Trends in cardiogenic shock: report from the SHOCK Study

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Aims We analysed time trends in patient characteristics, management, and outcomes of cardiogenic shock complicating acute myocardial infarction in the international, prospective SHOCK Trial Registry and pre-study Registry.

Background Despite therapeutic advances in its management, the incidence and high mortality of this complication has remained unchanged for decades. However, in recent years mortality was reported to decrease in one community concomitant with increasing use of revascularization.

Methods Thirty-six centres registered 1380 patients with suspected cardiogenic shock complicating acute myocardial infarction from January 1992 to August 1997. Patient and myocardial infarction characteristics, haemodynamics, medications, procedure use, and vital status at discharge were recorded.

Results In all, 79% of patients had shock due to predominant pump failure (non-mechanical aetiology). The aetiology, patient profile, and clinical characteristics of cardiogenic shock did not differ over time, except for increases in the incidence of prior bypass surgery (P=0.054) and transfers to tertiary centres (P=0.008). In all, 44% underwent revascularization (n=485), with angioplasty performed more often than bypass surgery (69% vs 31%). The revascularization rate increased over time (P=0.006) with a significant decrease in the time to revascularization (P=0.033). The use of Swan–Ganz catheterization decreased over time (P=0.018), as did the mean length of hospitalization (P=0.034). Overall in-hospital mortality was high (63%) but decreased over time in all patients (P=0.004) and those with pump failure (P=0.018). Mortality was lower for patients who underwent revascularization compared to those who were not revascularized (41% vs 79%, P<0.001).

Conclusions Cardiogenic shock complicating acute myocardial infarction is associated with a high mortality rate, but mortality decreased significantly from 1992 to 1997. This partly reflects the greater use of revascularization, which was associated with better outcomes. The reported international trend towards shorter admissions for myocardial infarction was also observed in this cohort.

Key Words: Myocardial infarction, cardiogenic shock, prognosis, and mortality.

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Introduction

Cardiogenic shock complicating acute myocardial infarction is associated with high morbidity and mortality. Pooled data from several non-randomized series have shown decreasing mortality in cardiogenic shock with the aggressive use of early revascularization[1–3]. Despite such therapeutic advances in the management of acute myocardial infarction, prior reports, including those from large thrombolytic trials, suggest no change in the incidence (5-5% to 7.5%) or overall mortality (55% to 80%) of cardiogenic shock in this setting[4,5]. A recent community-based study has reported enhanced short-term survival among such
patients during a 23-year follow-up period, although the incidence remained unchanged[8].

The SHould we emergently revascularize Occluded Coronaries for cardiogenic shock? (SHOCK) pre-study and Trial Registries provide a unique, prospective, international database of cardiogenic shock complicating acute myocardial infarction from January 1992 to August 1997. This analysis of these Registries was conducted to examine recent time trends in (1) the mortality of cardiogenic shock; (2) the patient profiles and clinical characteristics of shock, including its aetiology and time of onset; (3) the use of therapeutic interventions and their impact on mortality; and (4) the length of hospital stay.

Methods

Patients

We analysed (1) 190 of 231 patients from the SHOCK pre-study Registry who were enrolled by 19 participating centres in the United States and Belgium from January 1992 to December 1993, and (2) 1190 patients from the SHOCK Trial Registry. Patients enrolled in the pre-study Registry from January 1993 to April 1993 (n=41) were excluded due to incomplete data. The SHOCK Trial Registry enrolled patients at an additional 17 centres (a total of 36 centres) from April 1993 to August 1997. Of the 36 centres, 12 participated consistently from January 1992 to August 1997.

The pre-study Registry methods and results and the SHOCK Trial design have been reported[1,9]. Patients with suspected cardiogenic shock complicating acute myocardial infarction, whether or not they met strict criteria for shock, were prospectively registered while patients randomized in the SHOCK Trial were excluded from the Registry. The criteria for registration included a local discharge diagnosis of acute myocardial infarction and cardiogenic shock (DRGs 410 and 785.51), or a suspected diagnosis of cardiogenic shock complicating acute myocardial infarction regardless of final discharge diagnosis. Reasons for trial ineligibility (93% of registry patients) were recorded as failure to meet all inclusion criteria or due to patients who met one or more exclusion criteria (e.g. presenting outside the specified time windows). Non-randomized trial eligible patients comprised 7% of the registry. They were not randomized due to inability to provide, or refusal of, consent or rapid death. Centrally trained SHOCK study coordinators abstracted data from the medical records to complete standard study forms, collecting patient and myocardial infarction characteristics, haemodynamics, medication and procedure use, and vital status at discharge. SHOCK Trial mortality over time is reported for comparison[9,52].

