Journal of the American College of Cardiology Vol. 50, No. 18, 2007

Published by Elsevier Inc.
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.07.046

EDITORIAL COMMENT

# The Calm *After* the Storm

## Long-Term Survival After Cardiogenic Shock*

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Cardiogenic shock (CS) after acute myocardial infarction (MI) is a complex syndrome that involves a cascade of acute left ventricular dysfunction, decreased cardiac output, hypotension, and tissue hypoperfusion. In the past decade our understanding of this syndrome has been expanded, and important strides have been made in improving the survival of CS patients. Early mechanical revascularization, using either percutaneous coronary intervention or coronary artery bypass graft (CABG) surgery, along with supportive care, improves short-term survival in these patients when compared with initial medical stabilization using thrombolytic agents, intra-aortic balloon pump insertion, and intensive supportive care with or without delayed revascularization (1). However, CS remains a leading cause of death in patients hospitalized with MI. Even with early revascularization, the short-term mortality rate is high, and fewer than 50% survive to 1 year (1,2). But what becomes of those who survive beyond 1 year?

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In this issue of the *Journal*, Singh et al. (3) address this question and add to our understanding of the long-term outcome of patients with CS complicating MI who survive beyond 30 days by evaluating the large cohort of patients enrolled at U.S. sites in the GUSTO (Global Use of Strategies to Open Occluded Coronary Arteries)-I trial (3). Their analysis of patients treated with fibrinolytic therapy for ST-segment elevation MI compared the long-term survival of the 1,891 (8.3%) patients who developed CS with the 20,992 (91.7%) patients who did not by using the National Death Index, a large National Center for Health Statistics database.

The investigators found the 30-day survival of patients with CS to be expectedly poor at 50.4%, compared with 88.9% in those without CS. However, the remarkable finding of this study is that the mortality rate of patients with CS, although also high at 1 year, stabilized and approximated that of patients without CS between years 2 and 11, yielding annualized mortality rates of 2% to 4% per year for each group.

The observation that long-term outcome is relatively good for shock survivors is supported by smaller observational studies and the long-term follow-up of the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial (2,4–7). Although the mortality rate for patients in the initial medical stabilization group who survived to hospital discharge in the SHOCK trial was high in the first year, it was lower in the emergency revascularization group, and for both groups it stabilized over the 11-year follow-up (5). The older age at entry, lack of selection for fibrinolytic-eligible patients presenting within 6 h of MI, and other comorbidities likely explain the higher (~8% per year) late mortality rate for the early revascularization group in the SHOCK trial compared with the GUSTO trial shock survivors. Collectively these studies show that, although in-hospital survival was poor and the large majority of CS patients will not be alive at late follow-up, those who survived to discharge had a relatively low mortality rate at late follow-up.

The data in the GUSTO trial and other studies are insufficient to evaluate the potential further reduction in these mortality rates with current optimal therapy, including implantable defibrillators. In the GUSTO trial, independent predictors of higher mortality through 11 years for all 30-day survivors included age, shock, higher Killip class, cerebrovascular disease, prior MI, prior CABG, hypertension, diabetes, and anterior location of MI. Advancing age emerged as the most powerful predictor of both 30-day and 11-year mortality in both CS and non-CS cohorts. Remarkably, elderly 30-day survivors had similar 11-year outcomes whether or not they had shock. Age was not associated with worse functional status at 1 year after shock (8). These data and the long-term follow up of the SHOCK trial showing a similar treatment effect for early revascularization independent of age support the American College of Cardiology/American Heart Association 2004 Guidelines for the Management of ST-Segment Elevation Myocardial Infarction Class IIA recommendation for the elderly: "patients with good prior functional status who are eligible for revascularization and agree to invasive care may be selected for such an invasive strategy" (9).

It is noteworthy that the current study found overall mortality to be significantly lower in those receiving thrombolytic therapy <2 h from presentation, confirming the critical importance of very early reperfusion. This is the only

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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JACC Vol. 50, No. 18, 2007
October 30, 2007:1759–60

therapy known to prevent CS. Although the finding that percutaneous coronary intervention during the index hospitalization was associated with a significant improvement in survival in CS was expected (because of a treatment benefit as well as selection bias), a mortality benefit was not noted for patients treated with CABG surgery during the index hospitalization. This finding is in contrast to that of the randomized SHOCK trial and numerous registries and was observed despite the bias that reflects selection of less ill patients with shock for CABG, often after shock has resolved (1). The reason for this GUSTO finding is unclear but may be attributable to the small cohort or unidentified confounders. It is possible that the rate of perioperative deaths differs based on the volume of patients with CS who undergo surgery at a particular center and would suggest that regionalization of care may be appropriate for these highly complex and unstable patients.

A few other findings reported by Singh et al. (3) deserve mention. The average systolic blood pressure in the CS cohort at study entry was 116 mm Hg, and most (87.8%) were either Killip class I or II at baseline. Cardiogenic shock developed in the vast majority of patients after hospital presentation and presumably after initial therapy, raising the question, "How often is there an iatrogenic contribution to CS?" The CS cohort had an unusually high rate (43%) of severe bleeding. Patients with large infarcts will not tolerate bleeding, and a mixed shock picture may have been present in some.

The finding that long-term outcome for 1-year survivors of CS is similar to that of nonshock acute MI survivors points to the importance of improving short-term survival, which remains unacceptably low. This should place the focus on very early reperfusion in MI to prevent shock and novel therapies targeting patients with CS. Efforts to improve early survival are only made more important by the observation that survivors will likely enjoy good quality of life; most will be in New York Heart Association functional class I or II at 1 year of follow-up (1,4,8). Further improving short-term outcomes has proven challenging. Recent attempts to inhibit inflammatory cytokine and nitric oxide-mediated systemic inflammatory response syndrome pathways in CS have yielded disappointing results (10,11). Similarly, clinical outcomes were not improved in small trials of percutaneous left ventricular assist devices.

The similar long-term outcomes for survivors of MI with and without shock reported by Singh et al. (3) suggest that the cup can be viewed as half full—approximately one-half of patients with shock complicating MI will be alive at 1 year, with a long-term prognosis determined largely by typical CV risk factors. Most will lead active lives with good quality. We must rise to the challenge of preventing shock with very early reperfusion, avoiding iatrogenic shock, increasing use of early revascularization despite its potential impact on physician "scorecards," and developing novel therapies to treat shock.

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