Percutaneous mechanical circulatory support for treatment and prevention of hemodynamic instability
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CHAPTER 6.1

Mechanical circulatory support with the Impella 5.0 device for postcardiotomy cardiogenic shock: a three-center experience

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Submitted
ABSTRACT

Background
Postcardiotomy cardiogenic shock (PCCS) is associated with high mortality rates, despite full conventional treatment. Although the results of treatment with surgically implantable ventricular assist devices have been encouraging, the invasiveness of this treatment limits its applicability. Several less invasive devices have been developed, including the Impella system. The objective of this study was to describe our three-center experience with the Impella 5.0 device in the setting of PCCS.

Methods
From January 2004 through December 2010, a total of 46 patients were diagnosed with treatment-refractory PCCS and treated with the Impella 5.0 percutaneous left ventricular assist device at three European heart centers. Baseline and follow-up characteristics were collected retrospectively and entered into a dedicated database.

Results
Within the study cohort of 46 patients, mean logistic and additive EuroSCORES were 24±19 and 10±4. The majority of patients underwent coronary artery bypass grafting (48%) or combined surgery (33%). Half of all patients had been treated with an intra-aortic balloon pump before 5.0-implantation, 1 patient had been treated with an Impella 2.5 device. All patients were on mechanical ventilation and intravenous inotropes. The Kaplan-Meier estimate of overall 30-day survival was 39.5%.

Conclusions
Thirty-day survival rates for patients with PCCS, refractory to aggressive conventional treatment and treated with the Impella 5.0 device, are comparable to those reported in studies evaluating surgically implantable VADs, whereas the Impella system is much less invasive. Therefore, mechanical circulatory support with the Impella 5.0 device is a suitable treatment modality for patients with severe PCCS.
INTRODUCTION

Post-cardiotomy cardiogenic shock (PCCS) is a rare complication of cardiac surgery. Previous reports have suggested its prevalence to range from a historical 4-7% to 0.2-0.5% in more recent reports. Despite its low prevalence, PCCS is associated with high mortality rates, and it therefore represents an important therapeutic challenge. Besides optimal pharmacological treatment, intra-aortic balloon pump (IABP) placement and mechanical ventilation, more advanced mechanical circulatory support has been an important therapeutic modality for patients suffering from PCCS. A wide range of mechanical circulatory support systems have been applied in this setting, including surgically implantable ventricular assist devices (VADs) and extracorporeal membrane oxygenation systems. Although mortality rates vary amongst different reports, no advantage for a specific device has become clear from the currently available literature. Therefore, device choice largely depends on hospital-and patient-based characteristics. As the availability of large surgical VADs is limited, less invasive devices may play an important role in the field as well. Recently, several minimally invasive devices have been developed, including the Impella system (Abiomed Europe GmbH). The Impella pump is a microaxial catheter-mounted continuous-flow pump, which is usually inserted through the femoral artery and placed across the aortic valve with its inlet located in the left ventricle and its outlet just above the aortic valve. Two versions of this pump system have been developed, the first of which is the Impella 2.5 pump, which delivers a maximum flow of 2.5 liters per minute and which is inserted percutaneously. The other, larger pump is the Impella 5.0, which provides a maximum support level of 5 liters per minute but requires surgical cut-down of the femoral or axillary artery. The three centers participating in this registry have had a large experience with Impella treatment, which has become a part of routine care, especially in patients presenting with cardiogenic shock of various etiologies. As to date, only small reports have been published on Impella-support in PCCS, we aimed to describe our three-center experience in this setting.

PATIENTS AND METHODS

Patient population and data collection

The study population consisted of all consecutive patients who received the Impella 5.0 device between January 2004 and December 2010 for a PCCS indication at the Academic Medical Center in Amsterdam, the Netherlands, the Linköping University Hospital in Linköping Sweden and and the Westpfalz-Klinikum in Kaiserslautern, Germany. The total cohort consisted of 46 patients and included patients who underwent cardiac
surgery for various indications. Data on previous medical history, the presence of risk factors, hemodynamic status, laboratory measurements, inotropic therapy and duration of pump support were obtained through a validated ICU patient data management system (MetaVision®; iMDsoft, Massachusetts, USA) at the Academic Medical Center and through thorough chart review at the other 2 centers. For in-hospital deaths, information on date of death and death etiology were obtained through chart review in all three centers. For survivors, vital status was verified through the review of outpatient reports. In case of missing data, general practitioners or treating cardiologists were contacted by telephone.

Definitions

PCCS was defined as either the inability to wean successfully off cardiopulmonary bypass or a marginal hemodynamic condition in the early postoperative phase, within the first 24 hours after weaning from cardiopulmonary bypass. Treatment-refractory PCCS was defined as persistence of shock despite aggressive conventional treatment. Conventional treatment was at the discretion of the treating physician and included mechanical ventilation, IABP support, Impella 2.5 support and intravenous inotropes.

