Left Ventricular Assist Devices and Their Role in Cardiogenic Shock: Literature Review and Contemporary Data

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Abstract

Despite tremendous progress in the therapeutic algorithms of hemodynamically unstable patients, cardiogenic shock remains a clinical challenge with high mortality rate. Conservative management with inotropic agents remains the first-choice treatment, though it has been associated with serious adverse events and is not always adequate. Circulatory support with mechanical devices has been widely implemented in patients with cardiogenic shock during high-risk percutaneous coronary interventions or post-cardiac surgery complications and has been associated with favorable outcomes. In patients with acute decompensated heart failure, ventricular assist devices have been used to prolong the recovery period and reverse the cause of hemodynamic instability. In the present review, we discuss the current evidence on the use of percutaneous assist devices for the treatment of cardiogenic shock, plus we highlight the need for future evolution in this particular field that may permit the optimal choice of each device for different patients or clinical situations.

Keywords

Percutaneous circulatory support, Cardiogenic shock, Acute coronary syndrome, Left ventricular assist device, iVAC, Impella, ECMO

Abbreviations

CS: Cardiogenic Shock; MODS: Multiple Organ Dysfunction Syndrome; CAD: Coronary Artery Disease; AMI: Acute Myocardial Infarction; MCS: Mechanical Circulatory Support; PCI: Percutaneous Coronary Intervention; LV: Left Ventricle; RV: Right Ventricle; LVAD: Left Ventricular Assist Device; ECMO: Extracorporeal Membrane Oxygenation; VA: Venous - Arterial; IABP: Intra-Aortic Balloon Pump; ACS: Acute Coronary Syndrome

Introduction

Cardiogenic shock (CS) comprises a complex, critical clinical entity characterized by a dramatic decrease in cardiac output, resulting in peripheral tissue and end-organ hypoperfusion and subsequent multiple organ dysfunction syndrome (MODS) [1]. Widely accepted as a medical emergency, CS has garnered attention due to its markedly high mortality, which still exceeds 40%, despite progress in diagnostic and therapeutic algorithms [2].

In the 2016 European Society of Cardiology (ESC) guidelines on acute heart failure, CS is defined as a state of persistent hypotension (systolic blood pressure < 90 mmHg) despite adequate fluid replacement, with concomitant signs of hypoperfusion [3]. Other CS definitions have also been proposed in the literature, such as in the IABP-SHOCK II trial, where clinical signs of impaired end-organ perfusion, such as alterations of mental status and cold extremities, plus low urine output and high lactate concentration were taken under consideration for the establishment of the diagnosis [4]. Recently, in an attempt to classify CS with an eye towards the better understanding and establishing of more efficient therapeutic algorithms, the Society for Cardiovascular Angiography and Interventions proposed a simple, easy-to-use classification of CS, dividing patients into five distinct stages (A to E), intending to refine communication between clinicians and to categorize CS cases in order to provide the optimum treat-
The vast improvement in healthcare service quality through the past decades has led to significant demographic ageing of the developed countries, while coronary artery disease (CAD) still remains a major health burden with high death rates [6]. Acute myocardial infarction (AMI) belongs among the leading causes of CS, raising in-hospital mortality and healthcare costs [7]. Even so, one could highlight a variety of potential CS causes, namely acute decompensated heart failure, valvular and pericardial diseases, arrhythmias and toxicity [2].

CS has been an item of interest in international guidelines of clinical practice and published scientific statements [8]. Nevertheless, all available data point towards a particularly vague perception of CS as a clinical entity, while its recognition and its optimal therapeutic algorithm remain controversial; hence, one could highlight a plethora of inconsistencies between ESC and American Heart Association (AHA)/American College of Cardiology (ACC) guideline recommendations [1,3,9]. Those differences comprise the debate on the routine use of pulmonary artery catheter in CS for diagnosis and management and the use of inotropes as first-line vasoactive agents [9]. Notwithstanding, both guidelines agree on the application of mechanical circulatory support (MCS) when pharmacological therapy fails, despite the lack of strong clinical evidence on survival improvement [9].

The present review describes the use of MCS devices in the treatment of CS and summarizes all published cases of patients with hemodynamic instability undergoing high-risk percutaneous coronary interventions (PCI) or cardiac surgery who were managed with the aid of iVAC2L device.

