

# Weaning from Impella and mobilization of Impella patients

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## KEYWORDS

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Weaning of patients from Impella is complex and includes evaluation of the underlying disease, which is essential for estimating the potential for heart recovery. Monitoring during the weaning phase with echocardiography and pulmonary artery catheters will be discussed, as well as the use of intravenous and oral heart failure drugs. Patients who are candidates for weaning must be stable, without inotropes, and must have recovered from acute end-organ damage. Coronary artery disease and valvular heart diseases should be appropriately addressed before weaning to take the maximum advantage of haemodynamic stability provided by the support and to maximize the possibility of weaning. Tips and tricks for the mobilization of Impella patients will also be discussed.

## Introduction

The process of weaning from Impella is complex and multifaceted: the underlying disease can provide insights into the potential for heart recovery. For patients who are candidates for weaning, haemodynamic stability must have been reached without inotropes, end-organ function should be recovered, coronary artery disease must be addressed with revascularization therapy guided by the assessment of myocardial viability, and they must have received appropriate treatment for valvular diseases while still under support, taking advantage of the haemodynamic stability provided by the device.

Any weaning process must take into account pump durability to avoid the risks of pump malfunction or the need for emergent pump exchange. Moreover, patient candidacy for further therapies, such as long-term mechanical

circulatory support (MCS) and heart transplantation, should be carefully considered.

## Haemodynamic recovery vs. myocardial recovery

The difference between haemodynamic and myocardial recovery has received little attention and, to the best of our knowledge, has never been a specific study subject.

We can define *haemodynamic recovery* the progressive development, in a patient who was totally dependent from mechanical support, of a pulsatile systemic and pulmonary artery pressure waveform, still at high levels of Impella support, accompanied by an increase of native cardiac output. This definition prescinds from specific thresholds of left ventricular (LV) function index improvement. Cardiac power output (CPO), calculated as the mean arterial pressure  $\times$  cardiac output/451, is an important index of haemodynamic recovery and a strong predictor of mortality in cardiogenic shock (CS). An increase in CPO can

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be helpful during the weaning process. Pulmonary artery catheter (PAC)-derived indexes of right ventricular function, such as the pulmonary artery pulsatility index (PAPi), can have analogue value.<sup>1</sup>

*Myocardial recovery* is, instead, the improvement of ventricular contractility parameters, usually accompanied by haemodynamic recovery. It has been demonstrated that all mechanical support systems that are able to provide LV unloading can favour myocardial recovery through the reduction of mechanical power expenditure of the ventricle to minimize myocardial oxygen consumption and reduce haemodynamic forces that lead to ventricular remodelling and, in acute myocardial infarction (AMI), to reduce infarct size.

It is worth mentioning that, in terms of successful weaning from Impella, rather than a specific threshold of LV ejection fraction (LVEF) improvement, specific haemodynamic cut-off points of CPO, PAPi and central venous pressure seem to have predictive value.<sup>1,2</sup>

### Monitoring: echocardiography and pulmonary artery catheters

Multiparametric haemodynamic evaluation with comprehensive invasive and non-invasive haemodynamic monitoring should guide pump management and drug administration to provide adequate LV unloading and to detect the appropriate MCS weaning time.

Echocardiography offers a non-invasive real-time assessment of cardiac function at the bedside, making it the main modality for evaluating critically ill patients in the intensive care unit (ICU).

However, in Impella-supported patients, the most common Doppler-based measurements may be affected by the mechanical noise of the device and continuous flow. Furthermore, in patients with severe LV dysfunction, the most common biplane LVEF measurement is not sufficient for detecting myocardial recovery or guiding weaning strategies.

Therefore, combined monitoring with PACs in Impella-supported patients is strongly advised.

The routine use of PACs in acutely ill patients remains contentious. In the last decade, PAC monitoring adoption has progressively decreased following randomized trial results (PAC-Man and ESCAPE trials) comparing PACs with clinical assessment alone, which have suggested no overall benefit in terms of mortality and a high rate of catheter-related complications.<sup>3-5</sup> However, these trials have been criticized for their multiple potential confounders, particularly for the possibility of inappropriate patient selection. Indeed, a recent retrospective cohort study showed that the use of PACs in a subgroup of patients admitted with CS was associated with lower mortality, which may reflect the better selection of patients or the better use of information to guide therapies.<sup>6</sup>

Current heart failure European Society of Cardiology (ESC) guidelines recommend considering PAC monitoring in acute heart failure (HF) patients who present with refractory symptoms (particularly hypotension and hypoperfusion) despite pharmacological treatment (class IIb, level of evidence C).<sup>7</sup> Furthermore, in the setting of MCS, the use of

PACs for haemodynamic monitoring in Impella-supported patients was associated with higher survival in a US registry that included 15 259 AMI-related CS patients.<sup>8</sup>

However, PAC monitoring is associated with risks for procedural complications, infections, pulmonary infarctions, and pulmonary haemorrhages. Therefore, invasive haemodynamic monitoring should be positioned, managed and interpreted only by trained ICU physicians and nurses.

