Supported High-Risk Percutaneous Coronary Intervention With the Impella 2.5 Device

The Europella Registry

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Objectives
This retrospective multicenter registry evaluated the safety and feasibility of left ventricular (LV) support with the Impella 2.5 (Abiomed Europe GmbH, Aachen, Germany) during high-risk percutaneous coronary intervention (PCI).

Background
Patients with complex or high-risk coronary lesions, such as last remaining vessel or left main lesions, are increasingly being treated with PCI. Because periprocedural hemodynamic compromise and complications might occur rapidly, many of these high-risk procedures are being performed with mechanical cardiac assistance, particularly in patients with poor LV function. The Impella 2.5, a percutaneous implantable LV assist device, might be a superior alternative to the traditionally used intra-aortic balloon pump.

Methods
The Europella registry included 144 consecutive patients who underwent a high-risk PCI. Safety and feasibility endpoints included incidence of 30-day adverse events and successful device function.

Results
Patients were older (62% >70 years of age), 54% had an LV ejection fraction <30%, and the prevalence of comorbid conditions was high. Mean European System for Cardiac Operative Risk Evaluation score was 8.2 (SD 3.4), and 43% of the patients were refused for coronary artery bypass grafting. A PCI was considered high-risk due to left main disease, last remaining vessel disease, multivessel coronary artery disease, and low LV function in 53%, 17%, 81%, and 35% of the cases, respectively. Mortality at 30 days was 5.5%. Rates of myocardial infarction, stroke, bleeding requiring transfusion/surgery, and vascular complications at 30 days were 0%, 0.7%, 6.2%, and 4.0%, respectively.

Conclusions
This large multicenter registry supports the safety, feasibility, and potential usefulness of hemodynamic support with Impella 2.5 in high-risk PCI. (J Am Coll Cardiol 2009;54:2430–4) © 2009 by the American College of Cardiology Foundation

The rapid advances in percutaneous coronary intervention (PCI) technology and refinement in adjunctive pharmacological therapy have expanded and will continue to expand percutaneous treatment possibilities. Patients with complex or high-risk coronary lesions, due to extensive and diffuse multivessel, left main, or last remaining coronary artery disease (CAD)—that previously were not deemed suitable for PCI—are increasingly being treated with PCI (1). Furthermore, PCI is increasingly considered an alternative to coronary artery bypass grafting (CABG) in selected patients other than those who have been refused for cardiac surgery.
Because periprocedural hemodynamic compromise and complications can occur rapidly, a growing number of high-risk PCI procedures are being performed with mechanical cardiac assistance, particularly in patients with poor left ventricular (LV) function. Although, the exact role of mechanical cardiac assistance in periprocedural risk management of complex and high-risk PCI procedures remains a matter of debate, the recently introduced percutaneous left ventricular assist devices (LVADs) might be a superior alternative to intra-aortic balloon pump (IABP) (2,3). To date, no large series concerning prophylactic percutaneous LVAD therapy in elective high-risk PCI have been published. Therefore, the purpose of this study was to investigate safety and feasibility of the Impella 2.5 (Abiomed Europe GmbH, Aachen, Germany), a minimally invasive axial rotary blood pump (12-F), designed for short-term circulatory support. Through a femoral approach it is positioned across the aortic valve into the LV with fluoroscopy. Expelling aspirated blood from the LV into the ascending aorta, the Impella 2.5 at its maximal rotation speed of 51,000 rpm is able to provide flow up to 2.5 l/min, in elective high-risk PCI.

**Methods**

**Study design.** The Europella registry comprised patients from 10 tertiary PCI centers across Europe. It was designed to evaluate the safety and feasibility of all patients undergoing elective high-risk PCI with prophylactic mechanical cardiac support with the Impella 2.5. Patients with ST-segment elevation myocardial infarction (MI) within 48 h or cardiogenic shock, or patients undergoing emergent PCI were excluded. The registry was supported by Abiomed Europe GmbH. The investigators had access to the data, and control of the data analysis and monitoring plan.

**Impella 2.5.** As described earlier, the Impella 2.5 (Abiomed, Inc.) is a novel catheter-mounted (9-F) micro-axial rotary blood pump (12-F), designed for short-term circulatory support. Through a femoral approach it is positioned across the aortic valve into the LV with fluoroscopy. Expelling aspirated blood from the LV into the ascending aorta, the Impella 2.5 at its maximal rotation speed of 51,000 rpm is able to provide flow up to 2.5 l/min. The Impella 2.5 is CE (Conformité Européenne) marked for use up to 5 days and has recently received a 510(k) clearance for partial circulatory support for periods of up to 6 h from the U.S. Food and Drug Administration.