Mechanical Circulatory Support Devices

Percutaneously inserted MCS devices are designed to support the left ventricular dysfunction by reducing the pressures and volumes of the left ventricle (LV) as well as increasing end-organ perfusion and coronary blood flow in hemodynamically unstable patients [10,11]. The technical features of different types of percutaneous assist devices are presented in Table 1. The majority of these devices can be inserted percutaneously via the femoral or the axillary artery and aspirate blood from the LV to the ascending aorta, decrease LV preload and succeed the LV support. The devices with greater blood flow, as the IVC3L and the Impella 5.0 L are inserted with surgical preparation of the vascular site. While only the Impella RP and extracorporeal membrane oxygenation (ECMO) can support the right ventricular dysfunction according to the manufacturer, there are reports of other devices which have been used for the unloading of the right ventricle (RV) [12].

Extracorporeal membrane oxygenation (ECMO)

ECMO was the first device able to provide circulatory and simultaneous respiratory support, counting over seven decades of implementation. An ECMO device nowadays consists of the oxygenator, a gas exchange component, the inflow and outflow tubing, the pump and the hand crank. The closed ECMO circuit withdraws percutaneously via the femoral vein the deoxygenated blood from the right atrium or a central vein and returns the oxygenated blood via a second cannula to the arterial or venous system. More specifically, venous-arterial (VA) ECMO system reinfuses the fully saturated and decarboxylated blood to the iliac artery via the femoral artery. The cannulation of the femoral artery is demanding and needs careful, accurate manipulations in order to avoid limb ischemia [13]. An extra condition to be considered is the watershed phenomenon. The antegrade blood flow from the heart competes with the retrograde oxygenated blood flow from the cannula of the iliac artery of the ECMO. When the watershed phenomenon is formed low in thoracic aorta, the retrograde oxygenated blood from the ECMO does not contribute to the coronary and cerebral blood perfusion.

Over the last decades, a significantly increasing tendency in the use of ECMO has been observed. This might be a result of the easy way of implantation of the ECMO system, even at the bedside, and the ability of concurrent transportation of the supported patient to an advanced medical care unit.

Cardiopulmonary failure after cardiothoracic surgery, referred as post-cardiotomy CS, remains the most prominent indication of use of the ECMO system [14]. Although the benefit of ECMO implementation remains controversial in AMI-induced CS [15], it has been proven in refractory CS as a valuable temporary solution [16]. ECMO could be additionally employed as a bridge to lung transplantation in lung disease [17], and as a bridge to heart transplantation in fulminant myocarditis [18]. Another variant, the Veno-Venous ECMO is used in severe respiratory failure-like conditions [19,20]. Towards this direction, similarly demanding cases consist of patients in ECMO with shock, pulmonary edema and LV failure who need LV decompression. In order to reduce the effect of the watershed form, avoid coronary and cerebral hypoperfusion and increase cardiac output, a combination of ECMO and iVAC2L might be very profitable [21,22].

Impella

The Impella series are percutaneously catheter-based mechanical circulatory assist devices that can provide up to 6 L cardiac output and decrease LV preload. The Impella device is inserted in a peripheral artery, femoral or axillary, and is placed across the aortic valve in the LV. There are various types of Impella devices, depending on the provided stroke volume (Table 1). Impella RP is indicated in right ventricular failure after left ventricular assist device (LVAD) implantation, AMI, or acute pulmo-
### Table 1: Technical and clinical data of percutaneous mechanical circulatory support devices used for the treatment of cardiogenic shock.

