Progress made in cardiovascular treatment over the past several decades has been impressive. Combined invasive and pharmacological treatment strategies have improved clinical outcome in patients undergoing percutaneous coronary intervention (PCI), as well as in those treated for acute myocardial infarction and decompensated heart failure. In the case of acute myocardial infarction, dramatic reductions in the progression to cardiogenic shock and the rates of reinfarction and mortality have been seen.1–3 In particular, inhospital survival has improved by as much as 10 absolute percentage points, and cardiogenic shock after myocardial infarction has been cut in half.3,4 In addition, primary prevention strategies such as pharmacotherapy and aggressive risk factor modification have made significant headway in reducing the incidence of a first coronary event.4 Thus, not only do fewer patients present with acute myocardial infarction, but associated mortality has declined.

The improved survival after myocardial infarction, however, has resulted in more patients living with systolic dysfunction and associated congestive heart failure.5 Heart failure, indeed, is now the major cardiovascular disease that drives hospital admissions and produces significant patient morbidity.6 This is not to say that progress has not been made in the realm of congestive heart failure, however. Both invasive (implantable devices and revascularization) and pharmacological (β-blockers and renin-angiotensin-aldosterone system antagonists) therapies have improved outcome, including quality of life, heart failure symptoms, ventricular function, and survival.7–10

Finally, PCI outcomes have seen dramatic improvements since the initial angioplasties performed in the late 1970s. In particular, the development of bare metal stents and, more recently, drug-coated stents, modern angioplasty balloon catheters and equipment, and safer while more effective antiplatelet therapy has improved procedural success and reduced mortality.11 Indeed, patients with higher degrees of multivessel disease, as well as concomitant comorbidities, are increasingly offered PCI with maintained outcomes.11 This is confirmed by the dramatic shift toward PCI for the majority of patients presenting with coronary artery disease, as opposed to bypass surgery, as well as recent trends toward increased multivessel and left main PCI.12

However, progress in advanced PCI, as well as the management of acute myocardial infarction and advanced heart failure, including both acute decompensated failure and cardiogenic shock, has perhaps hit a plateau in the sickest patients. Chiefly, patients undergoing high-risk PCI, especially in the setting of severe ventricular dysfunction, clinical instability, or advanced age, and those presenting with cardiogenic shock or preshock, whether or not in the setting of acute myocardial infarction, continue to pose an especially high threat of progression to death or severe debility.13,14 In the case of high-risk PCI, such procedures are often either deferred or not considered entirely because of excessive risk, although finding actual rates of denial or deferral in real-world practice remains elusive. In the case of decompensated heart failure with low cardiac output or frank cardiogenic shock, available options have long been limited. Although inotrope and vasopressor therapy can improve short-term outcome, long-term survival is negatively affected.15,16 Furthermore, such management options may not work in all patients and may concomitantly impair peripheral organ perfusion and function, leading to multiorgan disease that may persist and affect clinical outcome after the acute hemodynamic insult has resolved.17–20 Finally, despite the incredible improvement in survival among those presenting with acute myocardial infarction, many patients are left with sizable infarcts that limit long-term survival and quality of life despite impressive short-term outcome. In addition, those in whom cardiogenic shock develops, mortality remains ≈50% despite revascularization.14

It is for these 3 patient populations (high-risk PCI, acute decompensated heart failure, and acute myocardial infarction, with or without cardiogenic shock) that use of percutaneous cardiac assist devices has been historically employed and that more powerful modalities of support are now being considered. For >40 years, the intra-aortic balloon pump (IABP) has remained either the only available or the most widely utilized percutaneous cardiac assist device for such situations. Developed in 1968, the device works on the concept of aortic counterpulsation, whereby diastolic inflation displaces blood both antegrade and retrograde in the aorta, improving diastolic mean arterial pressure and perfusion in both antegrade (systemic) and retrograde (great vessel and coronary) fashion.
During ventricular systole, active deflation of the balloon results in decreased afterload and associated ventricular wall tension, simultaneously increasing cardiac output (via an increase in stroke volume) and reducing myocardial ischemia through reductions in oxygen demand.\textsuperscript{21,22} Hemodynamic benefits are therefore a confluence of increased stroke volume (and cardiac output) and mean arterial pressure (diastolic augmentation), whereas ischemic benefits are a result of both increased coronary blood flow (CBF) (due to diastolic augmentation and reduction of left ventricular end-diastolic pressure) and decreased oxygen consumption (decreased wall tension). Importantly, these effects appear temporary and dependent on optimal timing of inflation and deflation to pressure- or ECG-based triggers.

