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VIEWPOINT

Microaxial flow pump for high-risk PCI: are we ready for the prime time?

Holger Thiele[1]*, MD; Divaka Perera[2], MD

**Corresponding author: Department of Internal Medicine/Cardiology, Heart Center Leipzig at University of Leipzig, Strümpellstraße 39, 04289, Leipzig, Germany. E-mail: holger.thiele@medizin.uni-leipzig.de*

The authors' affiliations can be found at the end of this article.

The Impella device (Abiomed) is a percutaneous transvalvular microaxial flow pump which traverses the aortic valve and pumps blood from the left ventricle (LV) to the ascending aorta. The percutaneous LV Impella systems include the Impella Cardiac Power (CP) and Impella CP SmartAssist, providing up to 3.5 l/min and 4.3 l/min (based on the manufacturer information) using a 14 Fr initial introducer sheath[1]. This degree of haemodynamic support makes the Impella an attractive adjunct when performing high-risk percutaneous coronary interventions (PCI), which could prevent hypotension or even the development of cardiogenic shock by maintaining cardiac output; it may also facilitate a better outcome in more complex interventions. However, to support such a strategy, evidence derived from randomised clinical trials (RCTs) is needed, since any intervention using large-bore access may also cause harm. The current endorsement for Impella-assisted high-risk PCI is largely based on observational registries, where the decision to utilise the device was driven by a variety of factors beyond carefully defined clinical indications. This article will address the current evidence and clinical practice as well as ongoing RCTs in this setting.

Current randomised evidence for Impella-facilitated non-emergent high-risk PCI

Impella-facilitated non-emergent elective high-risk PCI is increasingly being used to prevent haemodynamic deterioration due to ischaemia that can occur during coronary balloon and stent inflation, calcium modification techniques and unexpected complications such as coronary dissection or branch vessel occlusion. These risks are greatest when the myocardial jeopardy score is high (as in left main or last remaining patent vessel interventions), especially when there is reduced LV function at the outset[2].

One of the first RCTs to explore this was the Balloon Pump Assisted Coronary Intervention Study (BCIS-1) including 301 patients, which did not reveal an advantage of intra-aortic balloon pump (IABP)-supported PCI compared with non-supported PCI in high-risk patients[3]. Subsequently, the PROTECT II Trial randomised 452 patients (of an intended sample size of 654 patients) with either complex 3-vessel coronary artery disease (CAD) or unprotected left main CAD and severely compromised LV ejection fraction (≤35%) to Impella 2.5 versus an IABP-facilitated high-risk PCI[4]. Importantly, the trial was prematurely terminated by the data safety monitoring board because of its likely futility. The trial used an unusual 10-component primary endpoint combining efficacy and safety endpoints (all-cause death, Q wave or non-Q wave myocardial infarction [MI], stroke or transient ischaemic attack, any repeat revascularisation procedure [PCI or coronary artery bypass graft], need for a cardiac or vascular operation, acute renal insufficiency, severe intraprocedural hypotension requiring therapy, cardiopulmonary resuscitation or ventricular tachycardia requiring cardioversion, aortic insufficiency and angiographic failure of PCI). The intention-to-treat and per-protocol analyses did not show statistically significant differences in major adverse events at 30 days (primary endpoint: 35.1% Impella 2.5 vs 40.1% IABP)[4]. Interestingly, clinically important individual endpoints such as death and MI were numerically higher in the Impella group. The results of the *post hoc* per-protocol analysis at 90 days (40.0% vs 51.0%; p=0.023) have led to this being described as a positive trial by some, although this assertion is difficult to justify scientifically, given the neutral effect on the primary outcome of a trial stopped early for futility and its use of an unusual primary endpoint[4].

Nevertheless, the Impella 2.5 device received U.S. Food and Drug Administration (FDA) 510(k) clearance for high-risk PCI, and subsequently, other devices (Impella CP, Impella 5.0) have received approval with an expanded indication for cardiogenic shock. Approval of these devices by the FDA and by European regulatory agencies has led to a steadily increasing use of these devices.

