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Mechanical circulatory support for high-risk percutaneous coronary interventions and cardiogenic shock: Rationale and design of the multicenter, investigator-initiated IMPELLA-PL registry

Arkadiusz Pietrasik[1], Aleksandra Gasecka[1], Marek Grygier[2], Tomasz Pawlowski[3], Jerzy Sacha[4, 5], Janusz Kochman[1]

[1]1st Chair and Department of Cardiology, Medical University of Warsaw, Poland
[2]Department of Cardiology, Poznan University of Medical Sciences, Poznan, Poland
[3]Department of Invasive Cardiology, Central Clinical Hospital of the Ministry of Interior and Administration, Warsaw, Poland
[4]Department of Cardiology, University Hospital in Opole, Poland
[5]Faculty of Physical Education and Physiotherapy, Opole University of Technology, Opole, Poland

Background

Despite tremendous progress in the pharmacotherapy and interventional treatment for coronary artery disease (CAD), CAD and its complications, including acute myocardial infarction (MI), remain the main cause of morbidity and mortality worldwide [1]. Patients undergoing high-risk percutaneous coronary intervention (PCI) and those with MI complicated by cardiogenic shock frequently require short-term mechanical circulatory support (MCS) [2, 3]. Traditionally, an intra-aortic balloon pump (IABP) was used to assist failing left ventricle (LV) in these clinical scenarios, as it was initially demonstrated to decrease all-cause mortality, compared with unsupported PCI [4]. However, the results of subsequent clinical trials showed conflicting results regarding the beneficial effect of IABP on long-term survival [5, 6], leaving percutaneous MCS and a scope of greatly unmet needs.

The Impella device (Abiomed, Danvers, MA, USA) is a microaxial, continuous blood flow pump and the smallest catheter-based LV assist device, which provides up to 5.0 L/min cardiac output [7]. In contrast to IABP, which creates a reverse blood flow to coronary arteries during diastole, providing a non-physiological MCS, Impella facilitates blood flow from the LV into the ascending aorta during systole, reducing LV preload and providing hemodynamic support in a physiological way [7]. Preliminary evidence from randomized clinical trials suggested the advantage of Impella devices over IABP, both in patients with MI complicated by cardiogenic shock and those undergoing high-risk PCI [8–10]. Despite conflicting results provided by recent systematic reviews and registry-based analyses [11–14], Impella devices have received a Class IIa recommendation (should be considered) in the recent European Society of Cardiology (ESC) guidelines for the treatment of acute heart failure patients [15]. Whereas ESC guidelines for myocardial revascularization did not provide clear recommendations regarding the use of Impella during high-risk PCI [2], the American College of Cardiology (ACC) granted a Class IIb recommendation for Impella prophylactic use during elective high-risk PCI procedures [16].

Following the approval of Impella for clinical use in Europe in 2005, it has been adopted world-

Address for correspondence: Arkadiusz Pietrasik, MD, PhD, 1st Chair and Department of Cardiology, Medical University of Warsaw, ul. Banacha 1a, 02–097 Warszawa, Poland, tel: +48 22 599 19 51, e-mail: arkadiusz.pietrasik@wum.edu.pl

