

Defining the optimal revascularization strategy during protected high-risk procedures with Impella

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Complete revascularization (CR) in patients with multi-vessel disease improves outcomes. The use of percutaneous left-ventricular assist devices, such as the Impella heart pump, is useful to minimize the risk of haemodynamic compromise in complex higher risk and clinically indicated patients. The recently published data from the PROTECT III trial suggest more CR during Impella-protected percutaneous coronary intervention with more extensive lesion preparation and treatment, resulting in the reduced need for repeat revascularization. To achieve CR and improve survival, procedural guidance by intravascular imaging, extensive lesion preparation, debulking with atherectomy devices, advanced chronic total occlusion revascularization techniques, and post-interventional treatment with modern anti-platelet medication are essential.

Introduction

There is increasing evidence that complete revascularization (CR) in patients with multi-vessel disease improves outcomes, especially in patients undergoing primary percutaneous coronary intervention (PCI). The use of percutaneous left-ventricular assist devices, such as the Impella heart pump, may minimize the risk of haemodynamic compromise in complex, higher risk, and indicated patients (CHIPs) and allow for CR, thus improving outcomes.¹⁻³ The recently published PROTECT III (P-III) trial data suggest a more CR during Impella-protected PCI with more extensive lesion preparation and treatment, resulting in the reduced need for repeat revascularizations and improved survival.³⁻⁵

Extent of revascularization

Achieving CR is the ideal objective in all patients with multi-vessel coronary artery disease (CAD) undergoing myocardial revascularization. However, despite major improvements, a CR is not always possible in clinical practice. In the Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) trial, CR was achieved in 56.7% of enrolled patients undergoing PCI.⁶ The complexity of coronary lesions, left-ventricular ejection fraction, and clinical presentation at admission are the main factors influencing the decision-making process in myocardial revascularization.

Mechanical cardiac support with the Impella heart pump has been indicated in high-risk PCI patients.⁷ The haemodynamic stability provided by Impella may allow a patient to achieve CR; however, the clinical impact of pursuing an extensive revascularization in these

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procedures remains to be fully determined.⁵ Moreover, the lack of a universal definition of CR has also contributed to conflicting reports. Recently, the concept of a reasonable incomplete revascularization (IR) has been introduced, underlying the importance of residual burden of myocardium at risk.^{8,9} Nevertheless, in this setting, different scores have been proposed in order to better quantify the extent of coronary revascularization (*Figure 1*).

The predictive value of angiographic scoring systems prior to undergoing PCI has been validated in several subsets of patients with CAD.¹⁰ In the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial, the extent and complexity of residual coronary artery lesions remaining after PCI was assessed, and the residual SYNTAX score (rSS), correlated with clinical outcomes.¹¹ In particular, an rSS > 8.0 after PCI, identified a level of IR was strongly associated with increased mortality and adverse ischaemic events in patients. The British Cardiovascular Intervention Society myocardial jeopardy score (BCIS-JS) is a modification of the Duke Jeopardy Score scoring system and may be also applicable in patients with coronary artery bypass grafts (CABGs) or left main disease. The fundamental basis of BCIS-JS is an easy-to-apply classification of CAD extension according to the region of myocardium at risk, unlike other angiographic scoring systems that are more focused on lesion-specific characteristics like the SYNTAX score. This makes BCIS-JS and its derived revascularization index (range between 0=no revascularization and 1=CR) very suitable for critically ill patients. As such, this score is the only score used to evaluate the clinical

impact of revascularization extent in complex, high-risk PCI. In fact, data from the Roma-Verona registry, demonstrated a BCIS-JS revascularization index of ≤ 0.8 was an independent predictor of mortality at 14-month follow up in 86 high-risk PCI patients undergoing elective Impella-protected PCI.^{4,7} Additionally, the Impella Mechanical Circulatory Support Device in Italy (R-IMP-IT) study, identified that patients with a BCIS-JS revascularization index >0.67 had a lower occurrence of all-cause death, non-fatal myocardial infarction (MI), and non-fatal stroke at 1-year follow up with a more CR.¹² Thus, while achieving extensive revascularization requires longer and more complex PCI, the current data suggest a certain amount of revascularization of the myocardium is needed in order to positively affect clinical outcomes in Impella-protected high-risk PCI.