Although conceptually powerful and utilized liberally in all 3 aforementioned clinical scenarios, use of the IABP in clinical practice has shown equivocal or, at best, modest benefit. Indeed, although one might expect the combined perfusion and ischemic benefits to be strongest in patients with ST-segment elevation myocardial infarction and hemodynamic compromise, a recent meta-analysis of randomized and observational data failed to show a clear advantage to IABP placement in either clinical outcome or ventricular function, especially when patients received optimal care including primary angioplasty.\textsuperscript{23} Moreover, there was evidence that IABP placement promotes harm, including stroke.\textsuperscript{23} There are several limitations to the IABP that may explain these findings. From a hemodynamic standpoint, it is estimated that cardiac output is augmented by 0.5 L/min.\textsuperscript{24,25} Although the increases in stroke volume and mean diastolic pressure increase mean arterial pressure and result from coronary and systemic perfusion, such hemodynamic effects may not be sufficient to meet the demands of the sickest patients, especially those in developing or full-blown cardiogenic shock. Indeed, the benefit of the IABP may be more readily apparent in terms of myocardial ischemia, in which augmented diastolic pressure and diminished afterload and wall tension work to reduce myocardial oxygen demand while increasing oxygen delivery, thereby favorably affecting ischemic threshold. Yet even in this regard, more powerful devices theoretically mitigate ischemia to a greater degree. Furthermore, the IABP is limited by its reliance on innate cardiac function and a stable electric rhythm in order to achieve its full potential, features that may not be consistently present in the critically ill patient. Finally, the increased incidence of stroke seen with use of the IABP, perhaps related to repetitive aortic contact and retrograde diastolic blood flow, remains a cause for concern. Thus, cardiovascular practice has long awaited the arrival of newer, more potent ventricular assist devices that might advance outcomes in these 3 situations and perhaps even drive a paradigm shift in their management toward earlier device placement.

**Goals of Novel Percutaneous Cardiac Support Devices**

From the previous discussion, it is clear that novel devices must provide benefits above and beyond those attainable by counterpulsation, while minimizing any associated safety hazards, to positively affect outcome in the sickest and highest-risk populations. Not only will such devices need to be powerful modifiers of hemodynamic parameters and perfusion (hemodynamic support), but they must concomitantly markedly affect the ischemic threshold (myocardial protection).

**Hemodynamic Support**

Acute decompensated heart failure and cardiogenic shock have hemodynamic instability as a principal feature, whereas high-risk PCI and acute myocardial infarction have acute hemodynamic decompensation due to ischemia as a principal threat. More important to the former clinical situations than the latter, the ability to maintain hemodynamic stability remains a primary objective in cardiac support. In particular, this includes attainment and maintenance of physiologically appropriate mean arterial pressure, cardiac output, and pulmonary venous pressure for the given clinical state while ensuring adequate organ perfusion at the tissue level.

The field of hemodynamic support has evolved with regard to underlying concepts of adequate perfusion, cardiac output, and mean arterial pressure. Despite years of inotrope and vasopressor therapy, few positive benefits have been noted in patient outcome; indeed, most studies indicate higher morbidity and mortality with use of such agents.\textsuperscript{16–20,26–28} This has led many to believe that proper targets for hemodynamic support may not be fully characterized and that, as a result, patients may either be receiving insufficient or excessive support, with consequent poor outcome. Recently, the prognostic ability of a novel hemodynamic parameter, cardiac power output (CPO) measured in watts, has been elucidated. This parameter, defined as the mean arterial pressure multiplied by the cardiac output and divided by 451, accounts for both systemic flow and maintenance of physiologically appropriate blood pressure. The concept takes into account collective experience that cardiac output is necessary but likely not sufficient for end-organ perfusion; adequate mean arterial pressure appears to also be required.\textsuperscript{29}

Several recent studies have retrospectively corroborated the prognostic power of this novel hemodynamic parameter. CPO was able to predict mortality in various cardiac conditions, including myocardial infarction–related cardiogenic shock, both ischemic and nonischemic cardiomyopathy, and fulminant myocarditis.\textsuperscript{29–31} For lesser degrees of decompensation, CPO was able to predict worsening heart failure in patients admitted with heart failure or preshock. In these same studies, neither cardiac output alone nor other more traditional parameters were independently associated with mortality. Importantly, certain CPO cut points have now emerged as potential predictors of outcome, although not validated in prospective fashion; specifically, CPO <0.6 W predicted worsening heart failure in those admitted for heart failure exacerbation, whereas CPO <0.53 W predicted mortality in patients with cardiogenic shock.