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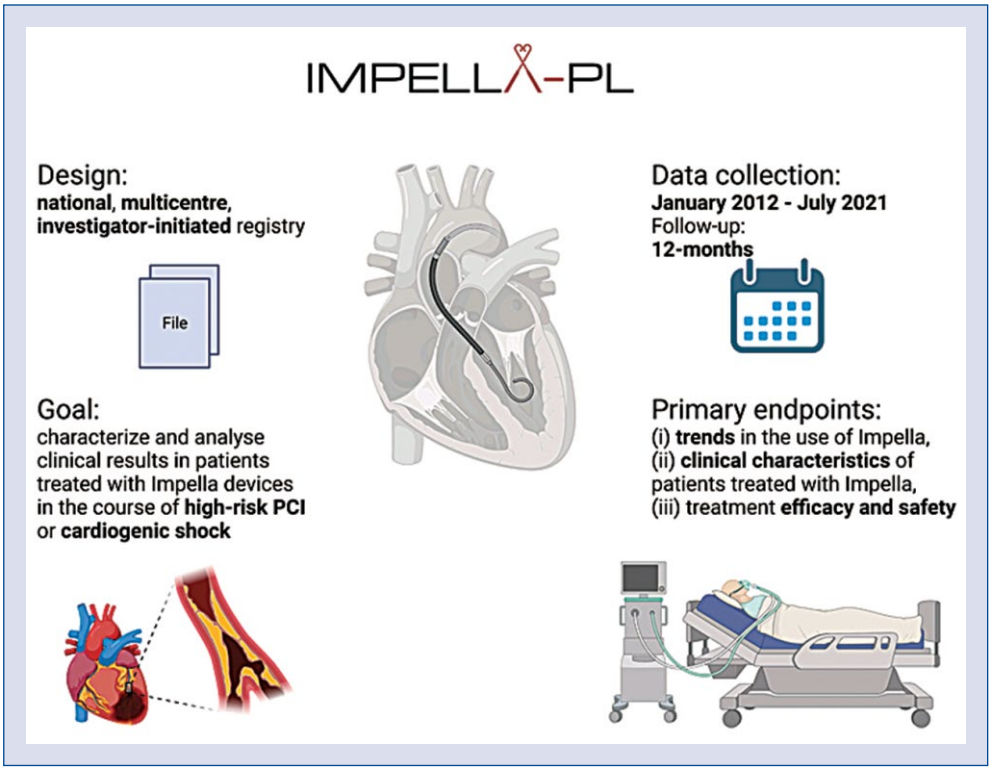

Figure 1. IMPELLA-PL registry scheme; PCI — percutaneous coronary intervention.

wide, with over 210,000 devices implanted up to date. Despite its widespread use, evidence-based data on the efficacy and safety of hemodynamic support with Impella in patients undergoing high-risk PCI and/or with cardiogenic shock are scarce. Therefore, the current landscape of Impella use is based on expert consensus, as acknowledged by recent position papers and consensus statements from various national societies [3, 17–20].

Since large randomized trials of hemodynamic support in patients undergoing high-risk PCI and with cardiogenic shock are challenging to conduct, few national registries have been launched which specifically focus on Impella devices: the Impella Italian (IMP-IT) Registry and German Impella Registry in Europe [21, 22] and the Catheter-Based Ventricular Assist Devices (cVAD) Registry in the United States (US) [23]. Considering various indications and types of Impella devices used in different countries and the lack of standardized algorithms for treatment qualification [19], it is crucial to establish new registries to further support decision making and form new recommendations in this challenging clinical scenario.

Regarding the growing complexity of percutaneous revascularization procedures in the recent decade, the use of the Impella devices have become a necessity in the interventional cardiology reference centres in Poland [24]. Careful monitoring of treatment with Impella, followed by analysis of the efficacy and safety of performed procedures are crucial to determine future directions of development for this emerging technology. To fill in this gap of knowledge, the IMPELLA-PL registry has been initiated.

Methods

Design

The IMPELLA-PL registry is a national, multicenter, investigator-initiated registry with the main objective to characterize the population of patients treated with Impella devices in the course of PCI and cardiogenic shock and to analyse the clinical results obtained in this patient population. The specific objectives include: (i) a description of trends in the use of Impella devices, (ii) clinical characteristics of patients treated with the device, including an in-depth analysis of indications for treatment, (iii) evaluation of Impella treatment efficacy and safety, according to the prespecified endpoint definitions, along with identification of independent predictors of outcomes based on clinical and periprocedural data. The registry scheme is shown in Figure 1.

