Finding Traction for Mechanical Circulatory Support During
Coronary Interventions

Running title: Stewart; Mechanical Support during PCI

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The management of acute cardiogenic shock remains one of the great challenges of contemporary cardiovascular care. Cardiogenic shock manifests as a vicious cascade of systemic hypoperfusion leading to multi-organ system dysfunction and is a hallmark of severe ventricular failure in the wake of extensive myocardial damage following acute infarction. Shock complicates between 5-8% of ST-segment elevation myocardial infarctions (STEMI) and 2-3% of non-STEMI. More than 80% of the time, shock arises from direct myocardial injury downstream from an occluded artery, with the remaining cases coming from later mechanical complications such as acute mitral regurgitation or ventricular septal defect. Despite remarkable advances in medical therapy for acute coronary syndromes over the last three decades, especially the emphasis on early recognition and reperfusion therapy, cardiogenic shock remains a leading cause of death after STEMI and carries with it a mortality rate between 40-50%. Timely revascularization is the mainstay of therapy for cardiogenic shock complicating an acute MI. Early resuscitation of patients with cardiogenic shock frequently includes intravenous vasopressors and inotropes, which can aid perfusion but often at the expense of increased myocardial oxygen demand. For patients who fail pharmacologic support or in those with frank hemodynamic embarrassment, mechanical circulatory support (MCS) devices can be deployed to augment myocardial performance and systemic perfusion. Since its introduction nearly 50 years ago by Kantrowitz et al., the intra-aortic balloon pump (IABP) has been used to support the failing circulation during acute MI. Inserted into the descending thoracic aorta and carefully synchronized to the cardiac cycle, the IABP delivers diastolic counterpulsation to augment coronary and systemic perfusion, coupled with presystolic deflation to reduce afterload. Despite its favorable effects on myocardial oxygen supply and demand, the IABP pump only minimally augments cardiac output. Yet, IABPs are ubiquitous, relatively easy to insert with...
low complication rates in experienced hands, and merited a longstanding Class I
recommendation in consensus guidelines for cardiogenic shock accompanying acute MI.\textsuperscript{6,7}

To clarify the role of IABP in the modern PCI era, the IABP-SHOCK II clinical trial was
completed in 2012. This landmark trial prospectively randomized 600 patients with cardiogenic
shock complicating an acute MI to receive either IABP or no IABP, with all patients expected to
undergo early reperfusion and optimal medical therapy.\textsuperscript{3} By 30 days after MI, approximately
40\% of patients in each arm had died (IABP vs. no IABP HR 0.96, CI 0.79-1.17). The IABP
resoundingly failed to reduce mortality in patients with acute MI and cardiogenic shock treated
with early revascularization in the trial. There was also no suggestion of IABP benefit in any
clinically meaningful subgroup. This striking evidence overturned the longstanding guideline
recommendations for cardiogenic shock complicating STEMI and use of an IABP was
downgraded to a Class IIA recommendation in the 2013 AHA/ACC Guidelines.\textsuperscript{8}

Even as evidence for the routine use of IABP in acute MI eroded, novel percutaneous
platforms for MCS were emerging. Percutaneous ventricular assist devices, or PVADs, are
continuous flow pumps that unload the failing ventricle, augment cardiac output, and maintain
systemic perfusion pressure. Two approved platforms are most often deployed: TandemHeart\textsuperscript{TM}
PVAD (CardiacAssist, Inc., Pittsburgh, PA) and Impella\textsuperscript{®} Recover System (Abiomed Inc.,
Danvers, MA). In addition, next generation oxygenators now allow safer veno-arterial extra-
corporeal membrane oxygenation (ECMO) powered by a number of different centrifugal
pumps.\textsuperscript{9} The TandemHeart\textsuperscript{TM} and Impella\textsuperscript{®} platforms have been shown in several small,
randomized trials to provide more robust ventricular unloading and augmentation of forward
flow compared to IABP.\textsuperscript{10,11} However, the short-term hemodynamic improvements after PVAD
have thus far failed to translate into a lower 30-day mortality when compared to IABP, relegating
PVADs to a Class IIB recommendation in current STEMI guidelines. Moreover, considerable concerns remain about the difficulty of PVAD insertion, concerns that include a prolonged implantation time, risk of limb ischemia, bleeding, and hemolysis, to say nothing of the considerable costs of these devices.

With these recent developments in mind, in this issue of Circulation, Sandhu et al. explore the current landscape of mechanical support at the time of PCI using data from the National Cardiovascular Data Registry (NCDR®) CathPCI® registry. Their manuscript describes the care of 76,544 patients with cardiogenic shock undergoing PCI between 2009 and 2013 in the United States. Cardiogenic shock was defined as a sustained episode of hypotension (systolic blood pressure <90mmHg) and/or reduced cardiac index (<2.2 L/min/m²). Among such patients with shock undergoing PCI, 54% received no mechanical support, 39% received IABP alone, 3.5% other MCS, and another 3.6% received both IABP plus other MCS device. Patients were significantly more likely to receive an MCS device other than IABP if they had heart failure in the preceding weeks, systolic dysfunction, or cardiac arrest within 24 hours. The timing of support device insertion was revealing. In general IABPs were placed later in the catheterization and most often during PCI itself (57%). This suggests that IABPs remain the device of choice for rapid insertion when there is evolving hemodynamic impairment or as a guarantor of vessel patency after PCI. In contrast, other MCS platforms were commonly placed at the start of the procedure (40%) or during the procedure but prior to PCI (37%). Prospective identification of high-risk candidates for these other MCS platforms may have relegated their use to a level of shock so severe that delaying time to reperfusion to insert the pumps was justified only in the sickest patients.

