Review

Percutaneous ventricular assist devices: clinical evidence

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Practice Points

- Intra-aortic balloon pumps, Impella Recover LP 2.5 and TandemHeart® are the three most readily available percutaneous ventricular assist devices.
- TandemHeart offers a maximum 3.5 l/min hemodynamic support, Impella Recover LP 2.5 a 2.5 l/min support, while IABP offers no hemodynamic support.
- Specific complications may be life threatening and contraindications differ for each device.
- Indications include support in cardiogenic shock, myocardial infarction without shock, prophylactic use in high-risk percutaneous coronary interventions, ventricular tachycardia ablation and percutaneous valvular implantation.
- Impella Recover LP 2.5 is most adapted for prophylactic use, whereas TandemHeart offers better support in cardiogenic shock.
- Specially adapted devices are required for the support of right ventricular failure.
- Percutaneous assist devices may be used as bridges until recovery from cardiogenic shock, long-term surgical ventricular assist device implantation as well as heart transplantation.
- Clinical evidence shows clear benefits on a patient-based level.
- There is no solid evidence-based data on increased survival or diminished morbidity.

SUMMARY Efficient therapy of cardiogenic shock and optimal protection in high-risk percutaneous coronary intervention are still orphaned to ideal management. Intra-aortic balloon pump and the newer percutaneous ventricular assist devices, such as TandemHeart and Impella Recover LP 2.5, have diversified the therapeutic arsenal with which one can tackle these clinical dilemmas. This article describes the characteristics of these three devices as well as the clinical evidence available for optimal and adapted use.

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Without a doubt, cardiology has been the theater of substantial and ongoing progress over the last two decades. Advances in treatment of acute coronary syndromes are multileveled, mainly: early detection of cardiovascular risk factors, elaboration of efficient pharmacological drugs and development of percutaneous coronary interventions (PCIs). PCI had a decisive role in the management and outcome of acute coronary syndromes, changing the paradigm upon which a myocardial infarct left the patient either moribund or dead. PCI is now safer and performed in more complex coronary disease configurations. Yet a consequence of this is that more patients suffer from congestive heart failure. Then again, progress has been substantial in the treatment whether through rehabilitation, pharmacotherapy or cardiac resynchronization therapy.

A subset of patients escape the bliss of this progress. Those with severe cardiac dysfunction, hemodynamic instability and those of extreme age are sometimes denied PCI due to excessive risk. The incidence of cardiogenic shock in acute coronary syndromes with ST-elevation myocardial infarction is unchanged at approximately 7% [1] and mortality stagnates at an upsetting 60% [2].

Researchers have generated the idea of ventricular mechanical assistance in answer to these needs (e.g., cardiogenic shock, high-risk PCI, extensive myocardial infarction without cardiogenic shock), initially, through the development of intra-aortic balloon pumps (IABPs) and more recently with other percutaneous ventricular assist devices (pVADs). The objective of this review is to describe device distinctiveness as to insertion, mechanism, advantages, limitations and complications. We will also describe the clinical evidence currently available.

Intra-aortic balloon pump

Originally introduced in 1968, the IABP was the fruit of two decades of research on ventricular assistance. The key principle is aortic counterpulsation, much like an alternating pump with the heart. Today, the 7.5-French (Fr) to 9Fr balloon is inserted percutaneously via the Seldinger technique using the femoral artery puncture. The balloon lies in the descending aorta with its tip classically situated below the left subclavian artery **(Figures 1 & 2)**. Diastolic inflation displaces the blood antegrade to the systemic circulation and retrograde to the coronary arteries and great vessels. Systolic deflation, schematically, suctions the blood, decreases afterload and ventricular wall tension, thereby increasing stroke volume and reducing oxygen demand. It is crucial that the balloon be synchronized with the patient's cardiac cycle. This is usually achieved using the R wave on the patient's electrocardiogram; alternative methods are the arterial waveform or intrinsic pump rate. This is why its reliance is dependant on the intrinsic cardiac function and stable rhythm.