<table>
<thead>
<tr>
<th>Device</th>
<th>Catheter Size (F)</th>
<th>Cannula Size (F)</th>
<th>Maximum Flow (L/min)</th>
<th>Pump Mechanism</th>
<th>Blood is aspirated from</th>
<th>Blood is ejected in</th>
<th>Access Site</th>
<th>Implantation</th>
<th>LV Support</th>
<th>Indications</th>
<th>Maximal duration of application</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>iVAC® 2.0 L</td>
<td>11</td>
<td>17</td>
<td>2.0</td>
<td>Pulsatile Flow - depend on HR</td>
<td>Left Ventricle</td>
<td>Femoral Artery</td>
<td>Percutaneous</td>
<td>+</td>
<td>High-risk PCI</td>
<td>Acute Myocardial Infarction</td>
<td>Up to 24 hours</td>
<td>++</td>
</tr>
<tr>
<td>Impella® 2.5 L</td>
<td>12</td>
<td>21</td>
<td>2.5</td>
<td>Axial flow - continuous pump</td>
<td>Left Ventricle</td>
<td>Femoral Artery</td>
<td>Percutaneous</td>
<td>+</td>
<td>Advanced HF</td>
<td>Cardiogenic shock</td>
<td>Up to 4 days</td>
<td>+++</td>
</tr>
<tr>
<td>Impella® 5.0 L</td>
<td>9</td>
<td>19</td>
<td>5.0</td>
<td>Axial flow - continuous pump</td>
<td>Left Ventricle</td>
<td>Femoral Artery</td>
<td>Percutaneous</td>
<td>+</td>
<td>Postcardiotomy</td>
<td>Cardiogenic shock</td>
<td>Up to 4 days</td>
<td>+++</td>
</tr>
<tr>
<td>Impella® 5.5 L</td>
<td>9</td>
<td>19</td>
<td>6.0</td>
<td>Axial flow - continuous pump</td>
<td>Left Ventricle</td>
<td>Femoral Artery</td>
<td>Percutaneous</td>
<td>+</td>
<td>Postcardiotomy</td>
<td>Cardiogenic shock</td>
<td>Up to 4 days</td>
<td>+++</td>
</tr>
<tr>
<td>Impella® CP</td>
<td>9</td>
<td>14</td>
<td>4.3</td>
<td>Axial flow - continuous pump</td>
<td>Right Atrium</td>
<td>Aorta</td>
<td>Percutaneous</td>
<td>+</td>
<td>Cardiogenic shock</td>
<td>High-risk PCI</td>
<td>Up to 4 days</td>
<td>+++</td>
</tr>
<tr>
<td>V-A ECMO</td>
<td>9</td>
<td>14</td>
<td>7.0</td>
<td>Centrifugal flow - continuous pump</td>
<td>Right Atrium</td>
<td>Aorta</td>
<td>Percutaneous</td>
<td>+</td>
<td>Cardiogenic shock</td>
<td>High-risk PCI</td>
<td>Up to 14 days</td>
<td>+++</td>
</tr>
</tbody>
</table>

F: French; LV: Left Ventricle; L: Liter; Min: Minutes; HR: Heart Rate; HF: Heart Failure; PCI: Percutaneous Coronary Intervention; EF: Ejection Fraction; CI: Cardiac Index.
nary embolism [23-35]. In patients with end-stage heart failure or in severe cases of myocarditis, Impella seems to be highly effective as a bridge both to recovery or to a final treatment, such as transplantation or surgical heart pump implantation [26,27]. Furthermore, Impella seems to be capable of aiding the stabilization of patients with aortic valve stenosis undergoing transcatheter aortic valve implantation [28].

Several published studies demonstrated the significant circulatory support and anti-ischemic myocardial protection that Impella could provide in the context of high-risk PCI [29-32]. Recent studies suggest the use of Impella devices in patients with CS or cardiac arrest caused by AMI in order to improve outcomes [33,34]. The early implantation of Impella prior to PCI is associated with prolonged survival and higher rates of successful revascularization [35]. In addition, no difference in 30 days mortality between Impella and ECMO was observed in patients with CS after AMI [36]. Nevertheless, the role of Impella in AMI-induced CS still remains a controversial issue, as highlighted in a recently published metaanalysis [37]; at the same time, another recent study suggested high mortality rates despite the use of Impella [38]. Well-organized, prospective, multicenter ongoing trials will shed light on this lack of data [39].

iVAC2L

The PulseCath iVAC2L (PulseCath BV, Amsterdam, Netherlands) is a novel pulsatile circulatory support system that accepts blood from the LV and ejects it in the ascending aorta. The device consists of a flow catheter with an extracorporeal pneumatic dual chamber and a patented rotating two-way valve [40]. The extracorporeal membrane pump is connected to a mainstream IABP console, acting as a pneumatic driver of the pump and generate up to 2.0 L/min output. The pulsatile mechanism of action is in synchrony with the cardiac cycle and aspirates blood from the LV simultaneously with the cardiac systole. At higher heart rate, the output will be decreased since the short-time of diastolic phase will not offer sufficient time for the ejection [40]. The main indication is CS due to AMI, while it has also been used in patients with post-cardiac surgery or viral infection-induced CS and for prevention of hemodynamic instability during high-risk PCI [41-43]. The device has been designed for the temporary support of the LV after percutaneous insertion through the femoral artery, while the support of RV after insertion through the pulmonary artery trunk during cardiac surgery has also been described [12].

Through a systematic search of the existing literature, several studies and case reports implying the iVAC device support were identified (Table 2) [12,21,22,23-48], while indications of use, type of vascular access, pre- and post-implantation hemodynamical parameters, as well as potential complications of the implantation, are presented in Table 1.

