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One-Year Survival Following Early Revascularization for Cardiogenic Shock

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CARDIOGENIC SHOCK (CS) is the leading cause of death for patients hospitalized with acute myocardial infarction (AMI),^{1,2} and mortality remains high during the following year.^{3,4} The SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) Trial demonstrated a nonsignificant reduction in 30-day mortality (56% vs 47%) when early revascularization (ERV) was compared with a strategy of initial medical stabilization (IMS), with a larger difference between the groups at 6 months.⁵ In this article, we report the 1-year survival, a prespecified secondary end point of the SHOCK Trial.

Context Cardiogenic shock (CS) is the leading cause of death for patients hospitalized with acute myocardial infarction (AMI).

Objective To assess the effect of early revascularization (ERV) on 1-year survival for patients with AMI complicated by CS.

Design The SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) Trial, an unblinded, randomized controlled trial from April 1993 through November 1998.

Setting Thirty-six referral centers with angioplasty and cardiac surgery facilities.

Patients Three hundred two patients with AMI and CS due to predominant left ventricular failure who met specified clinical and hemodynamic criteria.

Interventions Patients were randomly assigned to an initial medical stabilization (IMS; n=150) group, which included thrombolysis (63% of patients), intra-aortic balloon counterpulsation (86%), and subsequent revascularization (25%), or to an ERV group (n=152), which mandated revascularization within 6 hours of randomization and included angioplasty (55%) and coronary artery bypass graft surgery (38%).

Main Outcome Measures All-cause mortality and functional status at 1 year, compared between the ERV and IMS groups.

Results One-year survival was 46.7% for patients in the ERV group compared with 33.6% in the IMS group (absolute difference in survival, 13.2%; 95% confidence interval [CI], 2.2%-24.1%; $P<.03$; relative risk for death, 0.72; 95% CI, 0.54-0.95). Of the 10 prespecified subgroup analyses, only age (<75 vs ≥ 75 years) interacted significantly ($P<.03$) with treatment in that treatment benefit was apparent only for patients younger than 75 years (51.6% survival in ERV group vs 33.3% in IMS group). Eighty-three percent of 1-year survivors (85% of ERV group and 80% of IMS group) were in New York Heart Association class I or II.

Conclusions For patients with AMI complicated by CS, ERV resulted in improved 1-year survival. We recommend rapid transfer of patients with AMI complicated by CS, particularly those younger than 75 years, to medical centers capable of providing early angiography and revascularization procedures.

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METHODS

The SHOCK Trial design (an unblinded, randomized controlled trial) has been previously reported.⁶ Thirty-six referral centers with angioplasty and cardiac surgery facilities participated from April 1993 through November 1998. Patients with AMI who developed CS due to left ventricular failure at 36 hours or less were eligible if the electrocardiogram results showed ST-segment elevations or Q waves, posterior infarction, or

new left bundle-branch block. Clinical and hemodynamic criteria indicating CS and the absence of all exclusion criteria were required for patient inclusion.^{5,7} Patients were randomly assigned to undergo ERV, with either percutaneous transluminal coronary angioplasty

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(PTCA) or coronary artery bypass graft (CABG) surgery at 6 hours or less, or to IMS, which included patients undergoing thrombolysis, intra-aortic balloon counterpulsation (IABP) and subsequent revascularization with PTCA or CABG permitted 54 hours or more following randomization. The IABP procedure was performed in 86% of patients, thrombolysis in 63% of IMS patients, and subsequent revascularization in 25% of patients.⁵

Assignment of the New York Heart Association (NYHA) class was determined by a standardized telephone interview 1 year following AMI. Beginning in 1995, rehospitalization data were obtained via telephone.

Dichotomous survival end points were calculated based on survival times from randomization, without regard to heart transplantation. Fisher exact test was used to compare survival rates, and the normal approximation to the binomial was used to estimate the 95% confidence interval (CI) for the rate difference between groups. The Breslow-Day test of homogeneity of odds ratios was used to assess the interaction between treatment group and 10 prespecified subgroup variables.^{5,7} The Kaplan-Meier product-limit estimator and the log-rank test were used to analyze continuous survival times with censoring at the date of heart transplantation for 4 patients. In addition, 1 IMS patient who was lost to follow-up before 1 year was omitted from the survival analysis because of informative censoring (since this patient was not found in the Social Security Death Index, he/she is likely to be alive). All statistical analyses were conducted in SAS⁸ and S-Plus.⁹

RESULTS

The mean (SD) age of enrolled patients was 66 (11) years; 32% were female, 33% had history of AMI, 31% had diabetes mellitus, and 46% had hypertension. Fifty-five percent of patients were transferred from primary to tertiary care hospitals, by protocol 12 hours or less after CS.⁵ Eight patients (5 ERV and 3 IMS) were determined postrandomization to have aortic dissection, left ventricular free

wall rupture, tamponade, or severe mitral regurgitation. Vital status at 1 year was available for 301 of 302 patients.