Selection of participants

The study population consists of consecutive patients treated with Impella in the course of high-risk PCI or cardiogenic shock.

The subgroup of patients undergoing Impella--assisted revascularization includes hemodynamically stable patients with severe CAD undergoing elective or urgent, high-risk PCI, when a heart team, including a cardiac surgeon, has determined high-risk PCI is the appropriate therapeutic option. The Impella therapy will be used for temporary MCS to prevent hemodynamic instability, which can result from repeat episodes of reversible myocardial ischemia that occur during planned temporary coronary occlusions and may reduce peri- and post-procedural adverse events.

The subgroup of patients treated with Impella due to cardiogenic shock includes patients with ongoing cardiogenic shock that occurs immediately following acute MI or open-heart surgery or in the setting of cardiomyopathy, including peripartum cardiomyopathy, or myocarditis that is not responsive to optimal medical management and conventional treatment measures (including volume loading and use of pressors and inotropes, with or without IABP). Impella therapy will be used to improve organ perfusion and reduce ventricular loading necessary for heart recovery.

Study schedule

The data of consecutive patients treated with Impella between 2012 (introduction of the Impella device to Poland) until July 2021 are collected retrospectively. The follow-up data are collected until July 2022 to ascertain the 12-month follow-up of all patients, including the last patient included.

The registry has been launched under the patronage of the Association of Cardiovascular Interventions of the Polish Cardiac Society. The conducting of the study is coordinated by the 1st Chair and Department of Medical University of Warsaw. The capability of the coordinating center to initiate and execute the proposed project have been demonstrated with numerous previous registries launched by the coordinating center [25–27].

Data are collected in all Polish interventional cardiological centers which performed at least 5 interventions using Impella, i.e., 20 centers. The list of participating centers is available on the dedicated website of the registry (https://www.rejestrimpella.pl/). Site investigators enter the required data into password-protected, web-based electronic case report forms (eCRF). The eCRF is designed and maintained by a dedicated IT specialist. The quality of the collected data is monitored by an independent Study Monitoring Committee.

The following data are collected from the included patients: (i) demographical data, (ii) medical history and comorbidities, (iii) indications for Impella, (iv), baseline laboratory parameters, (v) scores (NYHA, EURO score II, SYNTAX score, Mehran risk score), (vi) echocardiography findings at admission, (vii) procedural details including type of Impella device, duration of support, access site, closure device, (viii) need for supportive treatment including extracorporeal membrane oxygenation (ECMO), IABP, invasive ventilation, catecholamine support, dialysis, (ix) medical therapy at baseline and during hospitalization, (x) efficacy of MCS using Impella determined as hemodynamic improvement and survival to hospital discharge, (xi) complications of MCS including acute renal dysfunction, aortic valve injury, bleeding, cardiogenic shock, cerebral vascular accident/stroke, death, hemolysis, limb ischemia, MI, renal failure, thrombocytopenia and vascular injury, (xii) clinical, laboratory and echocardiographic status at discharge. The 12-month follow-up data are collected from in-hospital and ambulatory medical records.

End-points

The study end-points are: (i) the trends in the use of Impella devices, (ii) clinical characteristics of patients treated with Impella, including treatment indications, and (iii) Impella treatment efficacy and safety. The clinical end-points will be prespecified and evaluated by an Independent Adjudication Committee.

Efficacy will be evaluated on the rate of in-hospital mortality, 1-year mortality and the composite of death, rehospitalization for heart failure, acute MI, stroke, left ventricular assist device (LVAD) implantation or heart transplant at 12-months. In addition, the need for cardiosurgical intervention, exacerbation of heart failure, acute MI, inflammatory complications, acute kidney injury and need for renal replacement therapy, need for mechanical ventilation, need for support escalation due to hemodynamic deterioration (use of advanced short-term mechanical support such as ECMO or long-term mechanical support such as surgical implantation of LVAD) will be assessed.