From a hemodynamic standpoint, therefore, one would theorize that cardiac assist devices should maintain both cardiac output and mean arterial pressure (CPO) at levels higher than these cut points, despite the underlying degree of cardiac dysfunction, to promote diuresis, optimize pulmonary...
venous pressure, maintain hemodynamic stability, and improve survival. The ideal device would be able to achieve these conceptual targets without concomitant vasopressor or inotrope therapy and thereby avoid the cardiotoxicity, multi-organ dysfunction, and acute and long-term morbidity and mortality of these agents. In current practice, use of the IABP does not appear to provide sufficient cardiac output and/or mean arterial pressure support to maintain adequate CPO without the additional use of deleterious vasoactive agents. Therefore, it seems clear that novel percutaneous support devices would need to affect both components of CPO to a greater degree than the IABP to provide substantive benefit in real-world practice.

Myocardial Ischemic Protection

Myocardial protection, or the ability to modify the oxygen supply-demand ratio favorably, is an important target of device therapy for patients undergoing high-risk PCI as well as those patients presenting with acute myocardial infarction. In both situations, prolonged ischemia can exacerbate diastolic and systolic ventricular dysfunction, extend infarction, and threaten hemodynamic stability. Novel cardiac assist devices must therefore be able to modify both oxygen demand and supply favorably, with the most powerful devices ideally suited for these 2 clinical situations.

Relying almost completely on aerobic metabolism, the heart extracts more oxygen from blood than any other organ in the body. As a result, under situations of increased oxygen demand, the heart must meet such demand by increasing CBF, or the clinician must meet the demand via supplemental oxygen or blood products (carrying capacity). In clinical practice, therefore, CBF augmentation is the principal mechanism whereby a percutaneous device might increase oxygen supply.

On the basis of the principles of fluid dynamics, CBF is directly related to the pressure difference across the vascular bed and inversely related to any resistance (myocardial microvascular resistance) to flow. Because coronary flow is primarily in diastole, the pressure gradient is the mean arterial pressure in diastole minus the downstream pressure, the latter being related to both right atrial and left ventricular end-diastolic pressure. The myocardial microvascular resistance, while tightly regulated by various neural, humoral, metabolic, extravascular compressive, and diastolic phase-related factors, approximates well with myocardial stiffness or wall tension, which also relates closely to left ventricular end-diastolic pressure. To increase CBF, therefore, novel devices must augment mean arterial pressure and/or reduce left ventricular end-diastolic pressure, affecting both perfusion pressure and myocardial microvascular resistance, with the most powerful devices significantly affecting both.

Consistent with this, the ability to manipulate myocardial microvascular resistance, through its effect on coronary flow velocity reserve and resultant CBF, has been linked to left ventricular recovery in acute myocardial infarction, validating this approach.

Reducing oxygen demand is an equally powerful mechanism to raise the ischemic threshold and therefore an equally important target for percutaneous assist devices. Although oxygen demand is related to heart rate, contractility, preload, afterload, and muscle mass, all components are interrelated and may be most conveniently discussed in terms of pressure-volume loop analysis (Figure 1). In Figure 1A, the 4 points A through D relate to ventricular systole and mitral valve closure (A), aortic valve opening and ejection (B), aortic valve closure (C) and mitral valve opening (D). Intervening segments are isovolumic contraction (from A to B), ejection (from B to C), isovolumic relaxation (from C to D), and ventricular filling (from D to A). B. Relationship of pressure-volume loop to ESPVR and EDPVR, the slope of the ESPVR (E_max), and the volume axis intercept (Vo). LV indicates left ventricular.

Although decreasing heart rate directly affects oxygen demand and consumption, the concept of pressure-volume area (PVA) has evolved as the strongest index of oxygen consumption per beat. The PVA is the area bounded by the ESPVR and ESPVR and the systolic portion of the pressure-volume loop and therefore represents both the area within the loop (stroke work or mechanical energy) and the area to the left of the loop (residual energy stored within the myocardium at the end of the beat, or potential energy) (Figure 2). Thus, devices that both reduce the area within the loop and shift the loop to the left favorably affect oxygen demand and consumption. Specifically, devices may decrease preload (left shift of the pressure-volume loop and modification of ESPVR) or decrease afterload and contractility (lower slope of the ESPVR and downward shift of ESPVR curve), resulting in marked reduction in PVA. Recent in vivo data appear to support these potential benefits.