Clinically, IABP are the most widespread, affordable and simplest assist devices. They are used in cardiogenic shock accounting for 20% of all insertions [3] but may also be helpful in high-risk PCI as well as myocardial infarction without shock. It is effective in the stabilization of patients by acutely decreasing ventricular afterload and improving coronary perfusion but does not provide cardiac support. Furthermore, no significant outcome improvement could be demonstrated [4]. Indeed, a recent Cochrane Database Review on the use of IABP in cardiogenic shock demonstrated little benefit in survival and heterogeneous results as to complications [5]. Euro Heart Survey findings on PCI also failed to show favorable survival outcomes [6]. Surprisingly, only 25% of the 653 patients benefited from IABP in postmyocardial infarct cardiogenic shock. Regarding high-risk PCI and despite initial positive trials [7,8], a recent randomized controlled study in 301 patients with severe left ventricular dysfunction demonstrated no reduction in major cardiac events or 6-month mortality [9]. These results challenge the 2009 AHA class 1 evidence guidelines which stated that IABP should be used in cardiogenic shock that is not quickly reversed by pharmacologic therapy [10]. The mediocre hemodynamic output achieved probably explains why IABP fails to show obvious benefit in the sickest patients with cardiogenic shock. The role of IABP in protecting from further or pending myocardial ischemia by diminishing oxygen demand has recently been questioned in the CRISP AMI trial [11]. A total of 337 patients presenting with acute ST-elevation myocardial infarction without cardiogenic shock were randomized between IABP insertion prior to PCI versus PCI alone. The trial failed to show differences in infarct size, its primary outcome and each group suffered similar mortality rates and vascular complications.

Thus, both growing interest and research have been invested in the development of devices thought to supplement the failing heart by improving hemodynamic parameters as well as ischemic threshold. Various ventricular assist devices are used for a large scope of indications. Range extends from long-term replacement of failing hearts to bridge-to-transplantation and, more critically, in the temporary support of cardiogenic shock (bridge-to-recovery). Prophylactic use has been studied in certain invasive coronary, valvular or electrophysiological procedures. One distinguishes between long- and short-term as well as surgically implanted versus minimally invasive pVADs. These have the advantage of availability, simplicity of use and installation. Two pVADs have received US FDA- and CE-approval for clinical use, the TandemHeart® (Cardiac Assist Inc, Pittsburgh, PA, USA) [12] and the Impella Recover LP 2.5® (Abiomed, Europe, Aachen, Germany) **(Figures 1 & 2)** [13]. Although singular in implantation, mechanism and complications, both improve hemodynamic parameters. Each device is optimally used in different clinical settings.

Impella Recover LP 2.5

■ Implantation & complications

Impella Recover LP 2.5 is a left percutaneous 2.5 l/min, 12-Fr axial flow pump that works on the principle of an Archimedean screw. The impeller is inserted through the femoral artery via a 13-Fr peel-away sheath. A 5-Fr catheter is usually used to cross the aortic valve, such as a pigtail catheter, Judkins right 4, Sones or Amplatzer left 1 or 2. This is then exchanged for the 12-Fr device through a dedicated 0.014 inch guidewire to suction blood out of the left ventricle, through the aortic valve and into the ascending aorta. The microaxial pump is rapidly connected ("plug and play") and rotates the impeller at high speed, thereby aspirating blood through the left ventricular inlet and ejecting it into the aortic outlet. Once the support is finished, the flow pump is withdrawn percutaneously with hemostasis achieved through manual compression. Overall, its implantation is user-friendly and rapid (taking 10–15 min). The single arterial puncture, and no extracorporeal pump is a central quality. Both Impella and the TandemHeart require cautious angiographic vascular assessment prior to insertion in order to ensure ample vessel diameter, patency and tortuosity. Anticoagulation with heparin is mandatory; recommended activated clotting time is 250 s during the implantation and 200 s during the support phase. Common complications to both pVADs include limb ischemia, bleeding, thrombocytopenia and thromboembolic risk. Infections, on the other hand, are seldom encountered and usually appear in long-term surgical cardiac assist devices [14]. Use of the Impella Recover LP 2.5 can lead to two specific life-threatening complications: hemolysis and ventricular arrhythmia owing to its

