

EDITORIAL COMMENT

Cardiogenic Shock

How Long Does the Storm Last?*



Adnan Kastrati, MD,^{a,b} Roisin Collieran, MB, BCH,^a Gjin Ndrepepa, MD^a

Cardiogenic shock, the most common cause of in-hospital mortality following acute myocardial infarction (AMI), complicates between 5% and 10% of cases (1). Although the past few decades have seen a decline in early mortality in patients with cardiogenic shock—largely due to increased rates of early revascularization (2) and improved adjunctive pharmacotherapy—in-hospital mortality remains high, at up to 50% (3). Although cardiogenic shock is more common among patients with ST-segment elevation myocardial infarction (STEMI), patients with non-ST-segment elevation myocardial infarction (NSTEMI) tend to have higher baseline risk profiles. Some registries report no difference in early mortality according to AMI subtype in patients with cardiogenic shock (4). Others report higher mortality for NSTEMI patients, potentially explained by their less favorable risk profiles and higher rates of early revascularization for STEMI (5). For patients who survive the index hospitalization, the effect of shock on adverse outcomes diminishes over time, with similar mortality beyond 1 year in shock and nonshock patients (6,7). However, very little is known regarding interim, early post-discharge outcomes in this population.

SEE PAGE 739

In this issue of the *Journal*, Shah et al. (8) address these knowledge gaps by providing prognostic

information regarding the first year following hospital discharge, emphasizing the early post-discharge period in patients with STEMI and NSTEMI complicated by cardiogenic shock. Using NCDR (National Cardiovascular Data Registry) ACTION Registry-GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry-Get With The Guidelines) data from 2007 to 2012 linked with Centers for Medicare & Medicaid Services for follow-up outcomes, they compiled a sample of 5,555 patients with AMI complicated by cardiogenic shock. Baseline characteristics and early (1 to 60 days) and late (61 to 365 days) outcomes of patients with cardiogenic shock were compared with those of 107,113 patients without cardiogenic shock. Their main finding was that hospital survivors of AMI who had cardiogenic shock had a higher risk of death and/or hospitalization during the first year after discharge. After accounting for differences in baseline characteristics, patients with AMI complicated by cardiogenic shock had a higher risk of all-cause mortality in the early post-discharge period (the first 60 days) versus nonshock patients, but shared a similar prognosis thereafter (between 61 days and 1 year). The same was true for the composite secondary endpoint of all-cause hospitalization or all-cause mortality. Conversely, higher early rates of heart failure-specific hospitalization or all-cause mortality in cardiogenic shock patients persisted into the late post-discharge period. Although patients with NSTEMI fared worse than those with STEMI, similar outcomes were observed in the adjusted analyses (for patient demographics and comorbidities, in-hospital interventions and events, discharge medications, and characteristics of the treating hospital).

This study's strength lies in its reliance on the large NCDR ACTION Registry-GWTG of contemporary patients with AMI, characterized by meticulous data collection. The investigators found that at 1 year, over

*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.

From the ^aDeutsches Herzzentrum München, Technische Universität München, Munich, Germany; and the ^bDZHK (German Centre for Cardiovascular Research), partner site Munich Heart Alliance, Munich, Germany. Dr. Collieran has received support from the Irish Board for Training in Cardiovascular Medicine sponsored by Merck & Co. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

50% of patients had died or been rehospitalized, regardless of the presence or absence of shock (59.1% with shock vs. 52.3% without). However, surprisingly few hospitalizations (less than one-quarter) were attributed to heart failure, which may reflect improvements in myocardial salvage in the acute phase and improved subsequent medical therapy, but also highlights the increasing effect of patient comorbidities predisposing to hospitalization due to noncardiac causes. Although proportions of cardiac and noncardiac mortality are not reported, this is consistent with findings from a previous registry reporting a steady increase in noncardiac causes of death over time in post-discharge myocardial infarction patients (4). These findings should prompt us to focus more on optimization of treatment of noncardiac conditions during the in-hospital and early discharge periods in patients with AMI complicated by cardiogenic shock.