Quality of revascularization (imaging/debulking)

To achieve CR during Impella-protected PCI, procedural guidance by intravascular imaging, extensive lesion preparation, and debulking with atherectomy devices is essential (*Figure 2*). In addition, there are advanced chronic total occlusion (CTO) revascularization techniques and post-interventional treatments with modern anti-platelet medication that reduce the odds of repeat revascularization and improve survival.^{3,5}

With the recent advances in functionally-based revascularization, adjunctive pharmacology such as modern anti-platelet therapy, and improved PCI techniques and

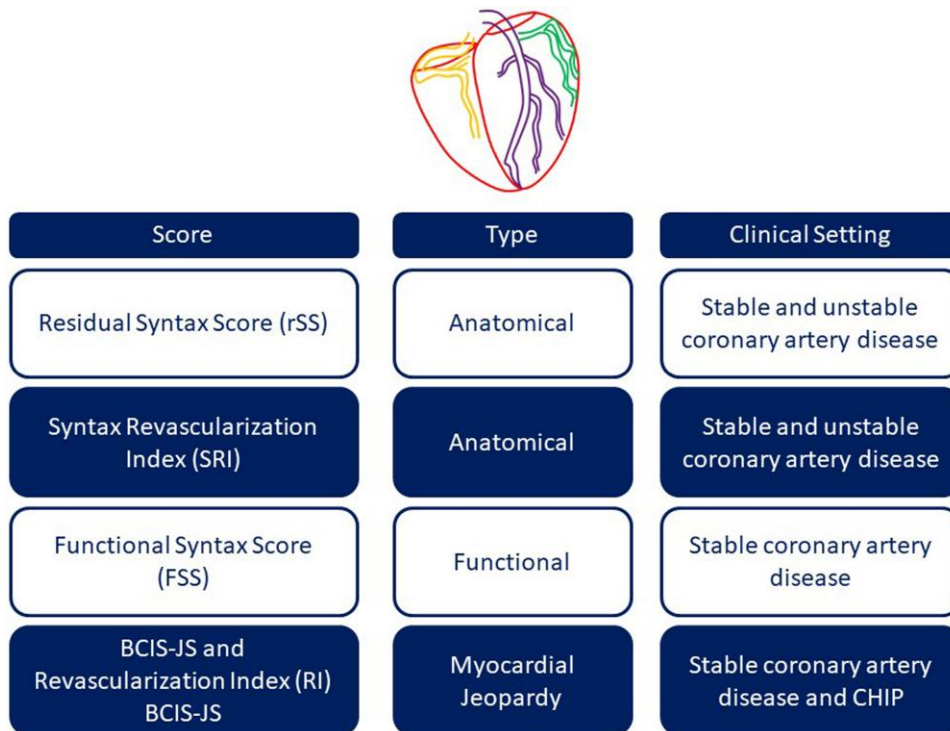


Figure 1 Determining the extent of coronary revascularization.