Definitions

Electrocardiographic myocardial infarction locations were defined as in the Global Utilization of Streptokinase and tPA (alteplase) for Ocluded Coronary Arteries (GUSTO-I) trial[10]: anterior myocardial infarction, leads V1 to V2; inferior myocardial infarction, leads II, III, or AVF; apical myocardial infarction, leads V2 to V3; posterior myocardial infarction, leads V1 to V2; or lateral myocardial infarction, lead I or AVL.

Statistical analysis

Linear trends between admission year and dichotomous or ordered covariates were tested with a Mantel extension test[11]. We examined comparisons by admission year after adjustment for another categorical factors using the Cochran–Mantel–Haenszel trend test. Pearson’s chi-square test was used to compare survival rates across categories. Analysis of variance was used to analyse log-transformed hospital stay by admission year. Tests of interaction based on logistic regression models were used to identify factors that had different mortality trends across admission years[12]. Multivariate logistic regression models were fitted to determine whether mortality trends persisted after adjustment for confounding factors such as age, type of admission, and treatment. All analyses were conducted using SAS® software[13].

Results

Demographics and clinical characteristics

(Table 1)

Among the 1380 patients, 32% were >75 years old, 41% were women, and the medical history included diabetes in 33%, hypertension in 53%, prior heart failure in 20%, prior angioplasty in 6%, and prior bypass surgery in 10%. Cardiogenic shock was due to predominant pump failure in 924 of the 1190 patients in the Trial Registry (78%) and in 166 of the 190 patients in the pre-study Registry (87%).

No significant changes over time were observed in patient demographics and haemodynamic status except for an increasing trend in the number of patients with prior bypass (P=0.054, Table 1). A similar absence of trends was observed in patients with pump failure of non-mechanical aetiology (79% of the cohort). There were no trends over time in the various aetiologies precipitating cardiogenic shock.

Patient management

(Table 2)

Direct hospital admissions were reported in 55% of all study patients while the remaining 45% were referrals
transferred to tertiary-care hospitals. There was a significant increase in the number of transfer admissions to tertiary centres over time ($P=0.008$, Table 2).

Swan–Ganz catheterization was performed in 66% of all patients. A significant decrease in the use of Swan–Ganz catheterization occurred over time ($P=0.001$, Table 2). Seventy-six percent of all patients received mechanical ventilation without any difference in use over time.

Overall, 62% of patients underwent coronary angiography, and its use increased significantly over the study period ($P=0.005$, Table 2). There was a concomitant decrease in the time from the diagnosis of shock to coronary angiography ($P=0.003$, Table 3). The overall rate of intra-aortic balloon-pump use was 53% with no time trends. Fifty-six percent of pump-failure patients did not undergo mechanical revascularization; among them, 23% received thrombolytic therapy alone, 29% received intra-aortic balloon pump support with or without thrombolysis, and 48% received neither therapy. Among the revascularized group, 8% received thrombolytic therapy alone, 80% received intra-aortic balloon pump support, and 12% received neither. Angioplasty accounted for 69% of all revascularization attempts and coronary artery bypass surgery for 31%. The total revascularization rate increased and the time to
revascularization decreased during the study period ($P=0.001$ and $0.033$ respectively, Tables 2 and 3).

**In-hospital survival** (Fig. 1)

The overall in-hospital mortality rate for all patients was 63%. A significant decrease in mortality occurred from 1992 to 1997 ($P=0.004$). Further analysis of this trend over time, restricting the data to a smaller number of centres (n=12) that participated consistently from January 1992 to August 1997, showed trends similar to the larger sample ($P=0.094$).

In-hospital mortality was lower among transferred patients than among patients admitted directly to the tertiary-care hospitals (55% vs 69%, $P<0.001$). Mortality was also lower among patients selected for angiography than among those not selected (48% vs 87%, $P<0.001$).
Overall the multivariate model, mortality still decreased over time; 95% confidence interval (CI), 0.89 to 0.96; \( P=0.002 \). When revascularization status was added to the multivariate model, mortality still decreased over time but less so (OR, 0.91 per year; 95% CI, 0.84 to 0.99; \( P=0.020 \)). The highest mortality rate was noted in 1992 (71%); when this year was excluded, mortality still tended to decline over time (\( P=0.099 \)). After adjustment for age, transfer status, and prior bypass surgery, however, a decreasing trend in mortality over time was observed among patients registered from January 1993 to August 1997 (OR for death, 0.90 per year; 95% CI, 0.82 to 1.00; \( P=0.054 \)) while after adjustment for the above factors and revascularization, mortality did not decrease over time (OR for death, 0.92 per year; 95% CI 0.83 to 1.02; \( P=0.119 \)). The reduction in mortality was not due to enrolment of more high-risk patients into the randomized trial rather than into the registry; trial mortality was constant from April 1993 to August 1997 (\( P=0.378 \)).