**Data collection.** Baseline characteristics including PCI- and Impella-related procedural characteristics were obtained from pre-specified clinical report forms. In addition, vital status and adverse events were collected at 30-day follow-up.

**Study end points and definitions.** The primary safety end point was the incidence of major adverse cardiac and cerebral events defined as death, major bleeding requiring transfusion or surgery, MI, urgent CABG, or stroke at 30 days. Secondary safety end points included device malfunction, infection, vascular complications, renal failure, and hemolysis requiring transfusion. The primary feasibility end point included successful deployment, operation, and explantation of the Impella 2.5. All events were based on clinical diagnoses assigned by the patient's physician and were centrally adjudicated by an independent clinician.

**Statistical analysis.** Data are presented as mean ± SD for continuous variables and as number of patients and frequencies for categorical variables. EuroSCOREs were estimated with the online version of the European System for Cardiac Operative Risk Evaluation. Patients with an additive score sum ≥6 are considered at high risk.

**Results**

Between July 2004 and December 2007, a total of 144 consecutive patients received prophylactic circulatory support with Impella 2.5 during high-risk PCI. The age of patients and the prevalence of comorbid conditions were high. Moreover, 54% of the patients had a left ventricular ejection fraction (LVEF) ≤30%. Baseline and hemodynamic characteristics are detailed in Table 1.

**Procedural characteristics.** All PCI cases were qualified by the attending operators as high-risk procedures. The mean EuroSCORE was 8.2 ± 3.4. In 43% of the cases, patients were refused for CABG. The procedure concerned left main coronary artery (LMCA) PCI, last patent vessel PCI, and complex multivessel disease (MVD) in 52%, 17%, and 82% of the cases, respectively. The procedural characteristics are detailed in Table 2.

**Primary and secondary safety end points.** At 30 days, the primary safety end point was reached in 12.4% of the cases. Death occurred in a total of 8 patients (1 intraprocedural death). There were no device-related deaths. MI did not occur, whereas stroke occurred in 1 patient during hospital stay. Major bleeding requiring transfusion or surgery occurred in 9 patients. With regard to the secondary safety end point, there were no cases of device malfunction. In 1 patient, an abscess developed at the groin where the Impella 2.5 was inserted. Vascular complications (i.e., spurious aneurysm, fistula) and renal failure occurred in 6 and 3 patients, respectively. Hemolysis requiring transfusion occurred in 1 patient.

**Primary efficacy end point.** Successful passage through the femoral artery and implantation of the Impella 2.5 into the LV was achieved in all 144 patients. Both implantation and explantation of the Impella were considered easy or suitable in >99% of the cases. The safety and efficacy end points are detailed in Table 3.

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**Abbreviations and Acronyms**

- **CABG** = coronary artery bypass grafting
- **CAD** = coronary artery disease
- **EuroSCORE** = European System for Cardiac Operative Risk Evaluation
- **IABP** = intra-aortic balloon pump
- **LMCA** = left main coronary artery
- **LV** = left ventricle/ventricular
- **LVAD** = left ventricular assist device
- **LVEF** = left ventricular ejection fraction
- **MI** = myocardial infarction
- **MVD** = multivessel disease
- **PCI** = percutaneous coronary intervention
Mortality stratified by type or extent of CAD and LV function. Because the myocardium at jeopardy and the extent of LV dysfunction are considered important indicators of the risk of PCI, we stratified mortality according to the type of CAD and LV function. Mortality at 30 days for patients with all MVD, MVD + LVEF <40%, and MVD + LVEF <30% was 5.3%, 6.7%, and 5.4%, respectively. LMCA or last remaining vessel, LMCA or last remaining vessel + LVEF <40%, and LMCA or last remaining vessel + LVEF <30% was 6.7%, 8.3%, and 9.1%, respectively. Mortality at 30 days for patients with all LMCA, LMCA + LVEF <40%, and LMCA + LVEF <30% was 8.3%, 10.8%, and 12%, respectively.

**Discussion**

This study reports on the Europella registry, which to date is the largest cohort of patients who underwent an elective Impella 2.5-supported high-risk PCI. The 144 patients enrolled reflect a representative population of patients presenting to PCI centers in contemporary practice for high-risk procedures (i.e., due to complex or high-risk coronary lesions and/or multiple comorbidities).