Discussion

In the last decades, technological evolution has enabled mechanical LV assist devices to play a major role in the treatment of CS and in the hemodynamic support during high-risk PCI procedures. Moreover, they seem to prevent circulatory collapse and provide the necessary time for the patient to overcome a potentially reversible condition. As previously described, percutaneously inserted assist devices for LV dysfunction have been additionally used for the support of RV in patients with post-cardiac surgery CS which were treated with IABP [12]. The insertion technique’s adequacy through the right cavities and the efficacy of these devices are still under debate, nevertheless, the patient would probably meet a significant benefit, potentially leading to a complete recovery. The simultaneous use of LVAD with VA ECMO has also been endorsed by a newly published case supporting the concept of potential future applications of dual assist devices. The EC-iVAC (simultaneous use of ECMO and iVAC) and ECMELLA (ECMO and Impella) approaches may be considered as an option among patients in CS in urgent need of immediate LV support [21,22]. Moreover, a recently published international multicenter cohort study evaluated the clinical outcomes in patients with CS treated with VA ECMO with or without LV unloading with the use of Impella showed that the mechanical LV support was associated with lower mortality [49].

Implantation timing

In all instances, there is general agreement that a patient in CS requires early recognition, resuscitation and stabilization; attentive monitoring is crucial, whilst fluid challenge and adequate pharmacologic support with vasopressors and inotropic agents are considered as first-line therapeutic options. In addition, MCS may be needed in order to maintain systemic perfusion, stabilize hemodynamic status and act as a bridge to further therapeutic actions [3,50,51]. Nevertheless, the correct timing of implementing MCS in CS patients still remains controversial [52]. The development and validation of a novel algorithm predicting the progression of CS as well as guiding the physician towards the optimal implantation of a MCS device is of paramount importance. The hemodynamical support at the early-stage of the CS is proven to hold a significant benefit for the patient and seem to offer a major time extension with an eye towards recovery [53].

Insertion and accurate placement in the LV

The different technical features of the various MCS device may constitute an obstacle in the selection of the assist device, since the size of the sheath and the diameter of the femoral or axillary artery could determine the incision site as well as the type of the device that
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>#N, pts</th>
<th>Age (years)</th>
<th>Device</th>
<th>Access</th>
<th>Indication</th>
<th>Pre-IVAC</th>
<th>Post-IVAC</th>
<th>Complications*</th>
<th>Vascular-site complications**</th>
<th>Survival n/NMAP (mmHg)</th>
<th>PCWP (mmHg)</th>
<th>CI (L/min/m²)</th>
<th>MAP (mmHg)</th>
<th>PCWP (mmHg)</th>
<th>CI</th>
<th>MAP (mmHg)</th>
<th>PCWP (mmHg)</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tschope, 2020 [22]</td>
<td>1</td>
<td>49</td>
<td>iVAC2L &amp; VA ECMO</td>
<td>Femoral Artery</td>
<td>CS</td>
<td>45</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>2.88 (CO)</td>
<td>75</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>0/1</td>
<td></td>
</tr>
<tr>
<td>Tzikas, 2020 [43]</td>
<td>1</td>
<td>46</td>
<td>iVAC2L</td>
<td>Femoral Artery</td>
<td>CS</td>
<td>19</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>1.27 (CO)</td>
<td>2.5</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>11/11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Samol, 2019 [42,44]</td>
<td>17</td>
<td>72 ± 9</td>
<td>iVAC2L</td>
<td>Femoral Artery</td>
<td>High-risk PCI</td>
<td>Femoral Artery</td>
<td>81 ± 17</td>
<td>N/A</td>
<td>N/A</td>
<td>1.29 (CO)</td>
<td>3.3 (CO)</td>
<td>2</td>
<td>No</td>
<td>No</td>
<td>0/1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Bastos, 2018 [45]</td>
<td>1</td>
<td>70</td>
<td>iVAC2L</td>
<td>Femoral Artery</td>
<td>High-risk PCI</td>
<td>Femoral Artery</td>
<td>45</td>
<td>N/A</td>
<td>N/A</td>
<td>2.88 (CO)</td>
<td>75</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td>Den Uil, 2017 [46]</td>
<td>14</td>
<td>72 ± 8</td>
<td>iVAC2L</td>
<td>Pulmonary Artery</td>
<td>High-risk PCI</td>
<td>Pulmonary Artery</td>
<td>66.5 ± 87.7</td>
<td>12.1 ± 6.4</td>
<td>22 ± 0.7</td>
<td>94.9 ± 9</td>
<td>11.2 ± 8.7</td>
<td>3 ± 4</td>
<td>2.8 ± 0.8</td>
<td>No</td>
<td>No</td>
<td>13/13</td>
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</tr>
<tr>
<td>Arrigoni, 2011 [12]</td>
<td>1</td>
<td>76</td>
<td>iVAC3L</td>
<td>Pulmonary Artery</td>
<td>High-risk PCI</td>
<td>Pulmonary Artery</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
<td>2.88 (CO)</td>
<td>75</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td>Anastasiadis, 2011 [21]</td>
<td>1</td>
<td>76</td>
<td>iVAC3L</td>
<td>Pulmonary Artery</td>
<td>High-risk PCI</td>
<td>Pulmonary Artery</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
<td>2.88 (CO)</td>
<td>75</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td>Amico, 2008 [47]</td>
<td>1</td>
<td>69 ± 7</td>
<td>iVAC3L</td>
<td>Pulmonary Artery</td>
<td>High-risk PCI</td>
<td>Pulmonary Artery</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
<td>2.88 (CO)</td>
<td>75</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td>Marianni, 2007 [48]</td>
<td>14</td>
<td>33</td>
<td>iVAC3L</td>
<td>Pulmonary Artery</td>
<td>High-risk PCI</td>
<td>Pulmonary Artery</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
<td>2.88 (CO)</td>
<td>75</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>1/1</td>
<td></td>
</tr>
</tbody>
</table>