Taken together, it is clear that devices that affect both oxygen supply and demand will provide clear myocardial protective advantages, particularly in situations in which ischemia seems likely to occur (high-risk PCI) or is ongoing (acute myocardial infarction). The ideal device for these indications would therefore maximally reduce oxygen consumption (demand) by reducing both stroke work and potential energy (and total PVA) while simultaneously augmenting oxygen supply (CBF).
The TandemHeart device (Cardiac Assist Inc, Pittsburgh, PA) is a percutaneous left atrial to iliac artery bypass, powered by an external centrifugal pump that provides up to 3.5 to 4 L/min of forward flow by standard implantation technique. It is designed for use in patients with cardiogenic shock.56,57 Although the approach appeared feasible, it had limitations in application and potential complications. Rather than being viewed as competing technologies, each may be beneficial in unique clinical scenarios, making a full understanding of each device imperative for both implanting and requesting physicians (Table).

**The Devices: Mechanism of Action, Cardiovascular Benefits, and Clinical Data**

Two novel devices dominate the current landscape and differ in implantation technique, mechanism of action, maximal flow rate, and resultant ability to modify hemodynamic parameters and ischemic threshold. They also differ significantly in ease of insertion and potential complications. Rather than being viewed as competing technologies, each may be beneficial in unique clinical scenarios, making a full understanding of each device imperative for both implanting and requesting physicians (Table).

**TandemHeart**

The TandemHeart device (Cardiac Assist Inc, Pittsburgh, PA) is a percutaneous left atrial to iliac artery bypass, powered by an external centrifugal pump that provides up to 3.5 to 4 L/min of forward flow by standard implantation technique.43,44 (Figure 3). It received 510(k) clearance from the Food and Drug Administration in the United States for extracorporeal circulatory support of procedures not requiring full cardiopulmonary bypass for up to 6 hours of continuous use, although reports have described utility up to 14 days. To access the left atrium as well as the iliac artery, both arterial and venous access must be obtained at the femoral vessels. After venous access, transseptal puncture is performed, and a 2-stage dilator (14F then 21F) is used to dilate the interatrial septum and implant the 21F inflow cannula into the left atrium. After this, a 15F (maximal estimated flow, 3.5 L/min) or 17F (maximal estimated flow, 4.0 to 5.0 L/min) outflow cannula is advanced to the iliac artery by way of the femoral artery, utilizing the standard Seldinger technique. Alternatively, two 12F cannulas can be utilized in bilateral femoral arteries, with potential for less vascular compromise at the expense of diminished maximal flow rates (≈ 2.5 L/min). The cannulas are deaired and connected to the external centrifugal pump, anticoagulation is provided, and flow is initiated. Because of the relatively complicated insertion technique, requiring transseptal puncture, insertion times on average exceed 30 minutes in the nonemergent setting.45 Complications have included tamponade, major bleeding, critical limb ischemia, sepsis, arrhythmia, and residual atrial septal defect, the latter at times requiring treatment. Contraindications include aortic insufficiency, ventricular septal defect, and significant peripheral vascular disease. For these reasons, the device is implanted only by physicians experienced in transseptal puncture, and distal aortography with bilateral iliac runoff is required before implantation.

Cardiovascular benefits of the device include both hemodynamic support and myocardial ischemic protection. Because near-systemic flow rates can be achieved (dependent on adequate filling pressure and cannula diameter), the device augments mean arterial pressure and systemic flow substantially and consequently CPO significantly.44 As a result, CPO augmentation appears superior to that achievable by the smaller Impella 2.5 device (described below) but likely inferior to what may be achieved with the larger Impella 5.0 device. In simulated continuous-flow models mimicking the Impella and the TandemHeart, which allow us to standardize baseline hemodynamic parameters and thereby compare the 2 devices conceptually, cardiac output and mean arterial pressure augmentation confirm the TandemHeart as performing midway between the 2 Impella devices, regardless of underlying hemodynamic state (preserved cardiac output or cardiogenic shock).56–54 (Figures 4 and 5). Thus, hemodynamic support appears to track directly with degree of continuous flow.

From a myocardial ischemic protection standpoint, the TandemHeart successfully, yet indirectly, unloads the left ventricle, decreasing PVA and oxygen consumption. Under normal cardiac output conditions, the reduction in PVA appears greater than that seen with the Impella 2.5 device but not as great as seen with the Impella 5.0 device (Figure 4). Interestingly, however, under conditions of low cardiac output and cardiogenic shock, the reduction in oxygen consumption of the TandemHeart appears offset by increases in afterload (which increase oxygen consumption), and in such cases the myocardial protective benefits of the TandemHeart appear inferior to those achieved by the directly unloading Impella devices, regardless of whether the Impella 2.5 or 5.0 is utilized (Figure 5).