The important finding of similar outcomes in STEMI and NSTEMI patients has implications. Although revascularization rates in early survivors with STEMI exceeded 94%, the revascularization rate for the whole group with shock (both STEMI and NSTEMI) was 84.3%. Notably, this implies lower revascularization rates in the NSTEMI patients with shock. Although not reported in this study, the expected revascularization rates for shock patients who did not survive the index hospitalization would have been even lower. This is consistent with recent findings from national inpatient sample data, reporting revascularization in only 72.5% of NSTEMI patients with cardiogenic shock (9). Thus, lower rates of revascularization, a more unfavorable cardiovascular risk profile, and increased frequency of comorbidities may explain the worse outcomes in NSTEMI patients, even though the degree of ischemic damage may be smaller than in STEMI patients. Hopefully, guideline changes subsequent to the period studied here—recommending an immediate invasive strategy in NSTEMI with cardiogenic shock (similar to that in STEMI) and eliminating age discrimination for early revascularization in elderly patients >75 years of age—will improve revascularization rates going forward (10).

This study's findings further support the theory that early survival is determined predominantly by the extent of damaged muscle (explaining its improvement with revascularization) and late survival by lower baseline risk ("survival of the fittest"). Although cardiogenic shock patients who survived hospitalization were sicker in the acute phase than their nonshock counterparts (with a strong preponderance of STEMI, at 62% vs. 29%, respectively; $p < 0.001$), they had more favorable cardiovascular

risk profiles at baseline. Moreover, twice the proportion of cardiogenic shock patients was discharged to nursing care facilities rather than home, implying that these patients remained more frail on discharge. It is not surprising, then, that early mortality was higher for these patients; however, having survived the early post-discharge phase, as they returned closer to their lower-risk baseline with time, so too did their risk of adverse events.

The very high mortality rates for myocardial infarction patients with cardiogenic shock demonstrate that conventional management is inadequate. This should motivate us to search for potentially modifiable factors that may lead to improved outcomes. Aside from early revascularization and medical therapy, most prognostic factors associated with 1-year mortality were unmodifiable. Other measures that warrant further investigation in these patients include the optimal revascularization strategy in multivessel coronary artery disease and the optimal mechanical therapy for reversal of cardiogenic shock. Although the majority of patients with myocardial infarction complicated by cardiogenic shock have multivessel disease, studies on the value of complete revascularization in these patients are discordant. Recent randomized trials investigating complete revascularization in STEMI excluded cardiogenic shock patients (11–13). Nonetheless, both American and European guidelines support complete revascularization (10,14). Furthermore, the optimal role of complete revascularization in NSTEMI with cardiogenic shock is unknown. Results of the CULPRIT-SHOCK (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) trial (NCT01927549) (15) will shed more light on this issue.

The study has limitations inherent to its registry design. Restricting inclusion to patients with Medicare claims data (i.e., ≥ 65 years of age) limits the generalizability of the findings to younger or non-Medicare patients. Because older age is an important predictor of long-term mortality in early AMI survivors (5,7), this may explain the exceedingly high 1-year mortality in the current study. The voluntary nature of participation in NCDR may introduce a bias toward high-performing hospitals, which may offer more comprehensive and advanced treatment of patients with AMI and cardiogenic shock. Moreover, outcomes such as hospitalization for heart failure may be under-represented due to reimbursement disincentives for coding for the same diagnosis. Finally, the study offers no information on cause-specific mortality or detailed treatment of patients in the acute phase, in particular, the use of mechanical circulatory support devices. However, the

effectiveness of intra-aortic balloon counterpulsation has recently been challenged by data from a randomized trial (16), and despite improved hemodynamic parameters with left ventricular assist devices, their effect on clinical outcomes remains to be demonstrated. Recent guidelines give Class IIa and IIb recommendations for the respective use of intra-aortic balloon counterpulsation and left ventricular assist devices in patients with STEMI complicated by cardiogenic shock (10).

