Percutaneous Transvalvular Micro-axial Flow Pump: Impella

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Abstract

The Impella is a small heart pump that can be implanted via percutaneous method thus is minimally invasive. The Impella utilizes catheter-based technology to provide hemodynamic support and unload ventricle, currently it is available in Taiwan. The indications of Impella including high-risk PCI and cardiogenic shock especially acute myocardial infarction-related cardiogenic shock. This review provides an overview of Impella technology and development, also summarizes the clinical evidence of the Impella

Keywords: Impella, high risk PCI, cardiogenic shock

What is Impella

Impella (Abiomed, Danvers, Massachusetts) is a percutaneous ventricular assist device (pVAD), that utilizes catheter-based technology to provide hemodynamic support. Impella has been approved by the U.S. FDA for high-risk percutaneous coronary intervention (PCI) and cardiogenic shock (CS) since 2008. The technology of Impella involves a so-called micro-axial flow pump, which pumps blood directly and continuously from the left ventricle (LV) across the aortic valve into the aorta, thereby unloading the LV. The mechanism of Impella is essentially an Archimedes' screw, a type of pump which was historically used for raising water.[1] Initial Impella prototypes introduced in 1998 consisted of an intra-cardiac pump catheter designed for ventricular support during coronary artery bypass grafting.[2] Subsequently, Meyns and colleagues conducted an experimental study to evaluate the usefulness of Impella in acute myocardial infarction (AMI).[3] They found that implanting Impella during periods of myocardial ischemia could reduce myocardial oxygen consumption and result in a significant reduction in LV infarct size in pump-supported animals. The Impella can provide 4.1 +/- 0.1 L/min in full support mode and significantly increase mean blood pressures, while reducing LV end-diastolic blood pressure. Also, the reduction in LV infarct size correlates with the degree of unloading during reperfusion. There are different types of Impella devices (Impella CP, Impella 5.5, Impella RP) available in Taiwan, all based on the same technology with different support capacities (2.5 L/min to 6.0 L/min) and designs (left heart or right heart support). A comparative summary is given in Table 1. As previously mentioned, Impella

Received: Jul. 8, 2024; Accepted: Jul. 22, 2024
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Table 1. Comparison of the Impella devices available in Taiwan

Impella device	Impella CP	Impella 5.5	Impella RP
Indication	High-risk PCI or CS	CS	Right heart failure
Introducer diameter	14Fr	23Fr	23Fr
Access	Percutaneous femoral or axillary	Axillary cutdown or femoral	Percutaneous jugular or femoral vein to pulmonary artery
Maximum flow (L/min)	3.7	5.5	4.4

continuously draws blood from the inlet (located in the ventricle) and pumps it to the outlet (located in the ascending aorta or pulmonary artery), thereby reducing both preload and afterload. The pressure-volume loop of Impella-assisted LV shifts leftward and the pressure-volume area is significantly reduced, representing reduced stroke work of the LV.[4] The Impella can therefore provide adequate hemodynamic support while also unloading the LV, which allows the heart to rest and recover.

First introduced in 2016, the Impella CP is now one of the most commonly used devices. Impella CP can offer a maximum of 4.3 L/min cardiac output and can be implanted percutaneously through the femoral artery with a 14 Fr sheath (Figure 1). The major advantages of the Impella device, compared to other mechanical circulatory support (MCS) devices, are greater hemodynamic support than is offered by intra-aortic balloon pump (IABP), and greater active unloading of the LV, compared to both IABP and veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

There are some contra-indications and limitations for Impella use. Absolute contra-indications include left ventricular thrombus and mechanical aortic valves. Significant peripheral arterial disease and aortic valve disorders are also contraindications for Impella use. The major limitations of Impella use are the need for adequate right ventricular output to provide LV filling, and the lack of active oxygenation. Thus, the use of Impella is less efficient in prolonged cardiac arrest status as well as electrical storms. Also, in the case of biventricular failure, Impella can only support either the left or the right heart. For patients with biventricular failure, Impella plus another MCS (VA-ECMO, or Impella CP + Impella RP) should be considered.

Clinical evidence of Impella use

The most common indications for Impella use are for high-risk PCI and cardiogenic shock (CS), especially in those with AMI related CS (AMI-CS). The clinical data mainly focuses on high-risk PCI and AMI-CS.