The clinical benefit of a transseptal ventricular assist device has been seen in animal models of acute myocardial infarction and cardiogenic shock, during which the bypass circuit both restored microvascular and epicardial blood flow and reduced infarct size.55 In a prospective feasibility trial of 18 patients with cardiogenic shock, use of the TandemHeart resulted in significant augmentation of mean arterial pressure while producing marked reductions in left ventricular end-diastolic pressure, stroke work, and resultant myocardial oxygen demand.44 In addition, 2 small multicenter, randomized trials comparing the TandemHeart with IABP have been performed in patients with acute myocardial infarction and cardiogenic shock.56,57 Although the approach appeared fea-
sible, with marked improvements in hemodynamic parameters, a small meta-analysis of the 2 trials did not show a difference in mortality, and bleeding complications ranged from 40% to 90%.56–58

For high-risk PCI, 1 single-center experience showed safety and feasibility, and several case series have also highlighted the potential benefits of this approach in various clinical and angiographic subsets at risk of hemodynamic collapse.43,45,59 To date, however, there has been no large, multicenter randomized clinical trial comparing TandemHeart with any other support device in high-risk PCI. Two somewhat larger case series have been published recently.60,61 The first evaluated the TandemHeart in 23 patients undergoing high-risk PCI. Implantation was successful in all patients, with PCI successful in 91%, although 5 patients died with the device in place, primarily because of preexistent cardiogenic shock. Access site bleeding and hypothermia were each noted in 25% of patients. In the other series, 37 patients received the device for either high-risk PCI or cardiogenic shock. In this sick population, with 97% in New York Heart Association class III heart failure or cardiogenic shock, PCI was successful in all patients, and 71% survived to discharge. However, 82% required blood transfusion because of procedure-related bleeding. To decrease risk of bleeding, more recent experience includes a “preclose” technique to expedite hemostasis at the arteriotomy. Whether bleeding rates will ultimately improve remains to be seen.

**Impella 2.5 and 5.0**

As opposed to the TandemHeart centrifugal flow pump, the Impella (Abiomed Inc, Danvers, MA) uses a miniaturized axial flow pump fitted onto a pigtail catheter to directly unload the left ventricle (as opposed to the left atrium) and deliver blood to the ascending aorta, simulating normal physiology (Figure 6). It received 510(k) clearance from the Food and Drug Administration in 2008 for partial circulatory support. Similarly approved in the United States for up to 6 hours, clinical trials allow use for up to 7 days in the United States and 10 days in Europe. There are 2 available devices that provide either partial (Impella 2.5) or full (Impella 5.0) hemodynamic support, indicating maximal flow rates of 2.5 and 5.0 L/min, respectively. Unlike the TandemHeart, the Impella requires 1 femoral arterial access and no venous access. Anticoagulation is obtained, and the aortic valve is

