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EDITORIAL

Another Nail in the Coffin for Intra-Aortic Balloon Counterpulsion in Acute Myocardial Infarction With Cardiogenic Shock

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Stuart D. Katz, MD
Nathaniel R. Smilowitz, MD
Judith S. Hochman, MD

Cardiogenic shock occurs in up to 5% to 10% of acute myocardial infarctions (MI) and is associated with high short- and long-term mortality risk. Since its introduction into clinical practice >50 years ago, intra-aortic balloon counterpulsion has been used empirically to provide hemodynamic support in patients undergoing coronary revascularization in the setting of MI and cardiogenic shock. In the landmark SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial, conducted between 1993 and 1998, intra-aortic balloon pumps (IABP) were placed in 86% of participants, irrespective of the assigned management strategy.[1] Although expert opinion supported clinical benefit of IABP use in cardiogenic shock, the first large randomized, multi-center trial of IABP, published in 2012, upended this conventional wisdom. The IABP-SHOCK II (Intra-aortic Balloon Pump in Cardiogenic Shock II) trial randomly assigned 600 participants planned for early revascularization of acute MI complicated by cardiogenic shock to either IABP placement or no IABP placement.[2] The primary end point was 30-day all-cause mortality. At 30 days, all-cause mortality was 40%, with no difference between patients randomized to receive an IABP versus those who were not. There were no differences between treatment groups in secondary outcomes, including bleeding, ischemic complications, stroke, time to hemodynamic stabilization, intensive care unit length of stay, and the dose and duration of catecholamine therapy. A previous intermediate-term report of IABP-SHOCK II trial outcomes demonstrated no difference between treatment groups for all-cause mortality at 12 months.[3]

In this issue of *Circulation*, Thiele et al[4] report the 6-year results of the IABP-SHOCK II randomized trial. At 6 years of follow-up, all-cause mortality was high and did not differ between the IABP and control groups (66.3% versus 67.0%) in intention-to-treat, per-protocol, and as-treated analyses. No signal for benefit associated with IABP use was observed in any prespecified or post hoc subgroups. There were no differences in the frequency of recurrent MI, repeat revascularization, stroke, or cardiovascular rehospitalization between the 2 groups. Quality of life, measured by the EuroQol 5D questionnaire and New York Heart Association classification, was favorable in survivors of cardiogenic shock. Four of 5 survivors had New York Heart Association Class I or II symptoms, with no difference between patients randomly assigned to IABP and no IABP therapy.

The 6-year results of IABP-SHOCK II are consistent with the study findings previously reported at 30 days and 12 months, and confirm lack of benefit associated with IABP placement. In agreement with previous reports from the SHOCK trial, early events account for the majority of fatalities, and the 6-year mortality of the IABP-SHOCK II and immediate revascularization arm of the SHOCK are near-

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ly identical.[4,5] The authors should be commended for their rigorous follow-up of 98.5% of the trial participants through telephone interviews and death registry queries. Outcomes reported at 6 years were clinically relevant and objective, and quality of life metrics were assessed using validated survey instruments.

There are several limitations of the IABP-SHOCK II study. The study was nonblinded, because sham IABP placement is not feasible. An open-label study design may have led to differential use of other therapies between groups; however, the absence of other interventions known to improve outcomes in cardiogenic shock mitigates the impact of this potential limitation. Moreover, there was little risk of ascertainment bias with the primary end point of all-cause mortality. It is notable that the IABP-SHOCK II investigators did not select for a high-risk shock cohort by requiring a minimum lactate threshold, the most potent predictor of long-term mortality after multivariable adjustment, nor was lactate level a prespecified subgroup.[6] Still, the substantial early and late mortality reported in the study population suggests that participants enrolled in IABP-SHOCK II are broadly representative of patients with cardiogenic shock with a sufficient burden of illness to test the effectiveness of IABP support.

The results of IABP-SHOCK II trial had a significant impact on clinical practice guideline recommendations. Based on the 30-day and 12-month outcomes of the IABP-SHOCK II trial, routine placement of IABP in the setting of cardiogenic shock is a Class III (level of evidence B) recommendation in the 2017 European Society of Cardiology Guidelines for ST-segment elevation myocardial infarction.[7] The long-term follow-up from IABP-SHOCK II reinforces this guideline recommendation. Thus, the IABP-SHOCK II follow-up data provide additional evidence to support a limited role for IABP in acute MI with cardiogenic shock in the modern era. The next iteration of North American cardiogenic shock guidelines should also be updated to reflect these randomized clinical trial data and put an end to the clinical inertia that has perpetuated routine use of IABP for cardiogenic shock.