Safety will be evaluated based on the rate of device-related complications (bleeding or limb ischemia, complications requiring endovascular interventions, stroke, life-threatening bleeding, haemolysis, aortic injury).

Regarding the previously reported impact of the learning curve and low volume on the overall

outcomes, additional pre-specified sub-analyses will be performed: (i) comparison of the outcomes of patients undergoing Impella-assisted interventions per year, from 2012 to 2021, and (ii) comparison of the outcomes of patients undergoing Impella-assisted interventions in low-volume centers (< 10 interventions per year), medium volume centers (10–20 interventions per year) and high-volume centers (> 20 interventions per year).

All analyses will be done separately for the use of Impella in patients undergoing high-risk PCI procedures and those with cardiogenic shock or other indications, as these are different conditions with different outcome expectations.

Statistical analysis

Statistical analysis will be conducted using IBM SPSS Statistics, version 24.0. Categorical variables will be summarized using frequencies and proportions and compared using the χ^2 test or the Fisher exact test, as appropriate. Continuous data will be summarized using mean ± standard deviation or median and interquartile range and compared using Student t-test or nonparametric U-Mann-Whitney test, depending on the type of distribution. The Kaplan-Meier method will be used to estimate overall and event-free survival and the log-rank test to compare survival distributions. The Cox proportional hazards model will be used to estimate predictors of mortality. All analyzes will be performed in a blinded manner regarding patient demographics by an independent statistician. Statistical tests will be two-sided, with a significance level of 0.05.

Legal considerations

The study protocol was approved by the Bioethical Committee of the Medical University of Warsaw. The study is conducted according to Good Clinical Practice, the ethical principles described in the Declaration of Helsinki, the requirements of the European Medicines Agency and local legal and regulatory requirements. Data storage is conducted in compliance with local data protection laws. Authorities may request access to the study documentation in case of an inspection or audit. Documentation can be copied during inspection or audit only in cases where the identity of the participant/s have been made unrecognizable.

Discussion

The IMPELLA PL registry is a unique registry specifically providing insights into a rapidly evolving Impella hemodynamic technology, increasingly used in a variety of applications. Hitherto, only three registries which focus specifically on Impella devices have been launched, collecting data from the population of Italian, German and US patients [21–23]. However, regarding the differences in clinical practice in Europe and the US and the fact that large randomized trials of hemodynamic support in patients undergoing high-risk PCI and with cardiogenic shock are challenging to conduct, it is crucial to establish new national and international registries to provide high quality data which would provide a solid base to support decision making and evidence-based recommendations. The preliminary experience of the present study group and the collaborating groups regarding the use of Impella have been published, mostly as case reports and case series', demonstrating the great interest of numerous investigators in Poland to perform Impella®-assisted interventions and accounting for the feasibility to perform this project [24, 28–31].

The proposed study has several limitations that need to be disclosed. Given its observational, non-randomized design, the findings will remain hypothesis-generating. However, they may be used to inform further studies in this field. Data collection will be retrospective and therefore subject to recall and ascertainment bias. In addition, in view of its retrospective design, despite the prespecified definitions of endpoints, event monitoring will not be standardized across clinical centres which may lead to underreporting of adverse events. Still, summary of the data from all patients treated with Impella over the last years in Poland will enable us to expand from the preliminary data derived from case reports to a national cohort analysis. In the future, data from the IMPELLA-PL registry could be linked to other national and international registries to expand the knowledge on Impella hemodynamic technology by sharing the obtained scientific and clinical experiences with other centers. Based on the retrospective results, the plan is to continue the registry in a prospective form, specifically targeting issues and problems identified in the retrospective phase of the study.

Altogether, the IMPELLA-PL registry will provide an extended evaluation of the Impella technology in various clinical scenarios, allowing for the optimization of treatment in patients with cardiogenic shock or undergoing high-risk PCI.

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Conflict of interest: None declared

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