The present study shows that periprocedural support with the Impella 2.5 for elective high-risk PCI is safe and feasible and extends to encouraging findings with this novel percutaneous LVAD from 3 smaller case series (Table 4) (2,4,5). There are currently many new percutaneous LVADs being developed, and supporters foresee that the growing accessibility of these devices will significantly expand the percutaneous treatment possibilities, particularly in high-risk PCI. However, 2 important questions need to be answered. First, what is the exact indication for mechanical cardiac assist in the setting of elective PCI? Second, what is the optimal device to be used during elective high-risk PCI procedures?

First, the guidelines are conservative with regard to the indications of mechanical cardiac assist in elective PCI, because they only recommend it in patients with very poor LV dysfunction or those considered at high risk of periprocedural hemodynamic collapse (6). However, is there a
uniform definition of high-risk PCI? The Europella registry shows that there were several reasons for qualifying the PCI procedure as high-risk, thus necessitating mechanical cardiac support according to the attending operators. Interventions in an unprotected LMCA or LMCA equivalent, in a last patent vessel and in patients with complex coronary MVD, and low LV function were put forward to be reasons for employing the Impella 2.5 during the PCI procedure. These criteria, in absence of well-defined criteria and randomized controlled trials providing evidence for specific indications, are also the consensus amongst experts in the field (1). Of note, employment of this rationale by the attending operators is retrospectively supported by the sub-group analysis in this study with regard to the mortality stratified by type of CAD and extent of LV dysfunction. Also criteria concerning comorbidities of patients seemed to be important in the decision to use periprocedural mechanical support, as shown by the high comorbidity profile of the patients included in the Europella registry. However, comorbidity was not frequently addressed as the main reason to use mechanical support. Important evidence for defining the indications of elective periprocedural support will likely emerge from 2 ongoing multicenter randomized trials—the PROTECT 2 (Prospective, Multicenter Randomized Controlled Trial) (NCT00562016) and the BCIS 1 (Balloon-pump assisted Coronary Intervention Study)—randomizing between IABP versus Impella 2.5 periprocedural support, and elective IABP use versus conventional treatment (bailout IABP use), respectively. The first trial includes patients who have either MVD and an LVEF <35% or an unprotected LMCA and an LVEF <30%, whereas the latter includes patients with an LMCA lesion or a jeopardy score >8 and an LVEF <30%. Interestingly, the inclusion criteria of both trials are based on the severity of LV dysfunction and the extent of myocardium at jeopardy.

Second, although mechanical cardiac assist might be an appealing treatment strategy for high-risk PCI, iatrogenic morbidity and complications due to the introduction of any invasive therapy should not outweigh the benefits. Currently, the most-used LV support device in elective high-risk PCI is the IABP. Reported usage rates of the IABP range from 4.9% to 64%, depending on the specific case mix of the studies. Although prophylactic IABP therapy for elective high-risk PCI is still debated, there seems to be a trend for improved survival when used, particularly due to a lower periprocedural complication rate (7,8). However, the IABP requires residual cardiac function and stable cardiac rhythm for effective use. In contrast, in safety and feasibility studies, percutaneous LVADs were shown to be capable of providing more adequate cardiac support compared with IABP, particularly during hemodynamic depression due to balloon inflation, in case of periprocedural emergencies such as coronary dissection or cardiogenic shock (4,9).

The main reasons impeding widespread implementation of percutaneous LVADs for use in elective high-risk PCI is not presented here.
PCI and other indications were the high complication rates and complex handling of earlier devices, such as the femoro-femoral cardiopulmonary support system, Hemopump (Medtronic, Minneapolis, Minnesota), and the Tandemheart (CardiacAssist, Pittsburgh, Pennsylvania) (1,10). Three small series of periprocedural Impella 2.5 support were encouraging with respect to safety and feasibility (2,4,5). However to date, large series of the use of Impella 2.5 in high-risk PCI were lacking. The Europella registry showed that the Impella 2.5 was easy to implant and explant, and was associated with a low rate of adverse events. The observed mortality of 5.5% in the registry seems to be consistent with the rate expected for this high-risk patient group (LMCA and/or MVD). For comparison, the 30-day mortality was 10% in the PROTECT I trial (4). In addition, in the SYNTAX (SYNergy Between PCI With TAXUS and Cardiac Surgery) registry for patients undergoing elective PCI, after being refused from CABG the 1-year mortality was 7.3%. Importantly, the rate of hemorrhagic and thromboembolic complications in the Europella registry was limited. Finally, there were no cases of device malfunction.

**Study limitations.** Among others, all adverse events were based on clinical diagnoses assigned by the patient’s physician. However, events were entered in a prospectively developed case report form and centrally adjudicated by an independent clinician.

**Conclusions**

This large multicenter registry supports the safety, feasibility, and potential usefulness of hemodynamic support with Impella 2.5 in high-risk PCI.

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**REFERENCES**


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