**Length of hospital stay (Table 4)**

There was a significant decrease in length of hospital stay for pump-failure patients over time (\( P=0.034 \)). Both survivors and non-survivors showed a significant decrease in length of stay over time.

**Table 4 Length of hospital stay in days in patients with pump failure**

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<tr>
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<tbody>
<tr>
<td>Overall</td>
<td>Mean</td>
<td>11.5</td>
<td>9.5</td>
<td>14.4</td>
<td>12.3</td>
<td>12.0</td>
<td>8.6</td>
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<tr>
<td></td>
<td>SD</td>
<td>±1.0</td>
<td>±0.8</td>
<td>±2.9</td>
<td>±1.9</td>
<td>±1.7</td>
<td>±0.9</td>
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<tr>
<td></td>
<td>Median (IQR)</td>
<td>5.5 (2.0–15.5)</td>
<td>5.1 (7.3–15.2)</td>
<td>6.1 (11.3–14.5)</td>
<td>6.0 (9.3–15.6)</td>
<td>6.7 (1.03–16.0)</td>
<td>5.9 (1.16–12.5)</td>
</tr>
<tr>
<td>Survivors</td>
<td>Mean</td>
<td>23.4</td>
<td>17.6</td>
<td>27.9</td>
<td>24.8</td>
<td>19.7</td>
<td>15.4</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>±1.9</td>
<td>±1.5</td>
<td>±9.4</td>
<td>±2.3</td>
<td>±1.6</td>
<td>±0.4</td>
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<tr>
<td></td>
<td>Median (IQR)</td>
<td>18.0 (12.0–30.0)</td>
<td>17.1 (11.1–20.0)</td>
<td>15.0 (11.8–30.1)</td>
<td>17.4 (12.2–29.8)</td>
<td>15.7 (9.7–22.4)</td>
<td>12.6 (7.8–22.0)</td>
</tr>
<tr>
<td>Non-survivors</td>
<td>Mean</td>
<td>6.2</td>
<td>5.0</td>
<td>5.4</td>
<td>5.5</td>
<td>5.8</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>±0.5</td>
<td>±0.7</td>
<td>±1.3</td>
<td>±0.8</td>
<td>±1.6</td>
<td>±0.6</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>3.0 (1.0–7.0)</td>
<td>1.3 (0.45–7.6)</td>
<td>2.0 (0.43–5.4)</td>
<td>2.2 (0.37–6.0)</td>
<td>1.4 (0.28–4.8)</td>
<td>1.6 (0.34–5.5)</td>
</tr>
</tbody>
</table>

*Analysis of variance in log-transformed length of stay in days; SD = standard deviation; IQR = interquartile range.

**Discussion**

This analysis of the SHOCK Trial and pre-study registries shows a significant reduction in in-hospital mortality from January 1992 to August 1997 among patients with cardiogenic shock complicating acute myocardial infarction. Mortality was reduced over time in all patients with suspected cardiogenic shock as well as in patients with shock due to pump failure. Two studies in the early and mid-1990s evaluated mortality for cardiogenic shock over time and reported no change in high mortality\(^{[5,7]}\). The Worcester, Massachusetts community report, the first time-trend analysis of cardiogenic shock, showed an unchanging, high mortality of 78% from 1975 to 1988. In a comparison of thrombolytic-treated patients in GUSTO-I in the early-1990s and those treated in the Global Use of Strategies To Open Occluded Coronary Arteries (GUSTO-III) trial in the mid-1990s, there was no reduction in the overall mortality of 55% to 62%. A recent follow-up study of shock patients in the Worcester community from 1975 to 1997, however, has shown an improvement in in-hospital survival over time, particularly during the mid- and late-1990s with a simultaneous increase in the use of coronary revascularization procedures and intra-aortic balloon pump\(^{[9]}\).