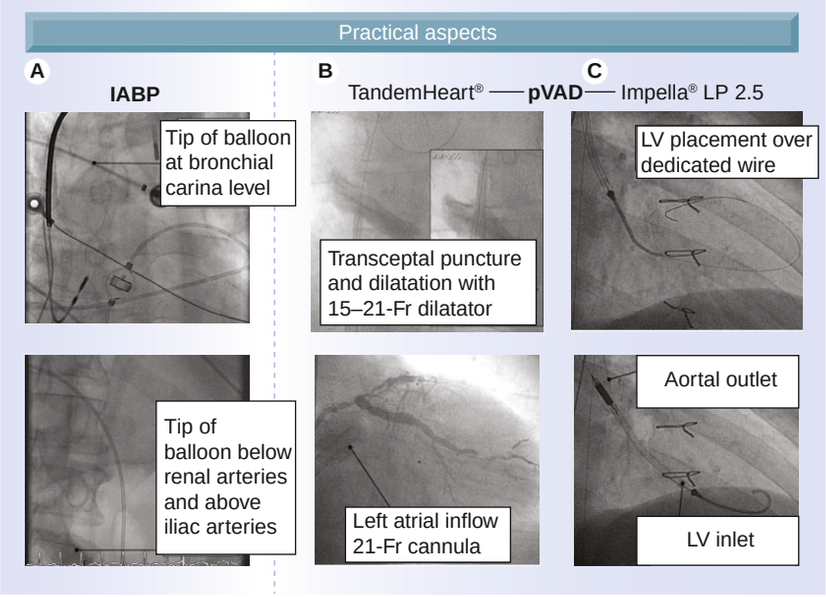

Figure 1. Fluoroscopic imaging and practical aspects of three commercially available percutaneous assist devices. (A) The intra-aortic balloon pump consists of a 7.5- to 9-Fr helium and carbon dioxide balloon. It is inserted in the descending aorta with its tip situated just below the left subclavian artery. It pumps the blood during diastole antegrade to the systemic circulation and retrograde to the coronary vessels. It deflates during systole and diminishes ventricular afterload. **(B)** The TandemHeart® pVAD consists of a 21-Fr left atrial inflow cannula, an extracorporeal centrifugal pump rotating at up to 7500 rpm, a femoral outflow cannula (15- to 17-Fr) that extends into the iliac artery, and a microprocessor-based pump controller, which can provide blood flow up to 3.5 l/min. The tip of the atrial drainage cannula is positioned under fluoroscopic guidance into the left atrium following trans-septal puncture. **(C)** The Impella Recover® LP 2.5 is a catheter-mounted device. The microaxial pump consists of an impeller driven by an integrated microelectric motor on the distal end of a flexible catheter. At a maximum speed of 33,000 rpm, the pump provides a maximum hydraulic capacity of 2.5 l/min. The Impella Recover LP 2.5 is retrogradely placed across the aortic valve into the left ventricle where it aspirates blood via a caged blood flow inlet, which is then ejected into the ascending aorta.
Fr: French; IABP: Intra-aortic balloon pump; LV: Left ventriular; pVAD: Percutaneous ventricular assist device.

intraventricular positioning. Logically severe aortic stenosis excludes its implantation.

Relative contraindications to both pVADs are severe aortic regurgitation, prosthetic aortic valve as well as aortic aneurysm or dissection. Severe peripheral vascular disease, left ventricular and/or atrial thrombi, severe coagulation disorders and uncontrolled sepsis further preclude their use.