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Observational data

Currently, there are a multitude of registry data on Impella-assisted PCI, including the following registries: Europella, USpella, cVAD, PREMIER, and CathPCI. The indications for Impella implantation in these registries are often much less stringent than the inclusion criteria of PROTECT II, and many include patients with only mildly reduced or even normal LV ejection fraction[2]. Based on the retrospective design and selection bias inherent in such series, it is difficult to draw robust conclusions regarding efficacy and, in our view, such results should only be considered hypothesis-generating.

Ongoing randomised clinical trials

There are 2 ongoing RCTs of Impella-assisted high-risk PCI, which both started recruitment in 2021. The Controlled Trial of High-risk Coronary Intervention with Percutaneous Left Ventricular Unloading (CHIP-BCIS3) is an investigator-initiated trial funded by the National Institute for Health and Care Research in the United Kingdom, which aims to enrol 250 patients undergoing complex PCI in patients with a high myocardial jeopardy score and severely reduced LV ejection fraction. The PROTECT IV Trial is an industry-funded, multicentre RCT comparing Impella-assisted PCI versus standard PCI with or without IABP. The results from both trials (which both have a minimum follow-up duration of 1 year) are expected to be available at the end of 2025 or in 2026. There are important differences and some similarities in the design of these trials, which are summarised in **Table 1**[5].

Complications

The most common complications of Impella support in elective clinical scenarios are access site bleeding, haemolysis and limb ischaemia due to the large-bore access with an almost mandatory need for therapeutic anticoagulation. The incidence of these complications can be reduced by mandating preprocedural vascular imaging and with the growing

Table 1. Randomised trials of Impella-assisted high-risk PCI.

Clinical trial	Impella-Supported PCI in High-Risk Patients With Complex Coronary Artery Disease and Reduced Left Ventricular Function: The PROTECT IV Trial (PROTECT IV)	Controlled Trial of High-risk Coronary Intervention with Percutaneous Left Ventricular Unloading (CHIP-BCIS3)
ClinicalTrials.gov identifier	NCT04763200	NCT05003817
Study start date	04/2021	08/2021
Study completion date	03/2026	06/2025
Location	USA	UK
Sample size	1,252	250
Condition	CCS, NSTEMI or STEMI ≥24 hours with LVEF ≤40%* undergoing complex PCI	CCS with 1) extensive CAD (BCIS-Jeopardy score >8) 2) LVEF ≤35% 3) undergoing complex PCI
Complex PCI definition	Complex PCI defined as ≥1 of: - PCI of distal LM bifurcation - MV PCI with 3-vessel disease - Last remaining patent vessel - 2-vessel PCI of complex lesions - 1-vessel PCI of complex lesion+non-treated CTO or - 1-vessel PCI of complex lesion (in non-infarct vessel) post-STEMI	Complex PCI defined as at least one of: 1) Unprotected left main intervention in the presence of - an occluded dominant right coronary artery or - a left dominant circulation or - disease involving the entire bifurcation (Medina 1,1,1 or 0,1,1) 2) Intended calcium modification (by atherectomy, lithotripsy or laser) - in multiple vessels or - in the left main stem or - in a final patent conduit or - where the anatomical SYNTAX score is ≥32 3) Target vessel is a CTO with planned retrograde approach
Interventional group	Impella CP or Impella 2.5 placement prior to PCI	Impella CP placement prior to PCI
Control group	Standard-of-care PCI with or without an IABP	Standard-of-care PCI
Primary outcome	Composite of all-cause death, stroke, durable LVAD/HTx, MI or hospitalisation for cardiovascular causes at 3 years Statistics: classical superiority analysis	Hierarchical composite: 1) death; 2) stroke; 3) spontaneous MI; 4) CV hospitalisation; 5) periprocedural MI Statistics: win ratio method
Funding	Abiomed	NIHR

*if STEMI, LVEF ≤30%. BCIS: British Cardiovascular Intervention Society; CAD: coronary artery disease; CCS: chronic coronary syndrome; CP: Cardiac Power; CTO: chronic total occlusion; CV: cardiovascular; HTx: heart transplant; IABP: intra-aortic balloon pump; LM: left main; LVAD: left ventricular assist device; LVEF: left ventricular ejection fraction; MI: myocardial infarction; MV: multivessel; NIHR: National Institute for Health and Care Research; NSTEMI: non-ST-elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction

experience of operators with closure techniques, but every published series to date has shown this to be an ongoing concern. These possible complications need to be weighed against the possible advantage of haemodynamic support during complex high-risk PCI.