<table>
<thead>
<tr>
<th>Insertion Technique</th>
<th>Major Complications</th>
<th>Effect on Circulation</th>
<th>Advantages</th>
<th>Limitations</th>
<th>Indications</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>IABP</td>
<td></td>
<td>Augment CO by up to 0.5 L/min</td>
<td>More prolonged support duration</td>
<td>Requires stable rhythm</td>
<td>Used in high-risk PCI, acute MI, and cardiogenic shock, although equivocal benefit</td>
<td>Moderate to severe AI, Aortic disease</td>
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<tr>
<td>Single arterial</td>
<td></td>
<td>Indirectly unloads LV</td>
<td>Lowest level of support</td>
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<td>Uncontrolled sepsis Coagulopathy</td>
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<td>8F to 9F</td>
<td></td>
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<tr>
<td>TandemHeart</td>
<td></td>
<td>Augment CO by up to 3.5 L/min</td>
<td>Prolonged support duration</td>
<td>Large arterial cannulas</td>
<td>All, but likely more useful in cardiogenic shock than high-risk PCI or acute MI</td>
<td>VSD, PAD</td>
</tr>
<tr>
<td>Transseptal puncture required</td>
<td>Aortic puncture, Limb ischemia (most risk)</td>
<td>Partial LV support</td>
<td>Indirectly unloads LV</td>
<td>Requires transseptal puncture</td>
<td>RV failure</td>
<td></td>
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<tr>
<td>21F inflow (venous)</td>
<td>Bleeding and transfusion (most risk)</td>
<td></td>
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<tr>
<td>15F outflow (arterial)</td>
<td>Residual ASD</td>
<td></td>
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<tr>
<td>Impella 2.5</td>
<td></td>
<td>Augment CO by up to 2.5 L/min</td>
<td>Prolonged support duration</td>
<td>Relatively large arterial cannulas</td>
<td>All, but likely more useful in high-risk PCI and acute MI than cardiogenic shock</td>
<td>LV thrombus, VSD</td>
</tr>
<tr>
<td>Single arterial access</td>
<td>Bleeding (minimal risk)</td>
<td>Partial LV support</td>
<td></td>
<td></td>
<td></td>
<td>Severe aortic stenosis, RV failure</td>
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<tr>
<td>13F</td>
<td></td>
<td>Directly unloads LV</td>
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For this comparison, the 3 most utilized devices are compared, including the IABP, the TandemHeart with 15F outflow, and the Impella 2.5. ASD indicates atrial septal defect; CO, cardiac output; LV, left ventricle; MI, myocardial infarction; VSD, ventricular septal defect; AI, aortic insufficiency; PAD, peripheral arterial disease; and RV, right ventricular.
crossed in retrograde fashion with the use of a multipurpose catheter and standard technique. An exchange-length 0.018-inch stiff wire is utilized to exchange for the 13F Impella 2.5 catheter with the monorail technique (21F Impella 5.0 catheter). The device is positioned with its elbow at the aortic valve, the wire is removed, and flow is initiated. Given its familiar implantation technique, sole arterial access requirement, smaller catheter diameter, and avoidance of complicated techniques such as transseptal puncture, implantation appears more rapid than TandemHeart (10 minutes), and complication rates appear lower.62 In particular, the absence of a transseptal puncture requirement makes tamponade an unlikely event. However, hemolysis has been reported more frequently in the first 24 hours, in 5% to 10% of patients.63 Contraindications to device placement include significant peripheral vascular disease, at least moderate (<1.5 cm²) aortic stenosis or insufficiency, ventricular septal defect, and left ventricular thrombus. As with the TandemHeart, distal aortography with runoff is required before device placement. Although both the smaller Impella 2.5 and the larger Impella 5.0 are utilized in clinical practice, the smaller device typically dominates the clinical landscape because of its smaller profile and autonomous implantation by the interventional cardiologist.

Cardiovascular benefits of the Impella devices similarly include both hemodynamic support and myocardial ischemic protection. Cardiac output and mean arterial pressure are increased, although the maximal CPO benefit of the Impella 2.5 falls short of that achievable with the TandemHeart in simulated models64 (Figures 4 and 5). In contrast, the Impella 5.0 device would provide superior CPO support compared with the TandemHeart. From a myocardial protection standpoint, Impella appears to exert uniquely powerful effects because of its direct unloading of the left ventricle, which appears to decrease oxygen demand and consumption to a larger degree at comparable flow rates than the TandemHeart while simultaneously increasing CBF through augmented mean arterial pressure and decreased left ventricular end-diastolic pressure.64–67 The greater effects are most notable when cardiac output is low or under conditions of cardiogenic shock (Figure 5). In these situations, on the basis of simulated models, both Impella devices appear to lower PVA to a greater degree than TandemHeart, with the latter paradoxically increasing oxygen consumption.

Clinical data appear more voluminous with the Impella and include randomized controlled trials and observational registries, reflecting the greater utilization of this device in real-world practice. The Prospective Feasibility Trial Investigating the Use of the Impella Recover LP 2.5 System in...
Patients Undergoing High Risk PCI (PROTECT) I trial was a safety and feasibility multicenter trial in 20 high-risk PCI patients (reduced ejection fraction combined with left main or last remaining conduit PCI). Hemolysis was noted in 2 patients within 24 hours, resolving spontaneously, but no other major safety concerns were noted. The Academic Medical Center Mechanical Support for Acute Congestive Heart Failure in STEMI Patients (AMC MACH)-1 trial corroborated these initial results. The subsequent AMC MACH-2 trial evaluated patients with anterior ST-segment elevation myocardial infarction without cardiogenic shock in nonrandomized fashion, comparing Impella 2.5 with IABP placement after primary PCI. More marked improvements in left ventricular ejection fraction were noted in the Impella 2.5 group, consistent with its myocardial protective benefits. Significant hemolysis was not noted. The Impella LP 2.5 vs IABP in Cardiogenic Shock (ISAR-SHOCK) trial randomized 26 patients with ST-segment elevation myocardial infarction and cardiogenic shock to the Impella 2.5 or IABP and showed greater augmentation of cardiac index and mean arterial pressure in those assigned to Impella. The ongoing PROTECT II trial is currently enrolling patients with reduced ejection fraction, multivessel, left main, or sole remaining conduit PCI, randomizing in 1:1 fashion Impella 2.5 and