Impella in high-risk PCI

Complex high-risk and indicated PCI (CHIP) is becoming increasingly common in the daily practice of interventional cardiologists. However, the definition of CHIP is based on expert opinion and lacks consensus. Protty et al. utilized the British Cardiovascular Intervention Society database, and promoted a CHIP score to define the level of risk of PCI.[5] Their identification of CHIP factors can facilitate risk stratification for PCI and guide potential further management. To facilitate the execution of high-risk PCI, several MCS devices have been developed, including Impella, IABP and VA-ECMO. The aims of MCS in high-risk PCI are to prevent low cardiac output and profound shock, and to provide sufficient time for optimal revascularization. According to a previous randomized study (BCIS-1) and meta-analysis,

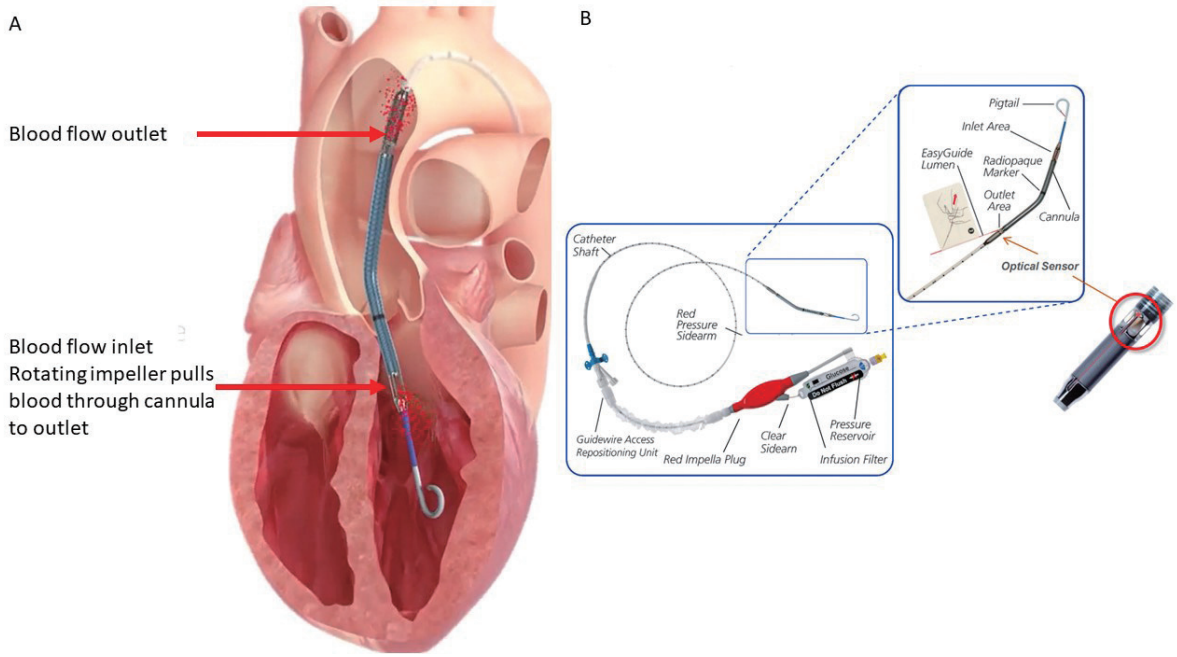

Figure 1. A: Impella CP is placed inside the LV. The rotating impeller draws blood from the LV, pumps it across the cannula and expels it into the aorta. **B:** Impella CP with SmartAssist.

IABP does not reduce MACE, compared with a control group, in high-risk PCI.[6,7] Data regarding the use of VA-ECMO in high-risk PCI is scarce. Thus, according to the expert consensus of the European guidelines, IABP and VA-ECMO are not recommended in high-risk PCI.[8]

Currently, Impella has the most abundant clinical data for high-risk PCI, and it is the only recommended MCS for patients receiving high-risk PCI, according to the European guidelines.[8] Table 2 summarizes the evidence regarding Impella-assisted high-risk PCI. The PROTECT I study is a pilot study which prospectively enrolled 20 patients who underwent high-risk PCI with Impella 2.5 support.[9] The Impella 2.5 was implanted successfully in 20 patients, and this pilot study demonstrated that Impella 2.5 is safe and can provide adequate hemodynamic support in high-risk PCI cases.