The optimal revascularization strategy during protected high-risk procedures

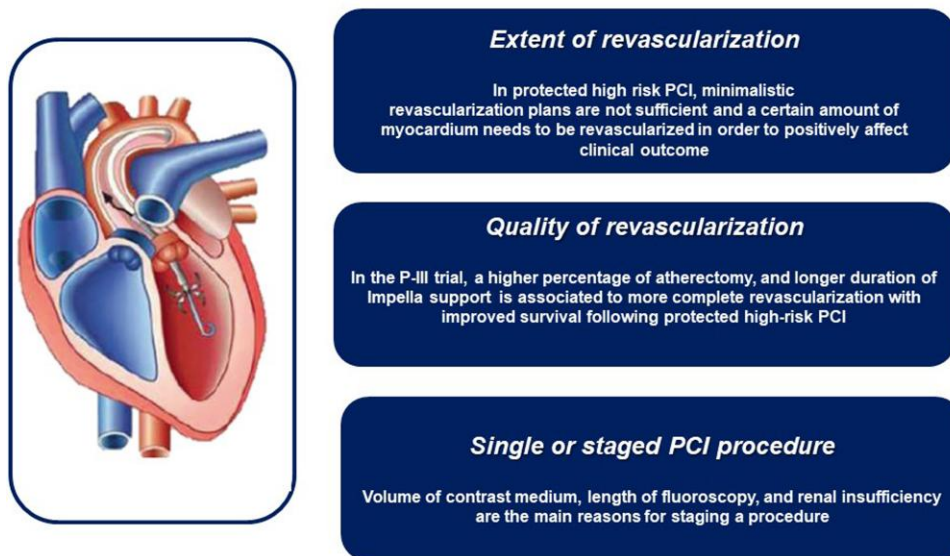


Figure 2 Optimal revascularization strategy during high-risk procedures.

devices, the success rate for treating the most complex lesions has improved among operators trained in specialized techniques, but have remained poor among average interventionists. To treat CHIPs safely and effectively, interventional cardiologists must possess the skills necessary to perform CR in complex cases such as CTO, calcified vessels, complex bifurcation disease, and in cases requiring haemodynamic support like protected PCI with the Impella heart pump.

It is important to recognize that there is a difference between complex intervention and high-risk intervention. Complex intervention requires advanced and specialized techniques, but not all of these will necessarily apply to high-risk patients. Therefore, successful establishment of specialized programmes must incorporate training in both complex techniques and the adequate assessment of procedural risk in order to achieve the most favourable clinical outcomes.²

In low- and intermediate-risk patients, the use of physiologically-guided revascularization has been shown to reduce the rate of major adverse cardiac and cerebrovascular events (MACCEs) in patients with multi-vessel disease. However, fractional flow reserve-guided PCI was recently found to be inferior to CABG with respect to the incidence of death, MI, stroke, or repeat revascularization at 1 year in the FAME III trial.¹³ While patients with anatomically more complex disease might have originally been considered for surgery, current clinical guidelines suggest that the risk of surgery is too high. Although not yet formally assessed in complex CAD patients, ischaemia and viability testing can be extremely helpful to determine if CR is possible in individual patients. Specifically, routine intracoronary imaging might be helpful to improve

procedural outcomes by optimizing stent implantation, reduce the incidence of stent under expansion, stent malposition, and edge dissection. Combining these strategies in the contemporary strategic approach based on the SYNTAX II study led to a significant reduction of device-related adverse events, such as repeat revascularization, MI and stent thrombosis.¹⁴

The SYNTAX II study confirmed that developments in PCI technology and techniques have translated into better outcomes since the SYNTAX I trial.¹⁴ The P-III trial, the largest non-randomized, prospective study of Impella-supported high-risk PCI, has also expanded knowledge in the field of CR in CHIPs. This study integrated the use of the Impella CP in a number of procedures and contemporary best practices for vascular access, closure, and haemodynamic support in patients with severely depressed left-ventricle ejection fraction. Although P-III patients were older and presented with more anatomically complex coronary disease (i.e. higher rates of three-vessel disease, longer and more calcified lesions), 90-day MACCE rates were improved in comparison with historical patients from the PROTECT II trial. This improvement is likely due to advances in best practices for haemodynamically supported PCI and a significant evolution over the last decade in how PCI procedures are performed.⁵

In summary, a more extensive single-stage complex revascularization and longer duration of Impella support in the P-III trial resulted in more CR and improved survival following high-risk PCI. Thus, outcome data that support previous studies have identified that a higher rSS is associated with poor long-term outcomes in patients undergoing complex multi-vessel PCI.⁵

