or CABG prior to shock are excluded.

sponds to the upper time limit for early revascularization after shock in the SHOCK Trial. Left ventricular assist devices were used in 0.8% (based on 856 with available data). Performance of coronary angiography, PTCA, and CABG were each associated with lower in-hospital mortality rates than in patients managed without these treatments (Fig. 2). Reports on IABP and thrombolysis (14), and angiographic findings (15), appear in this supplementary issue of the *Journal*.

Registry patients undergoing PTCA and CABG at any time during the shock hospitalization were younger (64.2 ± 11.6 vs. 72.0 ± 11.3 years, $p < 0.0001$), had a lower incidence of prior MI (35.3% vs. 44.2%, $p = 0.009$), diabetes (28.2% vs. 36.7%, $p = 0.009$), and prior CHF (12.8% vs. 25.7%, $p < 0.0001$), and a higher cardiac index (2.2 ± 0.8 vs. 1.9 ± 0.7 l/min/m^2, $p = 0.001$) and LV ejection fraction (32.1 ± 12.4 % vs. 28.5 ± 12.7 %, $p = 0.005$), and more often had CS diagnosis within 6 h of MI (48.2% vs. 39.6%, $p = 0.02$). The odds ratio (OR) for death, after adjusting for selection factors, for patients undergoing PTCA or CABG, compared with those without revascularization, is shown in Table 3. The effect of revascularization observed in the SHOCK Trial was obtained by comparing all trial patients undergoing a revascularization attempt at any time during hospitalization with those who did not (without regard to group assignment). The OR for death with revascularization in the SHOCK Trial was 0.35, similar to the adjusted OR of 0.30 observed in the SHOCK Trial Registry cohort. Table 4 summarizes the impact of revascularization within 18 h of CS, compared with no or late revascularization. In this analysis Trial patients were grouped according to their assigned treatment strategy because the upper time limit for early revascularization was 18 h (12). The adjusted OR for death with early revascu-

Table 3. Effect of Revascularization on Mortality
Odds Ratio for Death Revascularization vs. No Revascularization

	n	Odds Ratio	95% CI	Comments
Trial (30-Day mortality)*	302	0.35	0.22, 0.55	170 underwent a revascularization attempt vs. 132 who did not undergo revascularization†
Registry	800	0.18	0.13, 0.25	Unadjusted
(In-hospital mortality)	800	0.22	0.16, 0.30	Adjusted for age, diabetes, MI to CS <6 h
	389	0.30	0.19, 0.47	Adjusted for cardiac index, age, diabetes, prior MI

*Trial in-hospital and 30-day mortality were similar. †Revascularization was performed at any time during the hospitalization and includes all revascularized patients without regard to trial group assignment (11).
CI = Confidence interval.

Table 4. Effect of Early Revascularization on Mortality
Odds Ratio for Death Revascularization Within 18 h of Shock vs. No/Late Revascularization

	n	Odds Ratio	95% CI	Comments
Trial (30-Day mortality)*	302	0.69	0.44, 1.08	152 randomly assigned to early revascularization and 150 to no early revascularization
Registry	753	0.37	0.27, 0.51	Unadjusted
(In-hospital mortality)	753	0.46	0.33, 0.66	Adjusted for age, diabetes, MI to CS <6 h
	353	0.58	0.35, 0.98	Adjusted for cardiac index and age, diabetes, prior MI

*Trial in-hospital and 30-day mortality were similar.
CI = Confidence interval.

larization in the Registry was 0.46, again roughly similar to the Trial OR of 0.69.

DISCUSSION

Major causes of CS. The relative incidence of the various causes of CS has not been previously reported in a well-defined large prospective study. The most frequent cause of CS is predominant LV failure, most often with ECG findings consistent with recent total coronary occlusion MI with anterior location. Although inferior MI occurred often, it was associated with prior MI in more than one-third of the patients, or was associated with a mechanical cause of shock. This supports the view that inferior MI alone infrequently causes shock due to extensive LV dysfunction.

Mechanical causes of CS, including VSR, acute severe MR, and tamponade—all requiring early recognition and repair—accounted for 12% of cases. The mortality rate when VSR was the cause of shock was significantly higher than that associated with other categories, emphasizing the need for rapid septal repair before CS develops (16,17). It is worth noting that the mortality rate associated with cardiac tamponade, which is often due to sub-acute cardiac rupture, was relatively low (18,19). This emphasizes the potential for improving survival with early detection.