Hemodynamic support & physiology

The 50,000 rpm flow pump achieves a maximum flow rate of 2.5 l/min. At minimum speed, the pump compensates the aortic regurgitation induced by the catheter. The support is of short duration from several hours to 5 days and a maximum of 10 days for certain clinical trials. The desired benefits are hemodynamic support through increased cardiac output and myocardial ischemic protection. This is achieved through ventricular 'unloading', reducing oxygen demand and consumption. The initial study that addressed this question showed little unloading of the left ventricle [15]. Recently, hemodynamic studies on 11 patients undergoing high-risk PCI with pre-emptive Impella insertion exerted more promising results with significant left-ventricular unloading as well as decreases in end-diastolic wall stress and improved diastolic compliance [16].

Considering cardiogenic shock, Impella implantation is expected to increase cardiac output by as much as 37% [17]. In the same study mean arterial pressure increased by 30% and pulmonary capillary wedge pressure diminished by 38%.

Interestingly, an identical device, Impella 5.0 achieves full hemodynamic support with a flow rate of 5 l/min [18,19]. Unfortunately, the larger diameter imposes surgical access and removal, complicating emergent insertion. Clinical experience and *de facto* evidence is weaker; we will not discuss this device further.

Clinical results

The first randomized trial to have compared the Impella Recover LP 2.5 to IABP showed increased cardiac output in the Impella group but no differences with respect to 30-day mortality [20]. The Euroshock registry evaluated the use of Impella Recover 2.5 in 120 patients with cardiogenic shock post acute myocardial infarction [21]. The hemodynamic profile of patients was severe when compared to other studies reflecting the last-resort use of pVAD. Consequently, the 30-day mortality rate was high at 64.2%. Age (patients over 65 years old) and plasma lactate at admission greater than 3.8 mmol/l were demonstrated to be significant predictors of 30-day mortality. Major cardiac and cerebral events were reported in 15% of patients.

The Europella Registry published a retrospective study with 144 patients and 30-day mortality was found to be 5.5%. A total of 6.2% of patients had bleeding and 4% suffered vascular complications [22]. Recently, Protect II, a randomized controlled study, compared the use of IABP to Impella Recover 2.5 in high-risk PCI in 305 patients. Abiomed terminated the trial end of 2010 after determining it could not reach its composite primary end point of ten major cardiac adverse events. Temporary results failed to demonstrate the superiority of the Impella Recover LP 2.5 [101].

Another large observational study, the USpella registry, included 181 heterogeneous patients with either preventive placement for high-risk PCI and in acute myocardial infarction and/or cardiogenic shock. Preliminary results, not yet published, presented a 6% incidence of major cardiac events, and a 3% mortality rate at 30 days [23].

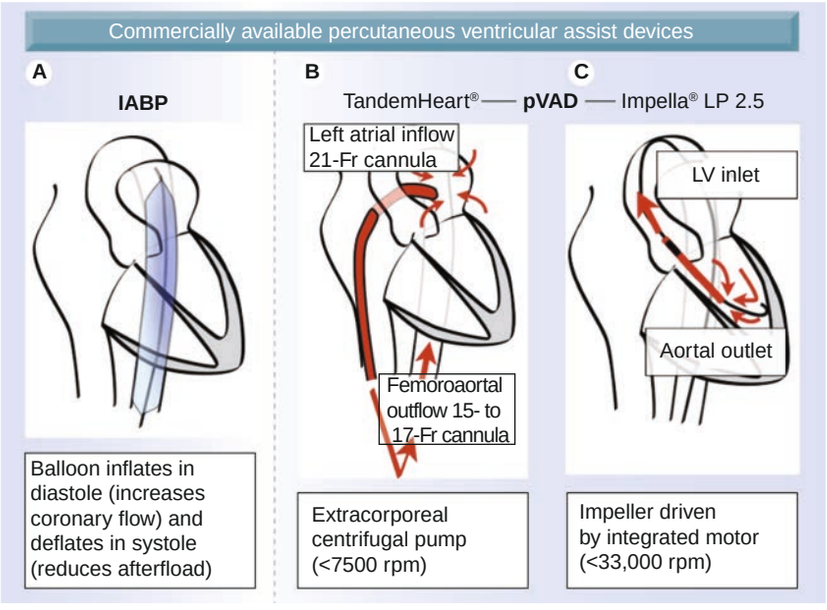

Figure 2. Commercially available percutaneous ventricular assist devices. **(A)** Intra-aortic balloon pump. **(B)** TandemHeart® **(C).** Impella Recover® LP 2.5. IABP: Intra-aortic balloon pump; LV: Left ventriular; pVAD: Percutaneous ventricular assist device.