Figure 5. Simulated models of continuous flow from the left ventricle (LV) to the aorta (Ao) (mimicking Impella) at the 2 flow rates of 2.5 and 5.0 L/min and from the left atrium (LA) to the aorta (mimicking TandemHeart) at the flow rate of 4.0 L/min, in cardiogenic shock (CGS). Cardiac output (CO) and mean arterial pressure (MAP) are increased most with simulated Impella 5.0 device, followed by TandemHeart and Impella 2.5. Myocardial protection in cardiogenic shock appears greatest with either Impella device. EDP indicates end-diastolic pressure; VAD, ventricular assist device.

Figure 6. The Impella device consists of a single pigtail 12F catheter with inflow positioned in the left ventricle, outflow in the ascending aorta, and an incorporated intravascular axial pump (maximal rotation 51,000 rotations per minute) that can deliver up to 2.5 L/min of continuous flow.
IABP therapies, with a combined major adverse cardiovascular end point of death, myocardial infarction, stroke, repeat revascularization, emergent surgery, acute renal failure, severe hypotension, and/or failure to achieve angiographic success.

Two large observational real-world registries utilizing the Impella 2.5 device have been either presented (USpella) or published (Europella). In both, the Impella was used in predominantly older patients with multiple comorbidities, who in many cases had already been denied coronary artery bypass grafting. The overwhelming majority of cases involved reduced ejection fraction <30%, and coronary interventions were performed on multivessel, left main, or last remaining conduit disease. In the Europella registry of 144 patients undergoing high-risk PCI, 30-day mortality was 5.5% and myocardial infarction and stroke <1%. Bleeding was seen in ~6%, vascular complications in 4%, and significant hemolysis in <1%. In the USpella registry of 181 patients undergoing device placement in various clinical situations, presented data showed 6% with a major adverse cardiac event and 3% mortality at 30 days. Interestingly, high-risk PCI patients evidenced marked improvements in their SYNTAX score after intervention compared with their initial score (mean score, 18 after intervention versus 38 before intervention), indicating that multivessel PCI was being performed routinely in these patients after device placement and was associated with a significant increase in ejection fraction from a mean of 29% to 34%. Of note, a similar increase in ejection fraction was also noted in the earlier PROTECT I trial. In contrast to the Europella registry of high-risk PCI, the USpella included patients treated for acute myocardial infarction and cardiogenic shock.

In such patients, Impella was utilized after more conservative measures had failed, including high-dose inotropes, IABP placement, and emergent revascularization in 88%, 68%, and 88%, respectively. Impella improved hemodynamics, including cardiac index, mean arterial pressure, pulmonary capillary wedge pressure, and systemic vascular resistance, and resulted in a significant increase in ejection fraction (37% in follow-up versus 29% at time of PCI). It is important to note, however, that confirmation of these preliminary results awaits the full evaluation and publication of the USpella data. In contrast to the Impella 2.5 device, experience with the 5.0 device has to date been limited to anecdotal experience.

Developing Indications for Percutaneous Cardiac Assist Devices: Choosing Between Devices

On the basis of the aforementioned available data, and as noted earlier, these novel percutaneous cardiac assist devices may create a paradigm shift in the manner in which we approach patients with advanced heart failure, those with acute myocardial infarction (with or without cardiogenic shock), and those undergoing high-risk PCI and may thus allow for opportunities to improve outcome in these difficult patient subsets. In all 3 populations, limitations of the current standard of care may potentially be mitigated with the initiation of safe and effective percutaneous cardiac support. Whether device therapy will ultimately prove beneficial and whether one device is superior to the other in each situation remain to be seen.