Patient profile. The characteristics of patients who develop CS in the SHOCK Trial Registry are remarkably similar to those in many other reports of CS (5,13,20–22). Patients with CS are often elderly and female and have high rates of prior MI, hypertension and diabetes. The timing of shock after MI onset, however, appears to be markedly shorter than previously reported (5,13,20). Whether this discrepancy results from the prospective nature of a registry dedicated exclusively to CS or from a change in the pathogenesis and/or the timing of CS is unknown.

Mortality. The overall mortality for patients with CS in this SHOCK Trial Registry is 60%, which is lower than the 80% to 90% rate in previous reports (21,22). This may be explained partly by the fact that 44% of the patients in the SHOCK Trial Registry were transferred from community hospitals. Not surprisingly, patients transferred to SHOCK Trial tertiary care centers had significantly lower mortality than direct admissions to the SHOCK Trial centers. This is attributed to the survival bias associated with transfer. Nevertheless, the mortality (67%) in the cohort with direct admission remains lower than previous reports, perhaps because of the increased utilization of IABP and revascularization. Although the mean LV ejection fraction was significantly lower for nonsurvivors, the 4% to 6% point difference carries no clear clinical import with respect to patient stratification or pathophysiologic understanding.

Outcome with thrombolysis and IABP. Patients selected to receive thrombolysis or IABP had lower mortality rates than those not receiving those therapies, and the combination appeared to be additive (14). Experimental evidence suggests that the depressed rates of thrombus dissolution are restored when IABP is used with thrombolysis in a hypotensive model (23,24). Similarly, nonrandomized clinical studies have reported lower mortality for these combined therapies (25,26). Whether this combination is superior to thrombolysis alone for pump failure complicating acute MI is being tested in the randomized Thrombolysis and Counterpulsation to Improve Cardiogenic Shock Survival Trial (TACTICS) and How Effective are Revascularization Options in Cardiogenic Shock Trial (HEROICS).

PTCA and CABG. Previous studies, largely retrospective, have demonstrated an association between the use of PTCA or CABG and lower mortality (6–10,27–34). The outcome of revascularization performed at the SHOCK centers very closely replicates the pooled rates from these studies. The mortality of LV failure patients undergoing PTCA at any time during the hospitalization for CS complicating acute MI is 45% for 646 patients in 22 studies (6–10,27), compared with 46% mortality for the 290 patients in the SHOCK Trial Registry. The 28% mortality rate for LV failure patients undergoing CABG in our Registry is remarkably similar to the pooled 35% mortality for 391 patients in 25 studies undergoing CABG at any time during the hospitalization for CS (27–33). Furthermore, the outcome with PTCA and CABG in the randomized SHOCK Trial was similar to these outcomes in the Registry (11). Our observation that the mortality rate associated with

revascularization is significantly lower than that associated with no revascularization is consistent with previous reports. The patient characteristics of those clinically selected to undergo revascularization are significantly different from those not selected and explain a large part of the mortality difference. In fact, the randomized SHOCK Trial demonstrated only 9% absolute and 17% relative mortality reduction at 30 days (similar to the outcome at hospital discharge) for early revascularization, compared with initial medical stabilization. The latter group often underwent IABP support and thrombolysis, and delayed revascularization was performed in 25% (11). The effect of early revascularization in the large Registry is somewhat greater than in the Trial after adjustment for differences in all characteristics except for hemodynamics, which were available only in a subset. After adjustment for the better hemodynamic profile of those selected for revascularization, the effect of early revascularization was similar in both the Trial and Registry. It is possible that the small difference between ORs in favor of a greater benefit of early revascularization in the Registry, compared with the Trial, is attributable to the more frequent use of IABP and thrombolysis in the initial medical stabilization arm of the Trial than in the Registry. Overall, the similarity of treatment effect in patients undergoing revascularization in the Registry and Trial provides strong support for the generalizability of the SHOCK Trial results to patients with CS complicating acute MI. Of note, the Trial reported increasing benefits of early revascularization over time, with a large and significant mortality reduction at six months consistent with 13 lives saved per 100 patients treated (11).

In summary, the overall mortality for CS complicating acute MI in this international registry is lower than previously reported, although CS due to VSR remains associated with very high mortality. This lower-than-expected mortality rate is likely due to higher revascularization rates in this Registry, consistent with similar findings in a recent population study and randomized trial (11,35).