There are a several hypotheses to account for the lack of benefit of IABP therapy on mortality in IABP-SHOCK II. First, balloon counterpulsion provides only a small augmentation of cardiac output in the setting of shock, and the device requires intrinsic left ventricular contractility for optimal benefit. Furthermore, balloon counterpulsion does not directly support right ventricular function, which may contribute to shock in some patients. In this context, IABP use may simply provide insufficient circulatory support to ensure end-organ perfusion. Once irreversible end-organ damage has occurred, outcomes are uniformly poor. Second, although 80% of participants in IABP-SHOCK II had multi-vessel coronary artery disease (CAD), nearly all underwent percutaneous coronary intervention for coronary revascularization. Residual ischemia from nonculprit coronary artery disease may also contribute to the substantial short- and long-term mortality.

If IABP does not improve survival in MI complicated by cardiogenic shock, which alternative strategies can effectively reduce mortality? Other than early coronary revascularization, no other interventions have been proven to provide clinical benefit. The results of a prespecified analysis of a small subgroup of the SOAP II trial (Sepsis Occurrence in Acutely Ill Patients II) suggest a benefit of norepinephrine over dopamine in cardiogenic shock, but dedicated robust trials of medical therapy in cardiogenic shock are still needed.[8] Newer mechanical circulatory support technologies have been developed to maintain end-organ perfusion and provide a bridge to left ventricular recovery, wearable ventricular assist device implantation, or cardiac transplantation in the setting of cardiogenic shock. Although promising, the percutaneous left ventricular assist device therapy has not been associated with improved clinical outcomes compared with IABP therapy in small clinical trials.[9] Larger trials of percutaneous left ventricular assist device therapy use in cardiogenic shock are needed. Venoarterial extracorporeal membrane oxygenation can provide complete biventricular mechanical circulatory support, but the optimal methods for catheter placement and unloading of the left ventricle remain uncertain. Randomized trials of extracorporeal membrane oxygenation for cardiogenic shock are currently being implemented, but results of these studies will not be available for years. Thus, the benefits of mechanical circulatory support for cardiogenic shock with percutaneous left ventricular assist device therapy and extracorporeal membrane oxygenation remain uncertain.

Approaches to coronary revascularization in the setting of MI with cardiogenic shock also deserve consideration. Data from the CULPRIT-SHOCK trial (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) recently demonstrated that multi-vessel percutaneous coronary intervention does not reduce mortality in patients with MI, multi-vessel CAD, and cardiogenic shock.[10]Although the majority of patients in IABP-SHOCK II had multi-vessel CAD, only 3.5% of trial participants underwent coronary artery bypass graft (CABG). In the original SHOCK trial, those who were referred for early CABG had a greater burden of CAD and diabetes mellitus, but had similar survival to trial participants who underwent early percutaneous coronary intervention.[11] Thus, complete revascularization with CABG is a promising path forward. A randomized trial of infarct-only percutaneous coronary intervention versus emergent CABG (with or without balloon angioplasty) in patients with MI, multi-vessel CAD of suitable anatomy, and cardiogenic shock might provide important insights into the optimal treatment of these complex patients. A trial to test whether CABG is superior is in development.[12]

The 6-year follow up of the IABP-SHOCK II trial demonstrates the stubbornly high short- and long-term mortality associated with MI and cardiogenic shock despite advances in cardiovascular care over the past decades. The study also confirms the feasibility of large clinical trials in this critically ill patient population in the modern era. These results should serve as a call to action to identify and test novel approaches to reduce short- and long-term mortality in cardiogenic shock. Large simple multicenter clinical trials are urgently needed to define optimal management strategies to improve outcomes in patients with cardiogenic shock complicating MI. All patients and care providers would ideally contribute to the evidence base.

ARTICLE INFORMATION

Correspondence

Judith S. Hochman, MD, Harold Snyder Family Professor and Associate Director of Cardiology, Senior Associate Dean for Clinical Sciences, Co-Director, NYU-HHC Clinical and Translational Science Institute, NYU School of Medicine, NYU Langone Health, 530 First Avenue, Skirball 9R, New York, NY 10016. Email judith.hochman@nyumc.org

Affiliation

Cardiovascular Clinical Research Center, Division of Cardiology, Department of Medicine, New York University School of Medicine, NYU Langone Health, New York, NY.

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Disclosures

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