The PROTECT II study is the only published large randomized study comparing IABP and Impella 2.5 in high-risk PCI.[10] The study planned to enroll 327 patients per treatment arm, but was terminated prematurely. Its primary endpoint was 30-day major adverse events (MAE). The MAE rates in per-protocol population showed no statistical difference at 30 days (34% vs. 42%, $p = 0.092$), but were significantly lower at 90 days in the Impella group than in the IABP group (40% vs. 51%, $p = 0.023$).

The PROTECT III study is a prospective, multi-center registry study.[11] PROTECT III included 1134 patients with severely depressed LV ejection fraction who underwent elective PCI with Impella at 45 sites between 2017 and 2020. Among the 1134 patients, 504 were "PROTECT II-like" (met the eligibility of PROTECT II) and were referred to as PROTECT III for comparative analysis. Compared with PROTECT II, PROTECT III demonstrated more complete revascularization, fewer bleeding events, and improved 90-day clinical outcomes which could be explained by further development of the device itself (from Impella 2.5 to Impella CP), along with increased operator experience.

The PROTECT IV study is an ongoing randomized study aiming to examine the performance of Impella in high-risk PCI. The

Table 2. Overview of the studies on Impella-assisted high-risk PCI

First Author	Year	Design/Number	Outcomes
O'Neil et al.[9] PROTECT I	2009	Prospective multicenter registry Enrolled: 20	Impella 2.5 is safe and easy to implant in patients receiving high-risk PCI
O'Neil et al.[10] PROTECT II	2012	Randomized study Impella 2.5 vs. IABP Enrolled: 452	30-day major adverse event (MAE) no difference Lower 90-day MAE in Impella than IABP
O'Neil et al.[11] PROTECT III	2022	Multicenter registry Enrolled: 1134	Improved completeness of revascularization and less 90-day MACE compared with last generation Impella-assisted PCI (PROTECT II)
Flaherty et al.[22]	2017	Retrospective study Enrolled: 230	Less acute kidney injury in Impella-assisted high-risk PCI than no-support group
Lansky et al.[23]	2022	Retrospective study Enrolled: 2156	Impella was associated with better survival than IABP in patients undergoing high-risk PCI

enrollment target is 1252 patients with reduced LV ejection fraction receiving Impella support vs. standard-of-care PCI with or without IABP. The estimated study completion date is 2027.

Impella in CS

CS is a state of severe systemic hypoperfusion due to cardiac dysfunction. Mortality is extremely high, ranging from 40% to 60% even in the contemporary era.[12] The pathophysiology of CS is complicated, but can be classified according to phenotype into LV failure or right ventricle (RV) failure. AMI accounts for 80% of CS in the clinical setting,[13] and the treatment of AMI-CS is the most common indication for Impella. Currently, Impella has yielded the most promising results in studies of AMI-CS, including randomized studies and registry data.[14,15] Table 3 summarizes the important studies on Impella use in CS. The USpella Registry (covering 38 MCS centers in the United States) reported the outcomes of 154 patients with AMI-CS treated with Impella-assisted PCI, whereby the in-hospital survival rate was 65%.[16] Several retrospective studies published by O'Neil et al., reporting on Impella-assisted PCI in AMI-CS, have demonstrated promising results. The survival rate is higher when Impella is used as the first support strategy and when patients are treated in high-volume Impella centers.[15,17] However, Schrage et al. reported that the Impella device was not associated with improved survival, compared to IABP.[18,19] They conducted a retrospective study using an AMI-CS database in European countries, selecting patients treated with the Impella device and fulfilling the inclusion/exclusion criteria of the IABP-SHOCK II trial. These patients were then matched to 600 patients selected from the IABP-SHOCK II trial. In total, 237 pairs of patients were included for final analysis. O'Neil et al. raised multiple concerns about the results reported by Schrage, questioning the obviously biased selection and matching process.[20]

In the face of all the controversial results on Impella in AMI-CS, the DanGer Shock trial offers a shot in the arm.[14] Møller et al. conducted an international, multicenter, randomized trial aiming to evaluate the effect of Impella in ST elevation myocardial infarction-related CS. A total of 355 patients were included for final analysis. Routine use of Impella in ST elevation MI-related CS led