TandemHeart

Implantation & complications

The TandemHeart® is a percutaneous left atrial-to-iliac bypass connected to an extracorporeal centrifugal pump powered by a microprocessor-controlled electromechanical unit, which enables rotation at 3500–7500 rpm. Both femoral artery and femoral vein puncture are required. By retrograde access, atrial septum puncture is performed through the standard Brockenbrough technique. It is crucial that interventional cardiologists be well trained in transseptal puncture to perform adequate implantation. Then, the interatrial septum is dilated using a two-stage (14–21-Fr) dilator to accommodate the 21-Fr left atrial drainage cannula. It is imperative that blood be properly suctioned from the left atrium. Common pitfalls include inflow cannula kinking or right atrium dislodgement, functionally corresponding to a right-to-left shunt and hypoxemia. The inflow cannula needs to be secured and immobilized in order to minimize the risk of dislodgement. Then, using the Seldinger technique, a 15–17-Fr femoral artery cannula is placed retrogradely in the iliac artery. Both cannulae are connected to the centrifugal pump under careful evacuation of any air within the tubing. Maximal estimated flow depends on the diameter of the inflow cannula. Evidently, the risk of limb ischemia and local vascular complications increases with the cannula diameter. Another option is bilateral femoral artery puncture with implantation of two 12-Fr inflow cannulae allowing for less vascular compromise but, equally, decreased maximal flow rate. In general, the implantation is more complicated and time-consuming than with Impella Recover LP 2.5; reports account for average insertion times of approximately 30 min.

Continuous use extends from hours to as much as 15 days. Weaning criteria are usually met when cardiac index and mean arterial pressure exceed 2.0 l/min/m^2 and 70 mmHg, respectively, in the absence of endorgan hypoperfusion and without inotropic support. Hemostasis is rarely achieved by manual compression, and surgical closure is frequently needed. Due to the larger cannulae, TandemHeart clearly exerts more vascular complications (18% of patients with cardiogenic shock at our institution), especially arterial occlusion and subsequent limb ischemia [24]. Owing to the transseptal puncture, atrial septal defect may persist. Aortic puncture and pericardial tamponade are extremely rare. Contraindications specific to TandemHeart are ventricular septal defect and right ventricular failure where implantation may hasten hemodynamic collapse.

Hemodynamic support & physiology

The 15-Fr cannula allows a maximal estimated flow of 3.5 l/min and the 17-Fr, 4–5 l/min depending on systemic vascular resistance. A group of investigators showed augmentation in mean arterial pressure and systemic flow [15]. They demonstrated significant increase in cardiac output by 37%, mean arterial pressure by 27% and decrease in pulmonary capillary wedge pressure by 50% [15,25]. Maintaining continuous supraventricular pressure while unloading the left ventricle in the case of very low cardiac output may cause transient, concomitant aortic and mitral valve closure [26]. Considering myocardial ischemia, TandemHeart decreases oxygen consumption by indirect ventricular unloading. However, in the situation of low cardiac output, the increased afterload may offset this beneficial aspect [27].

Clinical evidence

A group of investigators has recently studied the impact of TandemHeart in severe refractory cardiogenic shock of both ischemic and nonischemic origin [28]. In this observational study, 117 patients under IABP and/or high dose vasopressors were implanted with a TandemHeart, 56 of which underwent active cardiopulmonary resuscitation. The 30-day mortality after 6 months was between 40.2 and 45.3%, which is significantly lower than the ranges accounted for in previous trials such as the Shock Trial registry. Bleeding and limb ischemia were the most frequent complications.

