Optimized patient selection in high-risk protected percutaneous coronary intervention

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Percutaneous mechanical circulatory support (pMCS) is increasingly used in patients with poor left-ventricular (LV) function undergoing elective high-risk percutaneous coronary interventions (HR-PCIs). These patients are often in critical condition and not suitable candidates for coronary artery bypass graft surgery. For the definition of HR-PCI, there is a growing consensus that multiple factors must be considered to define the complexity of PCI. These include haemodynamic status, left-ventricular ejection fraction, clinical characteristics, and concomitant diseases, as well as the complexity of the coronary anatomy/lesions. Although haemodynamic support by percutaneous LV assist devices is commonly adopted in HR-PCI (protected PCI), there are no clear guideline recommendations for indication due to limited published data. Therefore, decisions to use a nonsurgical, minimally invasive procedure in HR-PCI patients should be based on a risk–benefit assessment by a multidisciplinary team. Here, the current evidence and indications for protected PCI will be discussed.

Introduction

There is increased use of percutaneous mechanical circulatory support in patients with poor left-ventricular (LV) function undergoing elective high-risk percutaneous coronary interventions (HR-PCIs), which is the last option in an increasing number of patients in critical condition and not suitable for artery bypass graft surgery.1 A universally accepted definition of HR-PCI remains elusive, but currently considers not only the anatomy of the coronary arteries (Table 1) but also clinical parameters such as advanced age, frailty, comorbidities, compromised haemodynamic status, depressed ventricular function, ventricular arrhythmias, and concomitant valvular disease (Figure 1). Given the variability in these parameters, this patient population is understudied and potentially underserved.4 The 1-year mortality rate of these patients has been shown to range from 1 to 11% due to associated comorbidities.5

Complex interventions often require long procedural times as well as special interventional skills and techniques such as rotational atherectomy or intravascular lithotripsy.6,7 Such interventions often carry the risk of haemodynamic deterioration especially in patients with reduced left-ventricular ejection fraction (LVEF).8 The use of percutaneous left-ventricular assist devices (p-LVADs) such as the Impella (Abiomed Inc.) has the potential to minimize the risk of haemodynamic deterioration. The feasibility, safety, and haemodynamic effects of Impella devices during HR-PCI have been

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demonstrated in the PROTECT-I, PROTECT-II (P-II), and PROTECT-III (P-III) trials as well as in multiple real-world studies.2,3,9–14 However, the use of Impella may carry risks for the patient and requires experienced interventional cardiologists.15,16

Patient selection is an essential key feature to a safe and successful outcome. Furthermore, since many patients present with severe comorbidities or advanced age, the indication should be discussed in an interdisciplinary team that considers the individual benefit and periprocedural risk.17 Although the use of p-LVAD is well established in HR-PCI, there is no clear guideline recommendation for indication due to limited published data. Here, the rationale, indication, and patient selection will be discussed.

Pre-procedural assessment to clarify contraindications of percutaneous left-ventricular assist device support in high-risk percutaneous coronary intervention

Pre-procedural diagnostics are discussed in a separate study. Briefly, echocardiographic visualization of the LV is recommended to exclude the presence of an LV thrombus. A mobile thrombus may result in systemic embolization as well as increase the risk for device malfunction due to thrombus aspiration in the inlet.18 Therefore, the presence of an LV thrombus is considered as an absolute contraindication. Severe aortic regurgitation is a relative contraindication. Due to the device mechanism, aortic insufficiency can be aggravated by the increase in aortic pressure. This leads to significant volume loading of the LV and may result in dilatation. Another relative contraindication is severe aortic valve stenosis, as it may be difficult to place the catheter in the LV. However, it must be noted that several groups have successfully used Impella in this subpopulation by employing balloon predilatation.19 Furthermore, an Impella device should not be used in patients with a mechanical aortic valve replacement. Patients with a hypertrophic obstructive cardiomyopathy or a ventricular septal defect (VSD) have a relative contraindication for Impella support. Despite the relative contraindication for VSD, Impella devices have been successfully used in patients with post-infarct VSD20 and their use is associated with improved haemodynamics.21 Peripheral artery disease is not a general contraindication, but its presence and severity should be assessed in elective cases to plan the appropriate access strategy.