PAC-derived information is particularly useful for making decisions concerning escalation therapy and support weaning. During the weaning phase, the monitoring of wedge pressure and pulmonary artery pressure is fundamental for safe de-escalation and the early detection of weaning failure. PACs can also provide important data concerning right ventricular performance and can aid in identifying the need for right ventricular support.<sup>9</sup>

### Medical therapy: inotropes and oral heart failure medications

#### Inotropes

According to the ESC guidelines, inotropic agents represent the initial therapy if there is a need to maintain systolic blood pressure in the presence of persistent hypoperfusion. However, rather than adding several inotropes, device therapy must be considered when there is an inadequate pharmacological response.<sup>7</sup>

In CS after Impella positioning, inotropes should be quickly weaned and stopped as soon as possible to avoid collateral effects and to maintain full mechanical unloading. During MCS support, inotrope cut-off values are extremely valuable for clinical purposes: inotropic scores >20 should warrant the evaluation of escalation, and similarly, requirement of inotropes after 48 h of Impella support should trigger a full haemodynamic re-evaluation.

In Impella-supported patients, the use of a calcium-sensitizer inotropic agent (levosimendan) should be considered: its long-lasting effect may be useful in the weaning phase, providing support for native heart function during MCS de-escalation, and its vasodilatory effect is useful in reducing pulmonary hypertension and improving right ventricular dysfunction if present.

#### Oral heart failure medications

Oral disease-modifying drugs, particularly beta-blockers and renin-angiotensin-aldosterone system blockers, are strongly recommended in the treatment of chronic HF by clinical practice guidelines.<sup>7</sup> The management with oral medications in the setting of acute decompensated HF and CS is less defined.

Current European guidelines recommend continuing oral therapies in cases of acute-on-chronic HF and initiating therapies as soon as possible in cases of *de novo* HF in the absence of haemodynamic instability (class I, level of evidence C). When haemodynamic instability is present (symptomatic hypotension, hypoperfusion, bradycardia), the daily dosage of oral therapy may be reduced or stopped temporarily until the patient is stabilized, particularly in those with a class III recommendation for beta-blockers in CS or low output states.<sup>7,10</sup>

A randomized controlled trial of 240 patients with ongoing CS demonstrated that 30-day mortality was higher in patients who received  $\beta$  or renin-angiotensin-aldosterone system blockers prior to CS resolution (27.3% vs 16.9%;  $P=0.035$ ), although a statistically significant difference was only observed in the subgroup of patients administered  $\beta$ -blockers ( $P=0.017$ ) but not among those only treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers ( $P=1.000$ ).<sup>11</sup> Similarly, a previous large randomized controlled trial showed that early intravenous  $\beta$ -blockers increased the risk of CS in high-risk patients with myocardial infarction.<sup>12</sup> Indeed,  $\beta$ -blockers have a recognized negative inotropic effect that can initially and transiently reduce LV systolic function in HF patients.

Therefore, in the setting of Impella-supported patients, the correct timing for the introduction of oral HF drugs is very important.

Given the previous evidence, beta-blocker agents should be avoided until complete weaning and removal of MCS have been accomplished. Control of heart rate should be obtained with ivabradine or digoxin. Instead, the gradual introduction of low-dose renin-angiotensin-aldosterone system blockers should be considered in Impella-support patients with persistent LV dysfunction (LVEF < 40%) after haemodynamic stabilization (low cardiac filling pressures) and end-organ damage recovery. Phosphodiesterase type 5 inhibitor (e.g. sildenafil) introduction should be considered before Impella removal in patients with pulmonary hypertension and right ventricular dysfunction.

## Management of coronary artery disease and valvular heart disease

According to the CULPRIT-SHOCK trial results, among patients with CS-AMI in multivessel coronary artery disease, culprit lesion-only percutaneous coronary intervention is indicated as the primary procedure.<sup>13</sup> MCS implantation is usually performed during the primary procedure. Impella insertion before primary PCI is strongly advised because it allows complete support during phases of haemodynamic or arrhythmic instability potentially occurring during coronary intervention and is correlated with improved survival.<sup>8</sup>

After culprit lesion revascularization, full-flow unloading with Impella is maintained in the ICU to achieve haemodynamic stabilization, weaning from inotropes and end-organ damage regression.

Before MCS weaning, the patient should be evaluated for the completion of coronary revascularization, which will be performed under device support. Myocardial viability assessment during MCS support is challenging due to practical management (often unstable and mechanically ventilated patients with high risk or impossible mobilization) and device interference (for example, with cardiac magnetic resonance). In this setting, two imaging techniques are available: echocardiography and cardiac positron emission tomography (FDG-PET). If myocardial viability is confirmed and major contraindications to antithrombotic therapy are excluded (for example, gastrointestinal

bleeding complications), second-stage coronary revascularization is performed while on device support before removal.

