Evaluating percutaneous support for cardiogenic shock: data shock and sticker shock

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This editorial refers to ‘Percutaneous left ventricular assist devices vs. intra-aortic balloon counterpulsation for treatment of cardiogenic shock: a meta-analysis of controlled trials’3, by J.M. Cheng et al., on page 2102

Cardiogenic shock, a state of systemic hypoperfusion resulting from cardiovascular dysfunction, is the leading cause of death in patients with ST-elevation myocardial infarction (STEMI). In spite of tremendous advances in cardiovascular care over the past two decades, mortality rates for patients with cardiogenic shock remain quite high, with some estimates as high as 50%. Given the underlying pathophysiology of cardiogenic shock, most commonly attributed to left ventricular failure resulting from STEMI, prompt institution of mechanical circulatory support seems intuitively important. The intra-aortic balloon pump (IABP) counterpulsation device was first introduced in the 1960s and has gained widespread acceptance as the device of choice for most patients with cardiogenic shock. Registry data suggest that cardiogenic shock is one of the most common conditions for which IABPs are used, accounting for 20% of all insertions. In fact, the ESC and ACC/AHA guidelines on STEMI strongly endorse the placement of an IABP in patients with cardiogenic shock refractory to pharmacological therapy. However, the evidence base from which these recommendations emanate is limited. There are no large randomized controlled trials which have rigorously evaluated the impact of IABPs in cardiogenic shock. Observational data from the Should We Emergetly Revascularize Occluded Coronary Arteries in Shock (SHOCK) trial registry as well as the National Registry of Myocardial Infarction (NRMI)-2 suggest that patients treated with an IABP in addition to thrombolytics had lower in-hospital mortality than those receiving thrombolytics alone. Notably, patients undergoing primary percutaneous coronary intervention (PCI) in NRMI-2 did not benefit from IABP placement. A recent systematic review of >10,000 patients with cardiogenic shock in the setting of acute myocardial infarction (AMI) published in the European Heart Journal presented similar findings and concluded by challenging contemporary clinical guidelines.

One of the theoretical shortcomings of the IABP is that while it favourably alters the balance between myocardial oxygen supply and demand, it provides no active mechanical augmentation of cardiac output. The advent of left ventricular assist devices (LVADs), which provide more direct haemodynamic support to the failing ventricle, therefore holds great promise (Figure 1). Relatively little is known, however, about the impact of percutaneous LVADs vs. IABPs in patients with cardiogenic shock resulting from AMI.

Cheng et al. begin to fill this conspicuous void in cardiovascular critical care through a meta-analysis comparing the efficacy and safety of percutaneous LVADs with IABPs in cardiogenic shock. Their analysis includes 100 patients from three recently completed randomized trials, two of which compared a miniaturized centrifugal pump (TandemHeart™) with IABPs and a third which compared a microaxial propeller pump (Impella®) with IABPs. Most patients had cardiogenic shock resulting from STEMI, were managed with primary PCI, and required mechanical ventilation in addition to inotropic and vasopressor support. The authors examined haemodynamic parameters and 30-day mortality, as well as safety endpoints such as leg ischaemia, major bleeding, and report of fever or sepsis.

Compared with patients managed with IABPs, those supported with percutaneous LVADs had a significantly higher cardiac index and mean arterial pressure with significantly lower pulmonary capillary wedge pressure. However, the improved haemodynamic profile, assessed 2 h after baseline measurement, did not translate into improved survival at 30 days, with a pooled estimate of the relative risk of 1.06 [95% confidence interval (CI) 0.68–1.66]. Furthermore, the IABP was found to have a better safety profile as compared with the LVAD, particularly when juxtaposed with the TandemHeart™, which was found to have significantly higher rates of leg ischaemia and bleeding.