The study period also straddled the dissemination of results from the IABP-SHOCK II
trial. After the trial was published, IABP use across the United States underwent a real though relatively small decline (-3.2%). This reduction was not offset by a concomitant increase in use of other MCS platforms. Even after the trial shed doubts about the added benefits of IABP, nearly 40% of patients with cardiogenic shock undergoing PCI were still being supported with a balloon pump, confirming the widespread acceptance of the IABP platform within the cardiology community. Despite the superior hemodynamic support of PVADs, use of other MCS at PCI remained flat between 2009 and 2013. Frequent use of IABP or MCS seemed to be clustered in a few hospitals, which tended to be large, university hospitals with teaching programs. Such hospitals may have more resources and expertise to facilitate MCS insertion, weaning, or transition to durable VADs. Recent data from the National Inpatient Sample suggested that overall utilization of percutaneous MCS devices actually increased over the past decade.\textsuperscript{14}

However, teaching hospitals made up nearly 80% of sites sampled and that study surveyed MCS use in all settings where cardiogenic shock is encountered.\textsuperscript{14} While there may well have been a genuine increase in overall PVAD use in recent years, it is clear from these NCDR® CathPCI® registry data that there has been no such rise in the use of PVADs during PCI for acute MI complicated by shock or even during high-risk PCI.\textsuperscript{13}

There are several important limitations to the CathPCI® registry data worth noting, most of which the authors address. First, the broad classification of reduced cardiac index and/or hypotension used to defined shock in the study captures a heterogeneous group of patients with varying degrees of impairment. There was no detailed patient-level information available on hemodynamics or use of vasoactive medications. Next, there was no ability to distinguish between the “other MCS” platforms in the registry, even though a full menu of devices is now available at many institutions. It would also be valuable to know how often support devices
were deployed in separate, later encounters for salvage therapy after initial PCI for shock was performed without support. Lastly, there are no outcome data presented for in-hospital or 30-day mortality to compare support strategies. Such data might eventually be available after linkage of the CathPCI® registry to claims data or the National Death Index.

These data highlight the many challenges confronting deployment of MCS during PCI for cardiogenic shock. Shock is a rapidly evolving state that can be confronted at all stages of post-MI care. This places a premium on support devices that can be easily inserted without delaying coronary reperfusion. After all, restoration of perfusion is the only treatment of cardiogenic shock shown to have mortality benefit.4 Entire regional health systems have been redesigned so patients can realize the proven benefits of early PCI. Yet whether or not a patient receives percutaneous support during PCI appears to have as much to do with where the ambulance happens to take the patient as how sick the patient might be. Protocols for the recognition of shock and triage to MCS often remain peculiar to each institution. Shock teams staffed by providers from multiple disciplines show promise, but their incorporation into routine STEMI care remains difficult. When it comes to use as an adjuvant during PCI, PVADs remain a niche therapy at select hospitals.

How do these data about the way we live now inform the future of short-term mechanical support? First, it will be difficult to justify wider deployment of PVADs during PCI in the absence of more robust trial data showing the impact of temporary support platforms on morbidity and mortality. In addition, we must redouble our efforts to classify the stages of cardiogenic shock. For example, the Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) profiles were developed to describe levels of advanced cardiac failure. In turn, these shorthand patient profiles have clarified decisions about the timing and
appropriateness of durable MCS. Better codifying the varying degrees of cardiogenic shock within INTERMACS Profiles 1 and 2 will allow us to learn more about when, how, and who to support with temporary devices. Lastly, enhanced pump designs will be required to translate hemodynamic support into improved outcomes. The ideal percutaneous support device would be versatile in its configuration for left- or right-sided support, small in caliber to reduce risk of limb compromise yet capable of high flow, and have low shear stress at the blood-pump interface to reduce hemolysis. A triumph of engineering will be required to propel temporary MCS into widespread use, as was the case when durable continuous flow VADs replaced pulsatile pumps for long-term support over the past decade. Without innovative pump design, a better taxonomy for acute shock, and more robust clinical trials, hope for improved outcomes in cardiogenic shock will be ever in the future, never reached but always coming.

Conflict of Interest Disclosures: None.

References:


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Mechanical Circulatory Support in Patients Undergoing PCI

Appendix Figure Legend

Appendix Figure 1: Temporal trends of IABP vs. O-MCS use for patients undergoing high-risk PCI (displayed by quarter).

Appendix Figure 2: Hospital variation in the use of IABP, O-MCS and no MCS among patients undergoing high-risk PCI.

Appendix Table Legend

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<table>
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<tr>
<th>Variable</th>
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<th>Other MV Support Only (N=6722)</th>
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Legend: STD = standard deviation; MI = myocardial infarction; CHF = congestive heart failure; CVA = cerebrovascular; PVD = peripheral vascular disease; COPD = chronic obstructive pulmonary disease; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; CM = cardiomyopathy; LV = left ventricular
Mechanical Circulatory Support in Patients Undergoing PCI