Two randomized trials have evaluated the TandemHeart in comparison to IABP in patients with cardiogenic shock primarily due to acute myocardial infarction [25,29]. In both, pVAD improved cardiac index and reduced pulmonary capillary wedge pressure significantly. Complications such as limb ischemia and severe hemorrhage were more frequent in the pVAD group than the IABP group ranging from 40 to 90%. A small meta-analysis of the two trials failed to show any mortality difference [30].

So far, there has not been a randomized controlled trial comparing TandemHeart with any

other support in high-risk PCI. Many observational, retrospective studies show safety of use, little device complications and lower than predicted mortality at 30 days [31,32]. In one series, for instance, 37 patients received hemodynamic support for either cardiogenic shock or high-risk PCI. PCI was successful in all patients and 71% survived at hospital discharge. A frightening 82% required blood transfusion due to procedure-associated bleeding [33]. Recently, an observational study retrospectively compared the TandemHeart with the Impella LP 2.5 in high-risk PCI. The 30-day MACE-rate was 5.8% and no difference between the two devices was detected [34].

Table 1 summarizes the in-hospital survival of patients having undergone high-risk PCI with either Impella or TandemHeart implantation. It also shows in-hospital survival of patients with cardiogenic shock due to acute myocardial infarction treated with either surgery or PVADs. The heterogeneity of the different studies forces a cautious interpretation of these global results but the trend clearly demonstrates cardiogenic shock's poor prognosis as opposed to high-risk PCI.

Additional indications & concepts

Ventricular tachycardia ablation

Advances in electrophysiology and invasive cardiology have allowed percutaneous management of the most threatening cardiac arrhythmias such as recurrent ventricular tachycardia. Whether in structural heart disease, for symptom management or in incessant ICD shocks, ablation is increasingly performed. Substrate-based approaches allow this without inducing arrhythmia, even in unstable patients. However, when this approach fails it may be difficult if not impossible to ablate hemodynamically unstable arrhythmias. In the past years, pVADs have been used to achieve hemodynamic stability and promote successful procedures. TandemHeart was first used in 2007 as a support for ventricular tachycardia ablation in a 55-year-old man [35]. Later, unstable ventricular tachycardia ablation was successfully achieved in three patients using Impella Recover LP 2.5 support [36]. Further case reports have been published including the use of pVADs in other types of arrhythmias such as unstable supra-ventricular tachycardias in the setting of congenital heart disease [37,38]. Again, when used as a 'prophylactic measure', the Impella Recover LP 2.5 may be more adequate in its risk/benefit equilibrium than the TandemHeart.

Right ventricular & bi-ventricular assistance

Acute right ventricular myocardial infarction may result in ventricular wall dysfunction and dramatic effects on biventricular performance. Transpulmonary cardiac output is diminished and inadequate left ventricular filling results in diminished cardiac output. Through ventricular interdependence, left ventricular compliance decreases as the right ventricle dilates. Key management lies amongst others in volume resuscitation and adequate pharmacotherapy. Clinical trials have rapidly unveiled the negative effects of left pVADs, such as TandemHeart, as they aggravate a fragile hemodynamic equilibrium. That is why dedicated TandemHeart cannulae have been developed for the right ventricle (pRVAD). One initial case report demonstrated the feasibility of pRVAD with TandemHeart [39]. Another case report showed successful 3-day support with an adapted right ventricular TandemHeart [40]. In both cases, the mean cardiac output was between 2 and 3 l/min. Successful bilateral percutaneous assist device support was accomplished via pRVAD with TandemHeart and left

Table 1. The 30-day survival in patients with cardiogenic shock and treated with surgical or percutaneous ventricular assist devices, and in preventive percutaneous ventricular assist device implantation for high-risk percutaneous coronary intervention.