Definition of high-risk percutaneous coronary intervention

To date, there is no clear definition of HR-PCI. In patients with coronary artery disease (CAD), the 2018 European
Therefore, measure haemodynamic status, LVEF, clinical characteristics and concomitant diseases, as well as the complexity of the coronary anatomy/lesions (Figure 1 and Table 1). In a study of >6000 patients, Brener et al. analysed PCI data and found four criteria for HR-PCI that were significant predictors of mortality. Each of these criteria was assigned points: age >80 years (3 points); dialysis (6 points); LVEF <30% (2 points); and number of lesions treated >2 (2 points). Based on this scoring system, patients were divided into three groups: low risk (0-1 points); intermediate risk (2-3 points); and high risk (>4 points). They observed that the 1-year mortality rates in these three groups were 1.24, 2.47, and 10.86%, respectively. However, the study does not provide information on the haemodynamic status of the patients and furthermore, patients with a p-LVAD were not investigated.

In addition to the above-mentioned factors, haemodynamic status can provide additional information for risk assessment. LVEF alone is not sufficient to assess the risk for haemodynamic deterioration, but additional factors may play a role for tolerance to PCI-related ischaemia. For example, LV end-diastolic volume (LVEDV) has been reported to significantly predict a decrease in mean arterial pressure (MAP) during HR-PCI in a small retrospective study. In this patient cohort, the mean LVEDV was 182 ± 47 mL. Therefore, measurement of LVEDV during the diagnostic work-up may be helpful to identify patients who may benefit from Impella support. In addition, left-ventricular end-diastolic pressure (LVEDP) can be considered as an indicator for LV wall tension and the potential of haemodynamic instability, myocardial dysfunction, or the development of cardiogenic shock, and thus may also be useful for decision-making. High LVEDP is associated with myocardial ischaemia, acute kidney injury and lower systolic blood pressure as well as cardiac output (CO). In contrast, Al Rashid et al. reported that pre-procedural LVEDP was not associated with peri-procedural haemodynamic deterioration or a higher rate of in-hospital major adverse cardiac and cerebrovascular events (MACCEs) in a study of 64 patients. In these patients, the mean LVEDP was 17 ± 8 mmHg before Impella insertion and start of PCI. However, the study has many limitations (small sample size, retrospective study design, and single centre experience). In contrast, Russo et al. observed that an increased LVEDV (and consequently elevated LVEDP) significantly predicted a decrease in MAP, as described above. Therefore, the authors recommend evaluating the LVEDV and LVEDP as an additional surrogate parameter for decision-making, as this may be helpful in a specific patient population. If available, information on the CO (cardiac index >2.2 L/min/m²), mean pulmonary artery pressure (>50 mmHg), as well as pulmonary capillary wedge pressure (>15 mmHg) should also be considered (Figure 1). Taken together, while data regarding patients’ haemodynamic pattern and device function during p-LVAD are scarce, available information on haemodynamic status should be evaluated and considered before starting the procedure.

The amount of jeopardized myocardium is another determinant in the decision-making of a protected PCI in HR-PCI patients. Indeed, a small retrospective study has demonstrated that a more significant jeopardized myocardium, assessed by the British Cardiovascular Intervention Society myocardial jeopardy score (BCIS-JS), is an independent predictor of critical pressure decreases during PCI. This suggests the importance of BCIS-JS during the diagnostic work-up in order to identify those who may benefit most from Impella support.

The authors recommend that in the presence of any of the criteria shown in Figure 1 alongside coronary angiographic criteria (Table 1) indicating high complexity, an increased interventional risk can be assumed, suggesting a classification of HR-PCI.

Evidence for the use of percutaneous left-ventricular assist devices in high-risk percutaneous coronary interventions

Impella support in the setting of HR-PCI (protected PCI) results in the following physiological effects: unloading, reduction in end-diastolic pressure and wall stress of the LV, and reduction in LV work and myocardial oxygen demand. This may increase CO, resulting in improved systemic perfusion and increased coronary flow. In addition, an increase in MAP can be achieved.

In the PROTECT-II randomized clinical trial, use of haemodynamic support devices during complex PCI did not meet the primary composite endpoint when the original definition of periprocedural myocardial infarction was used (troponin increase >×3 ULN). However, applying a more pragmatic definition (troponin increase >×8 ULN), a significant reduction in MACE among patients treated with the Impella device was observed. Although registry data show that protected PCI improved quality of life due to an increased ejection fraction, reduced New York Heart Association class, reduced adverse events, and reduced acute kidney injury requiring
dialysis, \(^3\) p-LVAD support is currently recommended by European guidelines only for patients in cardiogenic shock. \(^1\),\(^10\),\(^13\),\(^36\) However, the rationale for the use of p-LVAD support in a very high-risk cohort prior to the elective intervention is to prevent profound hypotension/low CO episodes and allow sufficient time to achieve optimal and complete revascularization. \(^18\),\(^24\),\(^32\)