Conclusions

The Impella device can be applied in different clinical scenarios including Impella-facilitated elective high-risk PCI. Besides numerous retrospective studies, there are almost no robust data on the impact of Impella use on outcome and complications, as adequately powered RCTs have not been completed as yet. Thus, Impella use has outpaced the quality of the available data and has been, in part, driven by the disappointing outcomes of other interventions used to support this critically ill population. The physiological rationale and some supporting data have led to substantial and growing use, despite other data suggesting that more caution may be warranted. In the absence of sufficient data from RCTs for the above-mentioned indications, the decision to use the Impella device should be made with caution and based on individual expertise.

The US and European agencies require high-quality clinical data to support approval of all high-risk invasive devices such as the Impella device, as is generally required for new drugs. Approval of these devices should be dependent on demonstrating clinical efficacy and safety in an adequately powered RCT and should not be based on physiological parameters. Additionally, coverage and reimbursement should also be related to clear evidence of benefit. Until such reforms are implemented and given the preponderance of existing evidence, use of the microaxial Impella device in individuals presenting a possible indication of high-risk PCI should be restricted to patients enrolled in RCTs. Whether there is any clinically meaningful benefit in hard endpoints, such as mortality and MI, and if this outweighs the associated harms, can only be addressed by data from such RCTs. In addition, this strategy would prevent a selection bias towards lower-risk patients if not all eligible patients are included. Whilst it is tempting for clinicians to want to be able to provide patients with more advanced therapies for complex high-risk interventional procedures, the interventional community also has a responsibility to ensure that interventions are evidence-based and safe. Therefore, the results of the PROTECT IV and CHIP-BCIS3 trials regarding Impella-facilitated PCI are eagerly awaited.

Authors' affiliations

1. Department of Internal Medicine/Cardiology, Leipzig Heart Science, Heart Center Leipzig at Leipzig University, Leipzig, Germany; 2. British Heart Foundation Centre of Research Excellence at the School of Cardiovascular Medicine and Sciences, King's College London, London, United Kingdom

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Thiele H, de Waha-Thiele S, Freund A, Zeymer U, Desch S, Fitzgerald S. Management of cardiogenic shock. *EuroIntervention*. 2021;17:451-65.
2. Zeitouni M, Marquis-Gravel G, Smilowitz NR, Zakroysky P, Wojdyla DM, Amit AP, Rao SV, Wang TY. Prophylactic Mechanical Circulatory Support Use in Elective Percutaneous Coronary Intervention for Patients With Stable Coronary Artery Disease. *Circ Cardiovasc Interv*. 2022;15:e011534.
3. Perera D, Stables R, Thomas M, Booth J, Pitt M, Blackman D, de Belder A, Redwood S; BCIS-1 Investigators. Elective intra-aortic balloon counterpulsation during high-risk percutaneous coronary intervention: a randomized controlled trial. *JAMA*. 2010;304:867-74.
4. O'Neill WW, Kleiman NS, Moses J, Henriques JP, Dixon S, Massaro J, Palacios I, Maini B, Mulukutla S, Dzavík V, Popma J, Douglas PS, Ohman M. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. *Circulation*. 2012;126:1717-27.
5. Ryan M, Ezad SM, Webb I, O'Kane PD, Dodd M, Evans R, Laidlaw L, Khan SQ, Weerackody R, Bagnall A, Panoulas VF, Rahman H, Strange JW, Fath-Ordoubadi F, Hoole SP, Stables RH, Curzen N, Clayton T, Perera D. Percutaneous left ventricular unloading in high-risk coronary intervention: rationale and design of the CHIP-BCIS3 randomised controlled trial. *Circ Cardiovasc Interv*. 2024;17:e013367.