The meta-analysis by Cheng et al. addresses a critical, clinically relevant, scientifically interesting question which practitioners undoubtedly face on a daily basis—namely, what offers the safest and most efficacious mechanical support for a patient with cardiogenic shock? Nevertheless, there are some shortcomings with the...
analysis which warrant further discussion. First is the limited patient population. Though this meta-analysis synthesizes the available data comparing percutaneous LVADs with IABPs, it includes only 100 patients from three trials, only one of which represents a multicentre experience. With a limited study population, the ability to detect any new effects, especially on clinical endpoints such as mortality, is markedly attenuated. Next, the authors compare two different LVADs, but pool the data for comparison with IABPs. The TandemHeart™ and Impella™ have drastically different insertion procedures, mechanical properties, and mechanisms of action. The former is placed via femoral access and uses centrifugal force to produce non-pulsatile flow, while the latter is placed via femoral access and uses a propeller device to drive non-pulsatile flow. Whether this heterogeneity would translate into important haemodynamic and clinical effects is unknown, but certainly cannot be excluded. Thus, the pooling of data across devices may obscure relevant differences in efficacy between LVADs (as was apparent for safety endpoints). Finally, one wonders whether a longer follow-up period may be necessary for true differences between support devices to become apparent.

So, we return to the question that underlies the analysis by Cheng et al., namely how should we manage patients who present with cardiogenic shock? Beyond early recognition and resuscitation, timely revascularization remains the mainstay of the management of cardiogenic shock. The SHOCK trial randomized 302 patients with STEMI complicated by shock to emergency revascularization (60% PCI, 40% surgical) or initial medical stabilization.® Mortality rates were lower among patients undergoing emergency revascularization, with a trend towards benefit at 30 days and a significant benefit emerging by 6 months.®

Unfortunately, promising pharmacotherapies that seemed logical, such as nitric oxide synthase inhibition, when rigorously tested have failed to show benefit.¹²

The utility of mechanical circulatory support devices in cardiogenic shock remains an unanswered question. As noted above, the evidence base supporting the use of IABPs in cardiogenic shock is somewhat fragile. It is understandable that practitioners place IABPs when facing this challenging clinical scenario given the ease of implantation, relatively low risk of complications, and favourable haemodynamic effects. They have become the de facto standard of care despite the absence of robust randomized data to support their use. The use of percutaneous LVADs to support patients with cardiogenic shock holds great promise and may herald the next major advance in cardiovascular therapeutics. However, the paucity of evidence supporting their use at present is notable. These devices are very expensive, and employed with increasing frequency in the USA and elsewhere without yet having undergone rigorous testing and evaluation.

We must avoid repeating the history of IABPs with LVADs. Large randomized trials comparing percutaneous LVADs and IABPs with each other as well as with appropriate controls need to be performed before we can more convincingly offer our patients evidence-based care. Acknowledging the complexity of performing randomized, clinical trials in cardiogenic shock, these trials should be adequately powered to examine hard, clinical endpoints rather than intermediate, haemodynamic endpoints which have too often led us astray. We eagerly await the results of ongoing clinical trials that will continue to inform our decision making in this challenging clinical circumstance. The IABP-SHOCK II trial, a follow-up study after a smaller trial of 45 patients with
cardiogenic shock examined haemodynamic parameters and inflammatory markers, will randomize patients with cardiogenic shock complicating STEMI to PCI with adjunctive IABP or PCI alone and examine 30-day mortality. Though not investigating patients with cardiogenic shock, the recently published PROTECT I trial provides new insight and reassuring data regarding the use of the Impella in high-risk PCI and provides the foundation for a larger randomized trial actively recruiting patients (PROTECT II). The temptation to be an innovator or early adopter is real, and the desire to do what is best for each patient is our common obligation, yet we must avoid the presumption that newer is necessarily better, that surrogate endpoints can supplant clinical outcomes, or that the intuition that drives us to rely on mechanical support is well serving. Finally, we must bear in mind that patients, providers, payers, hospitals, and healthcare systems are not immune to the challenges the global economy faces. The depth and length of this current economic downturn are unknown. With assets evaporating and budgets seemingly unbalanceable, major capital investments in untested technologies are difficult to justify.

In conclusion, Cheng et al. have furthered our pursuit of answering a question many of us face daily—whether to use IABPs or percutaneous LVADs to support our patients with cardiogenic shock. In doing so, they have also catalysed a broader debate—whether we are practising medicine based on what the data really support and what our economy can support.

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