At 1-year postrandomization, there was a significant difference in survival between the ERV ($n=152$) and IMS ($n=149$) groups (46.7% vs 33.6%, $P<.03$) (relative risk for death, 0.72; 95% CI, 0.54-0.95). The absolute difference in survival was 13.2% (95% CI, 2.2%-24.1%). The FIGURE demonstrates the increasing survival benefit of the ERV group after 1 month ($P=.04$). After exclusion of 8 patients with aortic dissection, tamponade, or severe MR, the 1-year survival rate was 47.6% ($n=147$) for the ERV and 33.6% ($n=146$) for the IMS groups, a 14.1% absolute difference (95% CI 2.9%-25.2%; $P<.02$).

Three ERV patients and 1 IMS patient underwent cardiac transplantation; 2 survived to 1-year postrandomization.

Most patients (64%) had 3-vessel disease⁵ and the mean (SD) left ventricle ejection fraction was 29% (11%) ($n=46$). Ninety-seven percent of ERV patients underwent coronary angiography and 87% underwent revascularization, including 55% ($n=84$) with PTCA and 38% ($n=57$) with CABG surgery. In the ERV group, the median time from randomization to revascularization was 0.9 hours for PTCA and 2.7 hours for CABG surgery.

Delayed revascularization was attempted in 32 IMS patients (21%) at a median of 103 hours after randomization, and 4% underwent revascularization at 54 hours or less.⁵ Initial medical stabilization patients who survived the first several days after randomization and were clinically selected to undergo revascularization had a 57% (21/37) 1-year survival rate. Their mean (SD) cardiac index was higher than IMS patients who did not undergo revascularization (2.02 [0.55] vs 1.68 [0.46] $L \cdot min^{-1} \cdot m^{-2}$; $P<.01$).

Only 1 of 10 prespecified subgroup analyses revealed a significant interaction with treatment (age <75 vs ≥ 75 years; interaction, $P=.03$). There was an 18% absolute difference in survival in fa-

Figure. Kaplan-Meier Survival Curve 1-Year Postrandomization

Survival estimates for early revascularization ($n=152$) and initial medical stabilization ($n=149$) groups. Log-rank test $P=.04$. ERV indicates early revascularization group; IMS, initial medical stabilization group.

vor of ERV patients for those younger than 75 years (51.6% for ERV vs 33.3% for IMS; 95% CI for the difference, 6.1%-30.4%) and no significant difference in survival between the 2 groups for those 75 years and older (20.8% for ERV vs 34.4% for IMS). There was no interaction between treatment effect and presence vs absence of the following variables: male sex, randomization 6 hours or less after AMI, anterior AMI, prior AMI, diabetes mellitus, hypertension, US site, transfer, and thrombolytic contraindication.

Among 1-year survivors ($n=90$), 83% were in the NYHA congestive heart failure (CHF) class I or II (85% of the ERV group and 80% of the IMS group). The overall rehospitalization rate was similar for 69 ERV and 51 IMS patients (20% vs 18%); CHF (9% vs 12%), angina (7% vs 2%), and recurrent AMI (0%) respectively.

COMMENT

In this randomized trial of patients with AMI complicated by CS, ERV resulted in a 39% improvement in 1-year survival compared with initial aggressive medical stabilization. The absolute benefit of ERV for CS, 132 lives saved for every thousand patients treated, is greater than¹⁰ or similar to the absolute benefit of CABG for left main vessel disease at 1 year.¹¹ However, the group difference of 9.3 percentage points in favor of ERV

at 30 days (reported previously as the primary study end point) did not reach statistical significance.⁵ The increasing survival difference over time is in contrast with other therapies for AMI, such as thrombolysis and primary PTCA, for which maximal benefit is manifested at 30 days.^{12,13} The early mortality difference between primary PTCA and thrombolytic agents decreases over time for AMI patients without CS.^{13,14} However, the angiographic substudy of GUSTO I (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries I) demonstrated divergence of the survival curves in the first year for those with normal vs abnormal coronary artery blood flow early after experiencing AMI.¹⁵ Our findings are consistent with results of randomized trials of CABG compared with medical therapy for high-risk patients with severe coronary artery disease, for whom an early hazard of surgery is more than offset only after long periods of follow-up.^{16,17}

The higher 1-year survival with ERV was remarkably consistent among subgroups. The notable exception was a differential treatment effect by age. The younger patients (<75 years) derived a large benefit from ERV, in contrast to an apparent lack of benefit for those 75 years or older. However, the experience of the small elderly cohort (n=56) in the trial is in contrast with results of the concurrent nonrandomized SHOCK Registry, which showed an apparent survival benefit for those 75 years or older who were clinically selected to undergo ERV.^{18,19} These data suggest that a routine strategy of ERV may not be appropriate for the elderly as a group but careful case selection might lead to increased survival in certain patients 75 years or older.

Based on the results of the SHOCK Trial, the American College of Cardiology/American Heart Association recently revised guidelines to recommend ERV for patients younger than 75 years with CS within 36 hours of AMI.²⁰

In summary, ERV improves 1-year survival for patients with AMI complicated by CS. We recommend rapid transfer of patients with AMI and CS,

particularly those younger than 75 years, to tertiary care hospitals with capabilities to perform urgent coronary angiography and revascularization.

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Dr Sleeper participated in the study concept and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and provided statistical expertise.

Drs White and Boland participated in the study concept and design, acquisition of data, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content.

Dr Dzavik participated in acquisition of data, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content.

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Ms Modur participated in the analysis and interpretation of data and drafting of the manuscript and provided statistical expertise.

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