APPENDIX

The following are committee members, principal investigators and study coordinators in the SHOCK Study. Executive Committee: J. Hochman, Study Chair; T. LeJemtel, Co-chair; P. Aylward, J. Boland, J. Col, O. Wayne Isom, S. McKinlay, M. Picard, T. Sanborn, L. Sleeper, H. White and P. Desvigne-Nickens (ex officio); Publications Committee: H. White, Chair; J. Abel, J. Hochman, T. LeJemtel, L. Sleeper and J. Webb; Clinical Centers: J. Webb, C. Thompson, J. Abel and E. Buller, St. Paul's Hospital (Vancouver, BC, Canada); J. David Talley, J. Harrell, M. Dearen, M. Rawert and R. Pacheco, University of Arkansas for Medical Sciences (Little Rock, AR); J. Slater, A. Palazzo, R. Leber, C. Connery, and D. Tormey, St. Luke's–Roosevelt Hospital Center (New York, NY); A. Jacobs, R. Shemin and M. Mazur, Boston University Medical Center (Boston, MA); C. Buller, K. Gin, E. Jamieson and R. Fox, Vancouver General Hospital (Vancouver, BC, Canada); D. H. Miller, T. Sanborn, R. Campagna, O.Wayne Isom and S. Hosat, New York Hospital/Cornell Medical Center (New York, NY); H. White, J. French, K. Graham and B. Williams, Green Lane Hospital (Auckland, New Zealand); M. Menegus, M. Greenberg, R. Brodman and B. Levine, Montefiore/Albert Einstein College of Medicine (Bronx, NY); J. Boland, R. Limet, S. Pourbaix, P. Baumans and M. Massoz, C.H.R. Citadelle (Liege, Belgium); J. Col, R. Dion and R. Lauwers, Cliniques Universitaires St. Luc (Brussels, Belgium); R. Forman, E. Scott Monrad, D. Sisto, M. Galvao and M. Jones, J.D. Weiler Hospital of the Albert Einstein College of Medicine (Bronx, NY); J. Ambrose, S. Sharma, T. Cocke, J. Galla, D. Ratner and E. Brown, Mount Sinai Medical Center (New York, NY); R. Steingart and S. Parker, Winthrop University Hospital (Mineola, NY); S. C. Wong, G. M. Gustafson, S. Papadakos, S. Lang, M. Brown and M. Claude Boileau, New York Hospital Medical Center of Queens (Flushing, NY); V. Dzavik, W. Tymchak, A. Koshal, C. Kee and L. Harris, University of Alberta Hospital (Edmonton, Alberta, Canada); M. Porway, J. Flack and B. Burkott, Baystate Medical Center (Springfield, MA); A. Moreyra, S. Palmeri, A. Spotnitz and M. Hosler, University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School (New Brunswick, NJ); P. Aylward, J. Knight and C. Thomas, Flinders Medical Centre (Adelaide, SA, Australia); J. Dens, F. Van de Werf, P. Sergeants and C. Luys, Gasthuisberg University Hospital (Leuven, Belgium); K. Baran, P. Koller, P. Filkins and C. Iacarella, St. Paul Heart Clinic (St. Paul, MN); L. David Hillis, J. Cigarroa and J. Kissee, University of Texas SW Medical Center (Dallas, TX); S. Graham, S. Raza and J. Celano, Buffalo General Hospital (Buffalo, NY); J. Brinker and V. Coombs, Johns Hopkins Hospital (Baltimore, MD); E. Ribeiro, A. Carlos Carvalho, C. Rodrigues Alves and A. Petrizzo, Paulista School of Medicine (Sao Paulo, Brazil); J. Dervan, W. Lawson and P.Montes, State University of New York at Stony Brook (Stony Brook, NY); D. Faxon and R. Singh, University of Southern California Medical Center (Los Angeles, CA); P. R. Paulsen and E. Miller, Hennepin County Medical Center (Minneapolis, MN); B. Weiner and M. Borbone, University of Massachusetts (Worcester, MA); E. Bates, University of Michigan Medical Center (Ann Arbor, myocardial Infarction); Clinical Coordinating Center: J. S. Hochman, T. H. LeJemtel and E. Godfrey, St. Luke's/Roosevelt Hospital Center (New York, NY); Data Coordinating Center: S. M. McKinlay, L. A. Sleeper, J. Lim and J. Nisbet-Brown, New England Research Institutes (Watertown, MA); Program Administration: P. Desvigne-Nickens, National Heart, Lung, and Blood Institute, National Institutes of Health (Bethesda, MD).

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