Early Revascularization and Long-term Survival in Cardiogenic Shock Complicating Acute Myocardial Infarction

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The incidence of cardiogenic shock complicating acute myocardial infarction (MI) has remained constant over 25 years. Although in-hospital mortality declined for the first time in the mid-1990s, the overall mortality rate is still 60%, and cardiogenic shock remains the major cause of death for patients hospitalized with acute MI. We previously reported the initial and 1-year results of the randomized Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial. This trial demonstrated that a strategy of early revascularization in patients with cardiogenic shock resulted in a nonsignificant reduction in 30-day mortality from 55% to 46% when compared with a strategy of initial medical stabilization, a significant 13 absolute percentage points reduction in 1-year mortality and good functional status at 1 year for the majority of survivors. We report here the

See also Patient Page.

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An intra-aortic balloon pump was used in 86% of patients assigned to each group. Median follow-up for 1-year survivors was 4.8 years (range, 1.0–10.7 years) in the initial medical stabilization group and 5.5 years (range, 1.0–11.1 years) in the early revascularization group. Detailed reporting of those not randomized is available elsewhere.1,2 The numbers screened and ineligible differ from those provided in the original report1 because 1 duplicate ineligible patient was discovered after publication of that report. CABG indicates coronary artery bypass graft surgery; PCI, percutaneous coronary intervention.

*Of the 1190 screened but not randomized, 884 had predominant left ventricular failure.
†This value does not include 9 of the 83 patients receiving PCI who also received CABG surgery.
‡Survivors count excludes 1 patient in the early revascularization group who underwent heart transplantation and was discharged alive from the hospitalization for shock.
§One patient in the initial medical stabilization group who successfully underwent heart transplantation after discharge but prior to 1-year post-randomization was censored at the date of transplantation.
Figure 2. Kaplan-Meier Long-term Survival of All Patients and Those Discharged Alive Following Hospitalization

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Years Since Randomization</th>
<th>Early Revascularization</th>
<th>Initial Medical Stabilization</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERV</td>
<td>56</td>
<td>33</td>
<td>18</td>
</tr>
<tr>
<td>IMS</td>
<td>42</td>
<td>33</td>
<td>18</td>
</tr>
<tr>
<td>Hospital Survivors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ERV</td>
<td>66</td>
<td>56</td>
<td>42</td>
</tr>
<tr>
<td>IMS</td>
<td>38</td>
<td>29</td>
<td>18</td>
</tr>
</tbody>
</table>

Among all patients, the survival rates in the early revascularization (ERV) and initial medical stabilization (IMS) groups, respectively, were 41.4% vs 28.3% at 3 years and 32.8% vs 19.6% at 6 years. With exclusion of 8 patients with aortic dissection, tamponade, or severe mitral regurgitation identified shortly after randomization, the survival curves remained significantly different (P = .02), with a 14.0% absolute difference at 6 years. Among hospital survivors, the survival rates in the ERV and IMS groups, respectively, were 78.8% vs 64.3% at 3 years and 62.4% vs 44.4% at 6 years.

Risk Stratification and Subgroups
Multivariable modeling revealed that older age (HR, 1.23 per 10 years; 95% CI, 1.06 to 1.43; P = .007), shock on admission (HR, 1.68; 95% CI, 1.12 to 2.52; P = .01), creatinine level of 1.9 mg/dL (170 µmol/L) or greater (HR, 1.56; 95% CI, 1.56 to 3.39; P < .001), a history of hypertension (HR, 1.40; 95% CI, 1.03 to 1.91; P = .03), and noninferior wall MI location (HR, 1.50; 95% CI, 1.06 to 2.12; P = .02) were independent risk factors for lower survival rates in a clinical model (n = 230). A model that also incorporated hemodynamic measurements and LVEF (n = 148) demonstrated that only older age (HR, 1.25 per 10 years; 95% CI, 1.02 to 1.52; P = .04), lower LVEF (HR, 1.22 per 5%; 95% CI, 1.10 to 1.32; P < .001), creatinine level of 1.9 mg/dL or greater (HR, 1.96; 95% CI, 1.16 to 3.34; P = .01), and a history of hypertension (HR, 1.56; 95% CI, 1.04 to 2.35; P = .03) were independently associated with death.

Early Revascularization for Cardiogenic Shock
Among hospital survivors who were assigned to receive early revascularization, there was no significant difference (P = .51) in long-term survival between PCI and CABG surgery as the primary emergency mode of revascularization (7.0 and 9.3 deaths per 100 patient-years, respectively), despite differences in coronary anatomy and rates of diabetes.13

The association in the revascularization group between 1-year mortality and timing of revascularization from MI onset was examined as a continuous variable and timing categories less than 4 hours post MI, in 2-hour increments thereafter, and 10 or more hours...
EARLY REVASCULARIZATION FOR CARDIOGENIC SHOCK COMPlicATING ACUTE MI

post MI. No statistically significant association was found due to small strata (11 patients per stratum, except for 99 patients at ≥8 hours), but 1-year mortality estimates increased from 0 to 8 hours and then decreased, presumably due to survivor bias (<4 hours, 36%; 4 to <6 hours, 55%; 6 to <8 hours, 82%; ≥8 hours, 48%).