	Device	Number of patients	30-day survival
Cardiogenic shock	sVAD[†]	157	92 (59%)
	pVAD[‡]	305	182 (60%)
High-risk percutaneous coronary intervention	pVAD TH[§]	161	142 (88%)
	pVAD IP[¶]	258	248 (95%)

[†]*Pooled data from 11 trials* [47,53–62].
[‡]*Pooled data from 11 trials* [18,19,21,24,25,29,48,63–69].
[§]*Pooled data from 11 trials* [31,34, 69,70–78].
[¶]*Pooled data from 10 trials* [15,32,34,69,79–87].
IP: Impella Recover 2.5 LP; pVAD: Percutaneous ventricular assist device; sVAD: Surgical ventricular assist device; TH: TandemHeart.

IABP counterpulsation in an acute biventricular myocardial infarction. The patient was under mechanical support for 48 h and was discharged 8 days after the procedure [41]. Finally, biventricular support with pRVAD TandemHeart and pLVAD with Impella Recover LP 2.5 allowed complete recovery of a patient with severe cardiac allograft rejection [42]. These isolated cases emphasize the life-saving potential of pVADs.

Bridging

Significant evidence shows pVAD utility in the bridge-to-recovery concept [43,44], when the assistance device supports the failing heart in potentially reversible causes of shock such as myocarditis, drug overdose, hypothermia, coronarography-related complications (e.g., air embolism, no-reflow phenomenon and dissections), incessant arrhythmia or postcardiotomy syndrome. Similarly, pVADs are reliable and can be used until more definitive measures can be undertaken, such as long-term surgical device implantation (bridge-to-bridge) and transplantation (bridge-to-transplantation) [45,46].

Conclusion

Certain key points should be withdrawn from the increasing literature published on pVADs. The Impella Recover LP 2.5 is evidently most adapted for high-risk PCI, and the lower complication rate outweighs the weaker yet sufficient hemodynamic support. These procedures are generally elective with patients being more stable.

With regards to myocardial infarction without cardiogenic shock, the goal is to alleviate the suffering myocardium from further injury and allow myocardial recovery. Impella LP 2.5's proven, direct, ventricular unloading capabilities appears to be an advantage. This could lead to the guideline shift of 'door-to-balloon' to 'door-to-circulatory assistance' time. The results from the ongoing IMPRESS in ST-elevation myocardial infarction study should bring further evidence on the subject.

In cases of pure cardiogenic shock, the TandemHeart achieves higher hemodynamic support and appears more adequate. Clinically, the earlier the assistance is initiated, the better the outcome, with mortality of 26% when initiated in the first 2 weeks as opposed to 40% after 2 weeks [47].

Even though it achieves the best hemodynamic support of all three pVADs and its early implantation in cardiogenic shock seems promising [48], the necessity for femoral surgical cutdown is an unfortunate disadvantage of the Impella LP 5.0.

The life-threatening complications are not trivial; our experience in local centers accounts for up to a fifth of patients with cardiogenic shock suffering from a significant cerebral vascular event. This, surprisingly, does not readily stand out in certain published series. Another aspect is that the better the hemodynamic support (i.e., TandemHeart) the more complications appear.

Other extracorporeal life support devices offer not only hemodynamic but also respiratory support. Newer, minimized systems such as the ELS-System and Cardiohelp (both from MAQUET Cardiopulmonary AG, Germany) have smaller priming volumes, may be rapidly inserted and have facilitated interhospital transport possibilities [49].

Case reports and observational studies abound but large randomized multicenter studies are rare. Trials tend to mix patients and pVADs with confounding results in cardiogenic shock and high-risk PCI, two drastically different conditions. From a patient-based point of view, pVAD implantation can undoubtedly be life-saving and numerous case-reports have shown successful outcomes [42,50,51]. Admittedly, from an evidence-based medicine standpoint, data is lacking further precluding pVAD use as a front-line mechanical therapy [52]. Larger cohorts are necessary to prove beneficial effects on mortality or morbidity and, considering the scarcity of patients and the financial burden, it seems unlikely that strong evidence will emerge within the next years. Some hypothesize that earlier pVAD implantation in cardiogenic shock or myocardial infarction would be most beneficial. Future research may concentrate on the matter and distance itself from aging pharmacologic and IABP support classics.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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