Notwithstanding these limitations, the study by Shah *et al.* (8) adds to our understanding of the risk trajectory of patients with AMI and cardiogenic

shock. The study underlines the persistent vulnerability of cardiogenic shock patients in the early post-discharge phase and urges us to address means of reducing the risk of adverse outcomes in these patients. It increases awareness of the importance of close medical surveillance of patients with AMI and cardiogenic shock in the immediate post-hospital discharge period.

REPRINT REQUESTS AND CORRESPONDENCE: Prof. Adnan Kastrati, Deutsches Herzzentrum München, Technische Universität München, Lazarettstrasse 36, 80636, Munich, Germany. E-mail: kastrati@dhm.mhn.de.

REFERENCES

- Anderson ML, Peterson ED, Peng SA, *et al.* Differences in the profile, treatment, and prognosis of patients with cardiogenic shock by myocardial infarction classification: a report from NCDR. *Circ Cardiovasc Qual Outcomes* 2013;6: 708–15.
- Hochman JS, Sleeper LA, Webb JG, *et al.*, for the SHOCK Investigators. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. *JAMA* 2006;295:2511–5.
- Thiele H, Ohman EM, Desch S, *et al.* Management of cardiogenic shock. *Eur Heart J* 2015;36: 1223–30.
- Kostis WJ, Deng Y, Pantazopoulos JS, *et al.*, for the Myocardial Infarction Data Acquisition System (MIDAS14) Study Group. Trends in mortality of acute myocardial infarction after discharge from the hospital. *Circ Cardiovasc Qual Outcomes* 2010; 3:581–9.
- Aissaoui N, Puymirat E, Simon T, *et al.* Long-term outcome in early survivors of cardiogenic shock at the acute stage of myocardial infarction: a landmark analysis from the French registry of Acute ST-elevation and non-ST-elevation Myocardial Infarction (FAST-MI) Registry. *Crit Care* 2014;18:516.
- Bagai A, Chen AY, Wang TY, *et al.* Long-term outcomes among older patients with non-ST-segment elevation myocardial infarction complicated by cardiogenic shock. *Am Heart J* 2013;166: 298–305.
- Singh M, White J, Hasdai D, *et al.* Long-term outcome and its predictors among patients with ST-segment elevation myocardial infarction complicated by shock: insights from the GUSTO-I trial. *J Am Coll Cardiol* 2007;50:1752–8.
- Shah RU, de Lemos JA, Wang TY, *et al.* Post-hospital outcomes of patients with acute myocardial infarction with cardiogenic shock: findings from the NCDR. *J Am Coll Cardiol* 2016; 67:739–47.
- Kolte D, Khera S, Dabhadkar KC, *et al.* Trends in coronary angiography, revascularization, and outcomes of cardiogenic shock complicating non-ST-elevation myocardial infarction. *Am J Cardiol* 2016;117:1–9.
- O’Gara PT, Kushner FG, Ascheim DD, *et al.* 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;61: e78–140.
- Engström T, Kelbæk H, Helqvist S, *et al.*, for the DANAMI-3-PRIMULTI Investigators. Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3-PRIMULTI): an open-label, randomised controlled trial. *Lancet* 2015;386: 665–71.
- Gershlick AH, Khan JN, Kelly DJ, *et al.* Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. *J Am Coll Cardiol* 2015;65:963–72.
- Wald DS, Morris JK, Wald NJ, *et al.*, for the PRAMI Investigators. Randomized trial of preventive angioplasty in myocardial infarction. *N Engl J Med* 2013;369:1115–23.
- Steg PG, James SK, Atar D, *et al.*, for the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology (ESC). ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012;33:2569–619.
- Thiele H, Desch S, Piek JJ, *et al.*, for the CULPRIT-SHOCK Investigators. Multivessel versus culprit lesion only percutaneous revascularization plus potential staged revascularization in patients with acute myocardial infarction complicated by cardiogenic shock—design and rationale of CULPRITSHOCK trial. *Am Heart J* 2016;172: 160–9.
- Thiele H, Zeymer U, Neumann FJ, *et al.*, for the IABP-SHOCK II Trial Investigators. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med* 2012;367: 1287–96.

KEY WORDS coronary artery disease, mortality, myocardial infarction, prognosis