N: Number; pts: patients; N/A: not available; MAP: Mean Arterial Pressure; PCWP: Pulmonary Capillary Wedge Pressure; CI: Cardiac Index; CO: Cardiac Output; CS: Cardiac Support; PCI: Percutaneous Coronary Intervention; LV: Left Ventriole; RV: Right Ventriole; CABG: Coronary Artery Bypass Graft; VAECMO: Venous - Arterial Extracorporeal Membrane Oxygenation; IABP: Intra-Aortic Balloon Pump.

*: any adverse event (acute kidney injury, stroke and transient ischemic attack)

**: vascular bleeding, puncture site infection or swelling

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**Table 2: Current experience with iVAC2L device.**
will be used. As presented in Table 1, the need of a larger sheath is mainly associated with the maximal output of each device, as larger devices demand wider sheath. Notwithstanding, the Impella CP is the only device with maximal blood flow greater than 4.0 L/min with a cannula size of 14 French which can be implanted for up to 4 days in patients with CS or for the prevention of hemodynamic instability during high-risk PCI procedures. The right placement of the device is crucial in order to properly aspirate blood from the LV and eject it over the aortic valve. The placement position of the device should be confirmed with the use of the transesophageal echocardiography or with aortography. The Impella system features a pig-tail loop in the top of the device rendering the implantation inside the LV easier. In the published literature, various methods for the right placement have been described, such as the insertion of a pigtail catheter over the aortic valve and subsequent aortography assessment in order properly place the two-way valve (outlet) over the aortic valve [44,54,55].

Complications of use and removal of the device

The disadvantage of axial flow Impella devices in contrast to the pulsatile iVAC, is that they have been associated with a significantly higher risk of hemolysis (10% of patients during first 24 hours) due to the high rotational speed of the axial flow pump [56-60]. Hemolysis has also been linked with worse prognosis in patients with acute coronary syndrome [61-63]. Tschope, et al. reported a case of significant hemolysis after the simultaneous use of VA ECMO and Impella devices, while the substitution of Impella with iVAC supported the hemodynamic status of the patient efficiently and resulted in a slighter hemolytic effect [22].

Furthermore, additional disadvantages of the percutaneous assist devices are the controversial selection of the most appropriate site for vascular catheter insertion, as well as the complications during the process or after the removal of the sheath. This depends on the size of the device, the diameter of the vessel, as well as the medical history of the patient. Moreover, the removal of the cannula is of paramount importance and should be performed by a trained physician as it might be accompanied by major complications. The most usual complications during the removal of the device are bleeding and arterial perforation which will need surgical reconstruction. Novel vascular closure devices for large-bore femoral arterial puncture have also been developed in the last years and can be valuable in order to provide safe hemostasis. In a recent meta-analysis, the use of these closure devices was associated with a significantly lower incidence of groin hematomas or pseudoaneurysms, as well as with impaired hemostasis time when compared to extrinsic compression [64].

All in all, there is lack of clinical studies that directly compare percutaneous assist devices. Further research ought to berendered in order to cover the gaps in evidence, provide guidance on device selection and way of implantation, depending on the hemodynamic status and individual history of each patient.

Conflict of Interest

Nothing to declare.

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