Moreover, before MCS weaning, major valvular dysfunction should be ruled out, particularly severe mitral regurgitation (MR) (functional or less frequent, organic), which can represent the underlying cause of weaning failure from Impella. The echocardiographic quantification of functional MR while on Impella support is challenging due to the unloading of the left ventricle: a 'weaning trial' by reducing the Impella speed (P2-P3) may unmask severe MR. Surgical or percutaneous MR correction may be helpful in achieving successful weaning. However, in patients with severe MR and a lack of LV function recovery with MCS weaning failure, long-term LV assist device implantation should be considered.

## Mobilization of Impella patients

The mobilization of critically ill patients represents a hot topic of current debate. There is a divide among ICU clinicians, depending on the prevalence of evidence about the benefits of this intervention or the traditional culture of bedrest for ICU patients.

Early mobilization of critically ill patients has no demonstrated effects on strong outcomes such as mortality and health-related quality of life,<sup>14</sup> but many advantages have been repeatedly observed: increased discharge-to-home rate<sup>15</sup>, prevention of bed-related complications, such as pressure ulcers, physical deconditioning, improved cough efficiency and pulmonary toilet, and patient mood.

Indeed, ICU patients inevitably develop severe muscle weakness over time due to muscle wasting secondary to the hypercatabolic state, sedation and immobility.<sup>16</sup> The vicious cycle is fuelled by decreased functional capacity, delayed recovery, myopathy onset, failed weaning from mechanical ventilation and increased length of ICU stay.<sup>17</sup>

Mobilization should be considered as a spectrum of physical therapies, active or passive, with various degrees of autonomy and caregiver assistance.

In this paragraph, the term 'mobilization' refers essentially to transfer activity, including from lying to sitting at the edge of the bed, from bed to chair sitting physical tolerance, from sitting to standing and walking away from the bed or chair, on each foot and with various degrees of assistance.<sup>18</sup>

Mobilization of patients under percutaneous MCS challenges clinicians, who, in addition to the traditional risks, must face the risk of pump dislodgement or malfunctioning in patients often totally dependent on extracorporeal flow. There are no studies specifically addressing the issue of mobilization of Impella patients, but many interesting insights can be drawn from the analysis of many published experiences. A recent study held out the prospect of a survival advantage in patients achieving the maximum mobility score during Impella 5.0 support, raising interest for further studies.<sup>19</sup>

New integrated approaches for patients suffering from CS have been recently described, in which a de-escalation strategy from veno-arterial extracorporeal life support to

Impella 5.0 was applied, allowing patients to be awake, weaned from mechanical ventilation, ambulating and orally fed.<sup>20</sup>

From a practical point of view, there are some prerequisites for safe mobilization: the patient must be cooperative, spontaneously breathing with or without oxygen supplementation, under conditions of haemodynamic stability, and without the need for inotrope/vasopressor escalation; additionally, the flow delivered by the pump must be stable, and the volume status should be optimized. The team responsible for the procedure will inform the patient about all the planned steps. The axillary access of the device and its safe fixation should be checked, and a well-trained team of physicians, nurses, and physical therapists should carry out the procedure.

This category of patients is frequently under invasive monitoring. Mobilization should always be performed at least under electrocardiographic, invasive blood pressure monitoring and peripheral oxygen saturation monitoring. The pump console will provide the usual device-related parameters. The risk of intravenous line dislodgment can be reduced by limiting the number of active infusion pumps to inotropes/vasopressors and anticoagulant drugs.

Rather than a predefined duration or distance, first sessions are useful for assessing the feasibility and the patient's tolerance. Tachycardia, dyspnoea, fatigue, haemodynamic changes, or pump alarms require the session to be ended. Over time, mobilization can translate into a stress test, which is able to directly evaluate the clinical and haemodynamic responses to physical activation, providing additional information about the possibility of weaning the patient from the device.

Mobilization and ambulation of Impella patients is not without risks: to the best of our knowledge, no catastrophic complications such as pump dislodgement or death have been described. However, the risks of pump dislodgement, malposition and malfunction induced by mobilization should be kept in mind. These risks are additive to intravenous line dislodgement, patient falls, and trauma.

In conclusion, mobilization of Impella patients by an expert team with precise planning can lead to many advantages, preventing patients from bed-related complications; however, the impact can also be strongly negative, especially in patients requiring long-term support as a bridge to candidacy, to durable supports or to heart transplantation.

## Conclusions

Weaning of patients from Impella is complex and includes evaluation of the underlying disease, which is essential for estimating the potential for heart recovery. Monitoring during the weaning phase with echocardiography and PACs is strongly advised. Patients who are candidates for weaning must be stable, without inotropes, and must have recovered from acute end-organ damage. Gradual introduction of oral HF medications (except for beta-blockers) should be considered in Impella-supported patients with persistent LV dysfunction after haemodynamic stabilization. Coronary artery disease and valvular heart diseases

should be appropriately addressed before weaning. Mobilization of axillary Impella patients is safe and beneficial if managed by a well-trained team of physicians, nurses, and physical therapists.

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