Table 3. Overview of the studies on Impella in CS

First Author	Year	Population/Design	Outcomes
O'Neil et al.[16] USpella Registry	2015	AMI-CS Prospective nationwide registry, enrolled: 154	Impella implantation prior to PCI was associated with better survival than implantation after PCI
Basir et al.[15]	2017	AMI-CS Retrospective study, enrolled: 287	Early Impella implantation before vasopressor use and before PCI independently associated with improved survival
O'Neil et al.[17]	2018	AMI-CS Prospective nationwide registry, enrolled: 15259	In AMI-CS, survival was higher when Impella was used as first support strategy Higher survival with right heart-catheter use Higher survival with pre-PCI MCS use
Schrage et al.[18]	2018	AMI-CS Retrospective study, enrolled: 474	Impella was not associated with lower 30-day mortality compared with matched patients from IABP-SHOCK II trial
Ogunbayo et a.[24]	2018	Non-AMI CS Retrospective study, enrolled: IABP (n=16619) vs. Impella (n=1414)	Impella group associated with lower survival than IABP group which may be due to indication bias
Hanson et al.	2024	AMI-CS Prospective single-arm registry, enrolled: 418	In AMI-CS treated with Impella, the 30-day survival was 52%, baseline CS stage was significantly associated with 30-day mortality
Møller et al.[14] DanGer Shock	2024	STEMI-CS Randomized study, enrolled: 360	Routine use of Impella CP in STEMI-CS led to lower risk of death at 180 days than standard of care alone
Nasu et al.[21]	2024	Fulminant myocarditis Nationwide registry Enrolled: 269	107 patients received Impella, and 162 used ECPELLA, the survival rate of Impella group was 83.2%, and 68.5% in ECPELLA

to a lower risk of death at 180 days than standard of care only (45.8% vs. 58.5%, hazard ratio: 0.74, $p = 0.04$). However, there were many limitations to the DanGer Shock trial, such as the strict inclusion criteria (ST elevation MI-related CS), small sample size with borderline p-value, and predominantly white patients. The DanGer Shock trial is the first randomized trial to show positive results of MCS in AMI-CS.

Notably, Data on MCS in patients with non-AMI CS is scant, recently Nasu et al. reported results from the Japanese Registry for Percutaneous Ventricular Assist Devices (J-PVAD), assessing the role of Impella in managing fulminant myocarditis.[21] The primary outcome of 30-day survival rate was 83.2% in the Impella only group, and 68.5% in the ECPELLA group (Impella + VA-ECMO). Adverse events were noted in 48.2% of patients, including major bleeding (32.0%) and deteriorated renal function (8.6%). The use of Impella in fulminant myocarditis demonstrated encouraging short-term outcomes.

Future direction of Impella application in Taiwan

Impella was approved by the Taiwan Food

and Drug Administration in 2022. The first Impella implantation in Taiwan was performed at the National Taiwan University Hospital for high-risk PCI. Currently, Impella does not qualify for national health insurance reimbursement in Taiwan, which limits its utilization. The most common indication for Impella in Taiwan is for high-risk PCI, representing 40% of cases, while its use for CS accounts for 60% (AMI-CS represents 60% of these cases). Impella will continue to be used in these two fields in Taiwan. In high-risk PCI cases, it is essential to identify situations where patients face the highest risks and consider using Impella during the PCI procedure. In contemporary CS management, MCS plays a crucial role, especially Impella, which should be considered for AMI-CS, especially in ST elevation MI-related CS. Current data supports the benefit of Impella in AMI-CS, emphasizing the importance of negotiating with the government to pursue reimbursement in these cases. In non-AMI CS cases, Impella has also shown promising results by providing adequate cardiac output and unloading of the left ventricle. After carefully evaluating the CS phenotype, Impella could be considered a viable treatment option.

Conclusions

Impella is a novel and minimally invasive MCS device, which provides adequate cardiac output and can directly unload the LV. It provides adequate support in high-risk PCI to facilitate complete revascularization. Impella also plays an important role in CS, and should be considered a first-line option in AMI-CS.

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