When to implement stage revascularization instead of single procedure and why

In patients with chronic coronary syndrome, who are candidates for multi-vessel PCI, operators must determine whether it is best to treat all lesions in one procedure or to stage revascularization (Figure 2). A substudy of the SYNTAX trial aimed to understand why staged PCI procedures were undertaken in a group of patients with complex CAD by comparing procedural differences and outcomes to those completing PCI in a single session. The results showed that volume of contrast medium, length of fluoroscopy, and renal insufficiency were the primary reasons for staging a procedure.¹⁵

Patients undergoing staged PCI have a higher incidence of MACCE (a composite of death, stroke and MI, repeat revascularization, and stent thrombosis), which is important to consider when determining revascularization strategy. The impact of staging in multi-vessel CAD patients with fewer comorbidities or less complex coronary anatomy, and the potential benefits of more modern stent technology, require further study. In the SMILE trial, multi-vessel patients with non-ST-elevation acute coronary syndrome had significantly lower MACCE with one-stage PCI during the index procedure than those with multi-stage PCI and complete coronary revascularization. This is mainly due to an unexplained higher incidence of target vessel revascularization.¹⁶

In selected cases, it may be useful to treat certain vessels in preliminary stages without the use of a mechanical support device. For example, this could be performed in simple Type A lesions or in lesions with smaller area of myocardium at risk. Similarly, some vessels can also be treated in a staged procedure after the protected PCI. Such an approach could be useful in individual cases of long procedure duration, high volume contrast medium consumption, or agitated patients. CR can be challenging especially in patients with heart failure and myocardial dysfunction. In cases of CTO or heavily calcified lesions, specific lesion preparation may be required, which can be time consuming and, thus, a staged approach might facilitate a more favourable outcome. However, given that IR has been shown to increase the incidence of adverse events in heart failure patients with or without haemodynamic support with Impella, CR should be the major aim of the intervention.^{12,17} Therefore, it is important to evaluate all treatment strategies that may have the potential to facilitate CR.

Which vessel should be treated first?

Due to a lack of related randomized data, it remains unclear on which vessel the intervention should be performed first in protected PCI patients. In patients suffering from cardiogenic shock or acute MI, the treatment of culprit lesions is clearly defined and associated with improved outcomes, whereas the timing of non-culprit lesion treatment during index PCI or as staged procedures still remains uncertain.¹⁸⁻²⁰ In stable conditions, there is no data that show a clear benefit to a

specific treatment order of lesions. Nonetheless, it may be useful to treat the simpler stenosis first and stabilize perfusion of the unaffected myocardium in the event of complications or low blood flow during treatment of the remaining, more complex lesions.

When and how do we have to treat chronic total occlusion in protected PCI patients?

Currently, there are no ongoing randomized trials comparing revascularization of CTOs in patients with heart failure and optimal medical therapy. Although CTO PCI has shown to improve the overall condition of the patient, it did not demonstrate clear benefits regarding mortality or MACCE.²¹ A sub-study of the SYNTAX trial identified CTO as the strongest independent predictor of IR in PCI patients, which was associated with increased mortality and MACCE at 4-year follow up.⁶ Interestingly, in the initial SYNTAX trial, the proportion of CR was significantly higher after CABG than after PCI (63.2 vs. 5.7%, $P=0.005$). Additionally, the prevalence of CTO correlated with less CR in the PCI group compared with the CABG group, which partially explains the lower CR rates in the PCI arm.⁶ Furthermore, a multi-variable analysis from the PROTECT II study comparing extensive and limited revascularization demonstrated reduced adverse events with extensive revascularization (41.9 vs. 54.0%; $P=0.023$).²² Together, data from these clinical studies suggest CR is associated with a reduction in MACCE.

In summary, the timing of when CTOs should be treated remains to be clearly defined. Data summarized above suggest that the non-CTO vessels should be treated first with haemodynamic support. If the duration of the procedure and the amount of contrast medium used are acceptable and patient is stable, the CTO PCI can be performed in the same session. If not, the CTO PCI should be performed as a second-stage procedure. Nevertheless, interventionist training and real-time experience with CTO PCI is crucial to achieve CR and to reduce adverse events.

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Data availability

The data underlying this article are available in the article or the references provided.

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