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EDITORIAL

Percutaneous Support Devices for Percutaneous Coronary Intervention

Having the Science Catch Up With the Technology

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Since the start of percutaneous coronary intervention (PCI), the field has seen a rapid explosion in technology from initial catheters, balloons, to metallic, now drug-coated stents. However, unique to the field of coronary intervention in comparison with other areas of technological advances in medicine, the iterative advances have been progressively tested, and when possible, randomized against control groups to determine the best and most appropriate care. In fact, the field has matured in such rapid fashion over the 40 years since inception,[1] in part, because of the scientific culture started by the initial report of angioplasty from Grüntzig et al[1] in which they concluded "A prospective randomized trial will be necessary to evaluate it usefulness in comparison with surgical and medical management."

Hence, each new therapy has been, in general, vetted and tested for improvements in patient outcomes from technologies such as coronary pressure wires, drug-eluting stents, to strategies such as primary PCI for acute myocardial infarction (MI). It is with these therapies and, more importantly, advances in effective medical therapy including antiplatelet and antithrombotic therapy, lipid-lowering drugs, and overall preventive care that cardiovascular mortality rates have fallen by 22% over the past decade.[2] However, in parallel with the maturation of coronary intervention has been the baby boom and aging population living with coronary heart disease and multiple comorbidities and more complex coronary anatomy. In fact, despite the noted improvements, patients presenting between 2011 and 2013 with acute MI and cardiogenic shock were significantly more likely to have comorbidities, including diabetes mellitus, dyslipidemia, previous PCI, and end-stage renal disease in comparison with similar patients between 2005 and 2006.[3] It is in this context that, as the clinical community attempts to determine how to best use percutaneous support devices, Kapur et al[4] provide the initial findings of the Door-to-Unload in STEMI Pilot trial in *Circulation.*

Based on prior preclinical studies demonstrating that mechanically unloading the left ventricle for 30 minutes before reperfusion leads to biological myocardial protective mechanisms reducing infarct size,[5–7] patients (n=50) with anterior ST-segment–elevation myocardial infarction were randomly assigned at 14 centers in the United States to either mechanical left ventricular unloading with an Impella CP system and immediate percutaneous reperfusion or left ventricular unloading with a 30-minute delay to reperfusion. The evaluation was specifically aimed at determining whether the unloading and delay were feasible and safe with regard to any increase in infarct size. The Impella was explanted after a minimum of 3 hours of support. All patients were followed for major adverse cardiovascular events, and the protocol aimed to have the patients undergo cardiac magnetic resonance imaging for infarct size at day 3 to 5 and 30 days post-MI.

Key Words: Editorials ■ drug-eluting stents ■ myocardial infarction ■ myocardial reperfusion ■ percutaneous coronary intervention

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Table. Randomized Trials With Percutaneous Support Devices

Trial Name	Description	Comparison	Sample Size	AMI	Shock	Trial Notes
MI without shock						
Ohman et al (1994)[8]	Primary PTCA in AMI	IABP + PTCA vs PTCA	96/86	Yes	No	Less reocclusion and MACE with IABP
PAMI II (1997)[9]	Primary PTCA in AMI	IABP + PTCA vs PTCA	211/226	Yes	No	No change in reocclusion or MACE with IABP
van't Hof et al (1999)[10]	Primary or rescue PCI in AMI	IABP + PCI vs PCI	118/120	Yes	No	No change in reocclusion or MACE with IABP
CRISP AMI (2011)[11]	Primary PCI in anterior AMI	IABP + PCI vs PCI	161/176	Yes	No	No change in infarct size
Kapur et al (2018)[4]	Primary PCI in anterior AMI	Impella CP + immediate PCI vs Impella CP + delayed PCI	25/25	Yes	No	Similar infarct size, similar MACE
High-risk PCI						
Vijayalakshmi et al (2007)[12]	High-risk PCI (hypotension, tachycardia, no-reflow, ST-segment elevation, pulmonary edema)	IABP + PCI vs-. PCI	17/16	No	No	No change coronary flow: TIMI grade
BCIS-1 (2010)[13]	High-risk PCI (LVEF ≤30%, unprotected LM, TV supply ≥40% of myocardium)	IABP+PCI vs PCI	150/150	No	No	No BCIS in MACE 30 days
PROTECT II (2012)[14]	High-risk PCI (last patent vessel PCI with LVEF ≤35%, unprotected LM, 3VD with LVEF ≤30%)	Impella 2.5 + PCI vs IABP + PCI	225/222	No	No	No difference MACE at 30 days; trend for Impella at 90 days (stopped for futility)
MI with shock						
Thiele et al (2005)[15]	AMI and shock	TandemHeart vs IABP	21/20	Yes	Yes	Improved cardiac power, more bleeding, similar 30-day mortality
Burkoff et al (2006)[16]	Cardiogenic shock; not all AMI	TandemHeart vs IABP	19/14	Some	Yes	Improved cardiac hemodynamics, similar 30-day mortality
ISAR-SHOCK (2008)[17]	AMI and shock	Impella 2.5 vs IABP	13/13	Yes	Yes	Improved Cardiac Index
IMPRESS in severe shock (2017)[18]	AMI and shock, 100% with mechanical ventilation, 100% with catecholamines at baseline	Impella CP vs IABP	24/24	Yes	Yes	30-day mortality; no difference
IABP-SHOCK II (2012)[19]	Primary PCI with shock	IABP + PCI vs PCI	300/298	Yes	Yes	30-day mortality; no difference