Currently, patient selection for protected PCI using Impella refers to the inclusion criteria of the P-II and P-III trials, results from registries, and personal experience of the treating physician. \(^10\),\(^13\),\(^15\)\(^33\)\(^35\) Inclusion criteria of PROTECT-II and PROTECT-III were: patients with none-mergent PCI of an unprotected LM, single remaining vessel with an LVEF \(\leq 0.55\%), or three-vessel disease and LVEF \(\leq 30\%\). \(^10\),\(^14\) Patients with ST-segment elevation myocardial infarction within 24 h of Impella placement, cardiogenic shock, renal failure with creatinine \(\geq 4\) mg/dL, or a platelet count of \(\leq 75\,000/mm^2\) were excluded in the PROTECT trials. In more recent studies, patients with an LVEF \(\leq 45\%)\) were also included. \(^1\),\(^35\) Retrospective data analysis of a multicentre registry showed that the following criteria were applied in a real-world cohort as indications for Impella support in the context of protected PCI: HR-PCI (70.8\%), followed by the personal impression of the treating interventional cardiologist (56.5\%), severely reduced LVEF (49.4\%), surgical turn down (30.5\%), and patient’s decision (25.3\%). \(^2\)

In complex interventions, it may be necessary to use special techniques. Case complexity is also reflected by the mortality rate, with in-hospital mortality ranging from 5 to 15\% in patients with impaired LVEF (<35\%), unprotected LM disease, severe three-vessel disease (SYNTAX score >33) or last remaining patent vessel. \(^16\) In contrast, the P-III study showed a lower inhospital mortality rate of 4.4\% in a comparable patient population treated with protected PCI. \(^14\)

Several studies have shown a potential benefit of Impella 2.5 and Impella CP in the treatment of unprotected LM. \(^3\),\(^16\),\(^12\),\(^14\),\(^17\),\(^37\),\(^38\) Data from the USpella registry showed that protected PCI could be performed safely and efficiently in 127 patients with an unprotected LM disease. The baseline SYNTAX score was 31, while the post-procedure SYNTAX score was 7.9 and the 30-day mortality was 2.1\%, and a rate of 0.8\% of vascular complications that required surgery. \(^17\)

In the case of MVD, a meta-analysis of 89 883 patients enrolled in randomized trials as well as observational studies revealed lower long-term mortality [relative risk (RR) 0.71, 95\% confidence interval (CI) 0.65–0.77, \(P < 0.001\)], lower rates of myocardial infarction (RR 0.78, 95\% CI 0.68–0.90; \(P = 0.001\)) and lower repeat revascularization (RR 0.74, 95\% CI 0.65–0.83; \(P < 0.001\)) in patients with complete revascularization compared with those with incomplete revascularization. \(^39\) These data are also confirmed by a recent meta-analysis, where complete revascularization had an incremental benefit when performed with state-of-the-art techniques in high-risk patients. \(^40\) The use of protected PCI can be advantageous due to the haemodynamic support in the event of complications or haemodynamic deterioration.

A study of 86 patients who underwent protected PCI with Impella 2.5 or Impella CP observed that a more complete revascularization was associated with significant LVEF improvement and survival. \(^13\) In this study, the long-term (14-month) follow-up all-cause mortality rate was 10.5\%. \(^13\) In the P-III trial, repeat revascularization up to 90 days was significantly lower compared with the P-II cohort (1.2 vs. 6.2\%; \(P = 0.015\)). This was due to more extensive single-stage revascularization in the P-III cohort compared with the P-II patient population, which led to a reduction in 90-day MACCE. \(^10\),\(^14\) Recently, a subgroup analysis of HR-PCI patients enrolled in the Revascularization Extent in IMPella Mechanical Circulatory Support Device in Italy (R-IMP-IT) study demonstrated that protected PCI patients receiving more complete revascularization, assessed by BCIS-JS revascularization index >0.67 (range 0–1), had improved survival free from a composite primary endpoint (all death, nonfatal MI, and nonfatal stroke) at 1-year follow up. \(^28\)