In the case of high-risk PCI, in which we have the most observational and randomized data, the threat of hemodynamic collapse due to prolonged ischemia or coronary complication is an overriding concern. In such patients, the procedure is most often elective, and therefore patients are hemodynamically stable at the start of the procedure. Therefore, a device with superior ability to increase oxygen supply and decrease oxygen demand would be preferable to one that prioritizes hemodynamic support (CPO). In addition, a device with widespread familiar implantation technique, minimal access sites, and smaller profile would be ideal. Recently, however, the IABP was tested in this context and was preliminarily found to provide no significant benefit in high-risk PCI despite fulfilling most of these criteria. As a result, the Impella 2.5 device has emerged as on balance most beneficial, providing stronger mechanical anti-ischemic therapy while maintaining ease of use. Indeed, at least in observational experience, the clinical stability afforded by this device appears to allow for multivessel single-setting PCI, more complete revascularization, and an increase in ventricular function, as seen in the USpella registry. Therefore, a developing indication for cardiac assist device placement in high-risk PCI may be for the safe and rapid performance of elective complete percutaneous revascularization, when coronary bypass surgery is contraindicated or considered high risk, to improve ejection fraction, quality of life, and overall survival. As with the IABP, however, confirmation of this application awaits results from the ongoing PROTECT II trial.

Similarly, in uncomplicated acute myocardial infarction, minimizing ischemia (and ultimately reducing infarct size) while facilitating rapid primary PCI is the primary goal. The Impella 2.5 device again seems ideally suited for this indication because of its direct effect on the ischemic threshold and shorter time to safe insertion and institution (which might only minimally affect door-to-balloon times). In acute myocardial infarction with mild to moderate degrees of congestive heart failure and reduced cardiac output, the Impella 2.5 again seems superior on balance because the hemodynamic support of the Impella 2.5 device would likely prove sufficient in such states to both rest the heart and normalize systemic perfusion and venous pressure while its myocardial protective effects concomitantly limit infarct size. Although current understanding and official guidelines of acute ST-segment elevation myocardial infarction care prioritize door-to-balloon times above almost all else (in effect, prioritizing improved CBF over reductions in myocardial oxygen demand), it will be interesting to see whether the marked benefit of device placement on oxygen consumption might ultimately prove more beneficial as an initial strategy in patients at risk for large infarction and resultant left ventricular dysfunction, such as those with proximal left anterior descending occlusions. In this regard, the ongoing European Impella Versus IABP Reduces Infarct Size in STEMI Patients Treated With Primary PCI (IMPRESS in STEMI) trial is a randomized comparison of IABP with Impella 2.5, and their respective effects on ejection fraction, in preshock ST-segment elevation myocardial infarction patients.
As the degree of heart failure worsens, however, and especially in those with frank cardiogenic shock (either due to acute myocardial infarction, acute on chronic heart failure, or fulminant myocarditis), hemodynamic support becomes the predominant concern. In these patients, the Impella 2.5 device may prove insufficient, and the TandemHeart or Impella 5.0 device would seem indicated to increase CPO to levels that would avoid end-organ dysfunction, despite their longer time to implantation and associated higher complication rates (both cardiac and vascular). When both hemodynamic support and myocardial protection are taken into consideration, the Impella 5.0 appears to outperform the TandemHeart device. However, because the larger Impella 5.0 may require surgical collaboration and thereby delay institution of therapy, the TandemHeart may prove to be the best initial option in such patients, despite an associated potential increase in oxygen consumption. Ultimately, reduced caliber of the 5.0 device over time, to a size that permits routine percutaneous placement without surgical assistance, may elevate this device as the preferred option.

Given that inotrope and vasopressor therapies in such patients have been shown to extend infarct size and reduce long-term survival (despite a modest improvement in short-term survival), as discussed earlier, further research is needed to determine optimal timing of percutaneous cardiac support device implantation to obviate the need for deleterious pharmacotherapy. By taking over the work of the heart earlier in the course of cardiogenic shock and allowing the heart to rest while maintaining acceptable systemic perfusion, such devices may ultimately reduce the incidence of end-stage heart and multiorgan system failure and improve quality of life and survival. Randomized controlled trials comparing early institution of device therapy to increasing doses of inotrope and vasopressor therapy are therefore needed.

Conclusions

Novel percutaneous cardiac assist devices have been utilized increasingly over the past several years and have forced a reevaluation of the patient populations that might benefit. Specifically, patients undergoing high-risk PCI, those with acute myocardial infarction, and those with higher degrees of heart failure and/or shock may stand to benefit from such devices. Although the benefit of one device over the other may be suggested by simulated models of flow and ischemic protection, the comparative merits and hazards of each device for these indications ultimately await further randomized and observational data. It appears likely, however, that continued refinements in technology and technique will usher in new device-based strategies to improve outcome in multiple patient populations.

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