Please note that selected randomized trials with percutaneous support and PCI are presented, observational data are not included in the table, and all devices are not represented. 3VD indicates 3 vessel disease; AMI, acute myocardial infarction; BCIS-1, Balloon Pump Assisted Coronary Intervention Trial – 1; CRISP, Counterpulsation or Reduce Infarct Size Pre-PCI in AMI Patients; IABP, intra-aortic balloon pump; IABP-SHOCK, intra-aortic balloon pump in cardiogenic shock trial; Impella CP, Impella Cardiac Power; IMPRESS, Impella CP vs intra-aortic balloon pump support in acute myocardial infarction complicated by cardiogenic shock (The IMPRESS in Severe Shock trial); ISAR SHOCK, Efficacy Study of LV Assist Device to Treat Patients With Cardiogenic Shock; LM, left main; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; PAMI II, Primary Angioplasty in Acute Myocardial Infarction-II study; PCI, percutaneous coronary intervention; PROTECT II, prospective, randomized clinical trial of hemodynamic support with Impella 2.5 vs intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention (the PROTECT II study); PTCA, percutaneous transluminal coronary angioplasty; TIMI, thrombosis in myocardial infarction; and TV, target vessel.

The investigators found that rates of major adverse cardiovascular events were rare and similar between groups, 3 (12%) in the unloading with a 30-minute delay to reperfusion group and 2 (8%) in the unloading with an Impella CP system and immediate percutaneous reperfusion group. The delayed group did undergo reperfusion at 97 minutes in comparison with 72 minutes for the immediate unload and reperfusion group, and the infarct size at 30 days was similar between the groups, 13% versus 15% for the unloading with a 30-minute delay to reperfusion versus the unloading with an Impella CP system and immediate percutaneous reperfusion groups. It should be noted that, by randomized chance, the ischemic time from symptom onset to unloading was 24 minutes longer in the immediate reperfusion group making the total ischemic time in the 2 arms, even after unloading and delayed reperfusion, similar between groups.

Kapur and colleagues should be congratulated for conducting an important and difficult-to-perform pilot randomized trial evaluating the feasibility and concept of reducing ischemia reperfusion injury and infarct size by unloading the left ventricle before primary percutaneous intervention. In concept and execution, studies

like this in patients with acute MI in which consent, randomization, and then potential delays for device insertion and possible planned delays are extremely difficult. Unfortunately, because of randomization differences in the ischemic times mentioned, it is not possible to make any substantive interpretations around the infarct size associated with delay. In addition, the critical lack of a standard-of-care control group (primary PCI without left ventricular unloading in patients with anterior MI) limits the ability to inform clinicians around the safety of the approach, namely, the rate of adverse cardiovascular events including vascular events. Nevertheless, this research group has provided the groundwork for a more pivotal study that should inform practice, a study in which they have indicated that a standard-of-care control arm would be recruited.

Although evaluating percutaneous support devices in rigorous randomized studies is difficult, the interventional community should continue our culture requiring these studies to help determine how best to change our practice and move the field to better serve our patients. As perspective, the Table shows some of the available randomized trial evidence comparing percutaneous support devices in the major indications for which they are being used, to support high-risk PCI, cardiogenic shock, or, being considered, specifically patients with MI without shock for reduction in ischemia-reperfusion injury and clinical events. It is evident from this table that there is a longstanding history and demand for clinical information from randomized studies, because they have substantially changed our perception of the utility of support devices such as the intra-aortic balloon pump. This is in conjunction with the continuous pace of improvement in PCI from improved systems of care for reperfusion, radial access, and other bleeding reduction strategies, to standardized periprocedural antithrombotic regimens.

Some have suggested with now-growing registry evidence from important investigator-initiated and eventual standardized larger observations such as the USpella Registry evolving into the sponsored quality improvement registry and subset of higher-density data in the cVAD Registry and Shock Initiatives that we have sufficient evidence and have lost our equipoise to continue to test percutaneous support devices in randomized trials. Although these registry and quality efforts have to be applauded because they have improved our overall care of patients with cardiogenic shock and high-risk PCI, substituting these observational data, which are compared with historic controls limited by patient selection and measurement bias, for randomized data demonstrating benefit would be a mistake. We have had encouraging observational data for devices or practices in the past that have not been borne out in randomized trials, with intra-aortic balloon pump or multivessel PCI in cardiogenic shock as the most recent examples. Because many thousands of patients have had percutaneous support devices placed with some level of clinical data collected, the interventional community must continue to push efforts and support investigators to perform large, simple, randomized comparisons aimed at demonstrating improved clinical outcomes. These studies are not easy to perform and will require both local community and clinician engagement, similar to ongoing resuscitation science. It is only with continued efforts such as those described by Kapur and colleagues that we will have science catch up to the technological advances so that clinicians and patients can have confidence to hopefully increase the use and meet the promise of the advances in percutaneous support devices.

ARTICLE INFORMATION

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