There is limited data for the use of Impella in complex chronic total occlusion (CTO)-PCI or intervention on the last remaining vessel. In a retrospective study of 1598 CTO-PCIs, a p-LVAD device was used electively in 69 procedures (4\%) and urgently in 22 procedures (1\%). In 62\% of the cases, Impella 2.5 or CP was used for p-LVAD. The authors observed that use of elective p-LVAD was associated with longer procedure and fluoroscopy times, and higher incidences of in-hospital major adverse cardiovascular events (8.7 vs. 2.5\%; \(P < 0.01\)) and bleeding (7.3 vs. 1.0\%; \(P < 0.001\)) with similar technical and procedural success rates. \(^41\) Of note, Davila et al. reported that CTO is associated with a higher probability of extended p-LVAD use. A small retrospective multicentre study of 57 patients reported the use of the p-LVAD during CTO-PCI in a patient cohort with a median LVEF of 20\%. The authors observed a technical success rate of 87.7\% and an in-hospital all-cause death rate of 5.3\%. \(^43\)

Due to the heterogeneous criteria for the indication of a protected PCI, the mortality rates vary from 2 to 20\%. \(^17\),\(^37\)-\(^44\),\(^45\) The invasive nature of the procedure also carries risks for the patient. \(^45\) For example, vascular complications, which was reported to be 13.5\% in a study including >30 000 p-LVAD placements. Of these complications, >50\% required surgical treatment. \(^15\) Acute limb thromboembolism and bleeding requiring transfusion accounted for 27.6 and 21.8\% of all vascular complications. \(^15\) In addition, Thiele et al. observed that the rate of bleeding was significantly increased in p-LVAD compared with intraaortic balloon pump. However, the p-LVAD indication in those patients was cardiogenic shock. In contrast, significantly lower rates of vascular complications requiring surgical treatment and rate of bleeding complications requiring transfusion are reported in the P-II and P-III studies, 2.4 vs. 0.9\% and 9.4 vs. 1.2\% (\(P = 0.001\)), respectively. \(^10\),\(^14\)

Conclusion: follow your heart or the facts?

The use of p-LVAD in cases of LM-PCI, MVD with complete revascularization, CTO-PCI, as well as in last remaining
vessel allows the interventional cardiologist to perform the procedure under optimal haemodynamic conditions with low risk of periprocedural complications, particularly in cases with severely impaired left-ventricular systolic function. These factors (Figures 1 and 2) should be considered when determining the indication for support, especially since performance of PCI in patients with impaired LV function is associated with a higher mortality rate, likely attributed to inadequate myocardial reserve. The indication for HR-PCI and protected PCI should be made jointly by the heart team and risk scores should be used to guide discussion (Figure 2). Furthermore, it is suggested that protected PCI/HR-PCI procedures only be performed in specialized centres by clinicians and teams with adequate training and experience in complex PCIs.

The decision should weigh the RRs, contraindications, and benefits of protected PCI vs. HR-PCI without p-LVAD vs. surgical revascularization. Selection of appropriate patients is particularly important given potential p-LVAD-associated complications. This is further supported by the retrospective analysis of 4782 patients, in which it was shown that Impella use was associated with higher rates of adverse events and costs. However, it is difficult to draw firm conclusions on protected PCI from this report due to the very different patient cohorts, especially given that Impella support was provided in approximately 50% of patients with cardiogenic shock or in bailout situation. These findings confirm the importance of a multidisciplinary team approach between the (interventional) cardiologist, intensivist/anaesthetist, and the cardiac surgeon. Here, local standards should be developed.

A number of European expert groups recommend considering the use of p-LVAD in the context of HR-PCI. In addition, the American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions acknowledged p-LVAD use in HR-PCI with a Class IIb recommendation. However, there is no clear recommendation in the European guidelines on myocardial revascularization due to limited data.

Due to the paucity of randomized clinical trials, the authors recommend the use of a p-LVAD as haemodynamic support be considered in patients with severely reduced LVEF and planned complex revascularization, and in patients with highly jeopardized myocardium, particularly for unprotected LM, last remaining conduit or multivessel disease. In cases where there is a pre-existing haemodynamic impairment, LV support is strongly recommended (Figures 1 and 2). Given the limited data regarding CTO-PCIs, the indication remains an individual decision, but the general principles mentioned above still apply.

In summary, the characteristics as shown in Figure 1 and Table 1 are intended to aid decision-making as depicted in Figure 2. In the absence of significant evidence-based knowledge, the multidisciplinary team, patient features, clinical conditions, and the respective experience of all team members play a major role in the decision-making regarding the use of protected PCI.
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No new data were generated or analysed in support of this research.

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