COMMENT

A strategy of early revascularization resulted in a 67% improvement in 6-year survival in this randomized trial involving patients with MI complicated by cardiogenic shock due to predominant left ventricular failure. The large survival benefit (130 lives saved per 1000 patients treated, or 8 patients needed to be treated to save 1 life) was sustained throughout the follow-up period of up to 11 years. After 1 year, the survival curves remained parallel, with an annualized mortality rate of 8.0 vs 10.7 deaths per 100 patient-years for early revascularization compared with initial medical stabilization. These annual mortality rates are similar to those reported for a comparably aged broad cohort of post-PCI patients and a few percentage points higher than a large cohort of unselected post-MI patients. The overall long-term survival of patients with cardiogenic shock who survived the early period (30 days) in prior studies varies widely, ranging from 32% at 6 years to 55% at 11 years, and is related to the definition of shock, risk profile, and management of the cohort.

In this report, the clinical and MI factors that were independently associated with a higher long-term mortality rate, regardless of treatment assignment, are similar to those associated with death at 30 days in the SHOCK Trial and Registry. In a model that also incorporated hemodynamics and LVEF, the latter was strongly independently associated with both short-term and long-term outcome. However, hemodynamic variables measured close to shock onset that are highly predictive at 30 days (eg, cardiac index, cardiac power, stroke work, and systolic blood pressure while receiving support) were not associated with long-term outcomes. In general, variables we observed to be independently associated with long-term outcome after shock (age, LVEF, and serum creatinine level) have been consistently demonstrated to be similarly associated with long-term outcome in patients with a variety of cardiovascular disease presentations.

The better long-term survival with early revascularization was remarkably consistent among multiple subgroups. The previously reported differential treatment effect at 1 year for the elderly patients (≥75 years) was no longer statistically significant. The findings at 1 year appear to be due to an imbalance that occurred by chance; ie, the elderly patients assigned to medical stabilization had a higher baseline ejection fraction than those assigned to early revascularization, and they also had an associated high survival rate, similar to patients younger than 75 years who were assigned to medical stabilization, despite the powerful prognostic importance of age. Furthermore, the larger nonrandomized SHOCK Registry demonstrated a markedly lower adjusted risk of in-hospital mortality for those aged 75 years or older (n=257) who were clinically selected to undergo early revascularization. Other large registries have shown similar results. The revised American College of Cardiology/American Heart Association ST Elevation MI guidelines indicate that primary or rescue PCI or CABG surgery is reasonable for selected patients aged 75 years or older with cardiogenic shock (class IIa recommendation).

The survival benefit of urgent revascularization is similar for patients who develop shock late after MI and those with early shock. Furthermore, there was benefit of revascularization throughout the SHOCK trial enrollment time window, which included up to 48 hours post MI and 18 hours post-shock onset. The current data are consistent with prior studies of time to reperfusion in acute MI with or without shock, which demonstrate a strong survival advantage for earlier reperfusion, although we did not observe a statistically significant relationship.

This is likely due to inherent selection bias, with the limited cohort size and more stable patients surviving to undergo later revascularization.

Our data demonstrate that the substantial survival benefit for early revascularization of patients with cardiogenic shock is maintained over long-term follow-up. These data therefore lend further support to the need to identify quickly all patients with cardiogenic shock who are candidates for early revascularization, as recommended in the guidelines. Early revascularization has been increasingly used in recent years in tertiary care centers, but only approximately 60% of those younger than 75 years received it in these select US centers in 2004. Furthermore, the rate of transfer of patients with cardiogenic shock out of hospitals that cannot perform revascularization is 38% and did not change from 1998-2001. The rate of revascularization for shock in Global Registry of Acute Coronary Events hospitals was only 43% from 1999-2001. These rates of revascularization are too low in light of the current study’s finding of the striking durability of treatment effect.

Limitations

One limitation of this analysis is the shorter follow-up period of patients from SHOCK centers that did not participate in the long-term follow-up component conducted from 2000 to 2005. However, all but 2 centers (3 patients) completed a vital status confirmation in 1999 regardless of randomization date, and only 18 patients had follow-up less than 2 years. The use of the Social Security Death Index may have led to overestimation of the long-term event rate, since patients lost to follow-up who did not appear in the index were recorded as alive only as of the date last seen at or contacted by the SHOCK center. We have limited information on the use of very late (ie, after hospital discharge) revascularization and implantable cardioverter-defibrillators.

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CONCLUSIONS

Patients with cardiogenic shock complicating ST-segment elevation MI undergoing early revascularization with PCI or CABG surgery have substantially improved long-term survival compared with patients undergoing initial intensive medical therapy followed by no or late in-hospital revascularization. These data further underscore the need for direct admission or early transfer of patients in cardiogenic shock to designated tertiary care shock centers with demonstrated expertise in acute revascularization and advanced intensive care of these high-risk patients.

Author Contributions: Dr Hochman and Sleeper had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Critical revision of the manuscript for important intellectual content: Hochman, Sleeper, Webb, Dzavik, Buller, Aylward, Col, White.

Statistical analysis: Sleeper.

Obtained funding: Hochman, Sleeper.

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Study supervision: Hochman, Webb.

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REFERENCES