We observed an increase in the use of coronary angiography and coronary revascularization, with coronary interventions performed sooner after shock diagnosis in the later study years. We have previously reported an independent association of revascularization and survival in this registry\(^{[14]}\). Unlike patients in the recent Worcester community report\(^{[8]}\) and recent GUSTO report\(^{[7]}\) our patients showed no differences in clinical profile over time. In the absence of trends in clinical profile, the improvement in survival over time is probably partially due to the increasing use of revascularization procedures\(^{[14–17]}\). This is further supported by our observation that the significant mortality trend over time after adjustment for confounding variables, especially increasing transfer rates, was mitigated after adjustment for revascularization status. The persistence
of a weak trend towards lower mortality rates over time after these adjustments suggests that unmeasured variables may also be playing a role. The GUSTO-I trial showed a greater use of invasive diagnostic and therapeutic interventions among U.S. patients with cardiogenic shock compared with other countries and a reduction in short-term mortality even after controlling for differences that affected treatment selection\textsuperscript{[19]}. In their recent comparison of GUSTO I and III studies, Menon et al. reported increasing revascularization rates but static shock mortality among U.S. patients. They speculated that this unchanged mortality rate might have resulted from the selection of sicker patients for aggressive revascularization which nullified its survival benefit\textsuperscript{[20]}. Among the non-revascularized patients in our study (the subgroup with the highest mortality), 48% did not receive thrombolytic therapy or intra-aortic balloon pump support. This may reflect that these patients were the sickest population, who died rapidly before therapy could be given. Non-randomized studies show low rates of intra-aortic balloon pump use despite trends towards lower in-hospital, 30-day, and 1-year all-cause mortalities associated with its use in cardiogenic shock\textsuperscript{[19,20]}. A recent report from this registry by Sanborn et al. shows lower in-hospital mortality among shock patients if treated with intra-aortic balloon pump alone or in combination with thrombolytic therapy irrespective of the timing of intra-aortic balloon pump insertion\textsuperscript{[21]}. However, the higher revascularization rate among patients receiving intra-aortic balloon pump was largely responsible for the lower mortality. We also found a decrease in the use of indwelling pulmonary artery catheterization, reflecting recent questions about its benefit and the increasing use of echocardiographic and Doppler studies\textsuperscript{[22,23]}.

Another important observation of our study was the decrease in length of hospital stay for both survivors and non-survivors over time. Aggressive strategies including early coronary interventions applied to eligible patients may have resulted in rapid clinical improvement and early discharge. The decreasing hospital stay of non-survivors over time may be due to a strategy of comfort care only for those not selected for aggressive management. Our findings also confirm the reported worldwide decreases in mortality and length of hospital stay for patients with coronary artery disease\textsuperscript{[24–27,31]}. Transfer rates of patients to tertiary-care centres increased over time, showing the potential for rapid stabilization and transfer from community hospitals for urgent revascularization\textsuperscript{[28]}. Similar favourable outcomes among high-risk patients transferred for revascularization have been observed by the Mid-American Heart Institute\textsuperscript{[29]} and by the Zwolle group in the Netherlands\textsuperscript{[30]}. Our study supports the observation that revascularization for eligible patients with cardiogenic shock improves mortality\textsuperscript{[6,16,31,32]}. The randomized SHOCK Trial demonstrated that early revascularization significantly reduced mortality at 6 months, with a trend toward lower in-hospital and 30-day mortality rates\textsuperscript{[32]}. This further supports the hypothesis that the increased rates of both overall and early revascularization procedures observed in our study may partially explain the decreasing mortality. An ongoing randomized trial—Thrombolysis And Counterpulsation To Increase Cardiogenic shock Survival (TACTICS) (TACTICS Web page.http://dcri.mc.duke.edu/research/current/tactics.html)—will define the role of stabilization with intra-aortic balloon pump before transfer of patients to tertiary centres.

**Limitations**

The highest mortality rate was observed in 1992 (71%); when this year was excluded, the trend for declining in-hospital mortality persisted ($P=0.099$). This high mortality for 1992 is consistent with other reports\textsuperscript{[8,15]}. Because the pre-study registry was a pilot study to assess the feasibility of the SHOCK trial\textsuperscript{[11]}; the data collected were more limited, as noted. Furthermore, there was recruitment of new centres and withdrawal of a few participating centres over time. However, analysis of the 12 centres that participated throughout showed the same trends for the overall cohort. Importantly, the declining mortality over time is consistent with that reported in a contemporary community study\textsuperscript{[30]}.

**Conclusions**

Cardiogenic shock complicating acute myocardial infarction is associated with high mortality rates, but the rates appear to be decreasing significantly over time. This trend may be partially due to the increased use of revascularization procedures. Early diagnosis of shock and selection of eligible patients for early institution of aggressive strategies including intra-aortic balloon pump use, transfer to a tertiary-care facility and revascularization may further reduce mortality for this highest-risk subgroup of myocardial infarction patients.

We acknowledge the dedication and outstanding performance of the SHOCK investigators and coordinators. A full list appears in the appendix of reference \textsuperscript{[32]}.

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**References**