Treatment

The decision for implantation of an Impella 5.0 device was made upon the diagnosis of treatment-refractory PCCS. Impella 5.0-implantation was performed as soon as possible after the diagnosis of treatment-refractory PCCS. Further treatment according to routine care was at the discretion of the treating ICU-physician and included, mechanical ventilation, renal replacement therapy and intravenous inotropes and vasopressors and continued IABP support in some cases.

Impella system

The Impella system (Abiomed Europe GmbH, Aachen, Germany) has been described previously. It is a catheter (9 Fr) mounted micro-axial rotary blood pump, designed for short-term mechanical circulatory support, which is inserted through the femoral artery and positioned across the aortic valve into the left ventricle preferably using fluoroscopy. The driving console of the pump allows management of pump speed (by 9 gradations) and displays the pressure difference between inflow and outflow, which gives an indication for pump position. Two versions of this system are currently available, the Impella 2.5 and the Impella 5.0. The 21-Fr Impella 5.0 device provides a maximum flow of 5.0 L/min, which is twice the amount of flow generated by the 2.5-device. Considering its large diameter, the Impella 5.0 is inserted through a Dacron graft which is sewed onto the femoral artery or right axillary or subclavian arteries. The axillary/
subclavian approach may be more compelling implantation strategy in case of severe peripheral vascular disease or for early patient mobilization and rehabilitation\cite{8,12}.

**Statistical analysis**

Data were analyzed using the statistical Package for the Social Sciences (SPSS inc., Chicago, IL, USA; version 16.0.2). Continuous data are presented as mean +/- standard deviation (SD) (median and interquartile range for skewed variables). Categorical data are presented as percentages. A Kaplan-Meier curve was constructed for 30-day survival.

**RESULTS**

**Patients**

The study cohort consisted of 46 patients who were treated with an Impella 5.0 device for treatment-refractory PCCS. Baseline and treatment characteristics are detailed in Table 1. Mean age was 61 ± 13 years, and the majority of patients were male (85%). Mean logistic and additive Euroscores were 24 ± 19 and 10 ± 4, respectively (n=28). Almost half of all patients had undergone CABG-surgery, 6 of whom underwent CABG for acute myocardial infarction.

One-third of patients had undergone a combined surgical procedure. Half of all patients had received treatment with an IABP before Impella 5.0 implantation, whereas all patients were on mechanical ventilation and intravenous inotropes. In the majority of cases, Impella 5.0 implantation occurred perioperatively. One patient had been

**Figure 1** Thirty-day survival in patients who received Impella 5.0 support for treatment-refractory postcardiotomy cardiogenic shock
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Table 1 Baseline characteristics of patients with Impella 5.0 support for treatment-refractory postcardiotomy cardiogenic shock

<table>
<thead>
<tr>
<th>Variables</th>
<th>N=46</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>61 ± 13</td>
</tr>
<tr>
<td>Male (%)</td>
<td>39 (84.8)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>30 (65.2)</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>19 (41.3)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>19 (41.3)</td>
</tr>
<tr>
<td>Known family history of CAD* (%)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>Known previous myocardial infarctions (%)</td>
<td>25 (54.3)</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>26 (56.5)</td>
</tr>
<tr>
<td>Logistic Euroscore** (mean ± SD)</td>
<td>24 ± 19</td>
</tr>
<tr>
<td>Additive Euroscore** (mean ± SD)</td>
<td>10 ± 4</td>
</tr>
<tr>
<td>Surgery type</td>
<td></td>
</tr>
<tr>
<td>CABG (%)</td>
<td>22 (47.8)</td>
</tr>
<tr>
<td>Valve (%)</td>
<td>7 (15.2)</td>
</tr>
<tr>
<td>Combined (%)</td>
<td>15 (32.6)</td>
</tr>
<tr>
<td>Other (%)</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>Mechanical circulatory support</td>
<td></td>
</tr>
<tr>
<td>Impella support (hours), median, IQR</td>
<td>74 (25 – 120)</td>
</tr>
<tr>
<td>Impella implantation*</td>
<td></td>
</tr>
<tr>
<td>Perioperatively</td>
<td>31 (81.6)</td>
</tr>
<tr>
<td>Within 6 hours postoperatively</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>Between 6-24 hours postoperatively</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>After 48 hours postoperatively</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>Impella 2.5 support before Impella 5.0 implantation</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>IABP support before Impella implantation</td>
<td>25 (54.3)</td>
</tr>
</tbody>
</table>

*n=25; **n=28; ***n=38; SD denotes standard deviation; IQR denotes interquartile range; CAD denotes coronary artery disease; CABG denotes coronary artery bypass grafting; IABP denotes intra-aortic balloon pump

supported with an Impella 2.5 device before Impella 5.0-implantation. Median duration of Impella support was 74 hours, with an IQR of 24 – 120 hours. The Kaplan-Meier estimate for thirty-day survival was 39.5% (Figure 1).

DISCUSSION

This study is the largest to date to report on Impella 5.0 treatment for treatment-refractory PCCS. Our main finding is that mechanical circulatory support for treatment-refractory PCCS with the Impella 5.0 is a feasible treatment option, with 30-day survival rates of 39.5%.
PCCS and mechanical circulatory support

Mechanical circulatory support has played an important role in the treatment of PCCS. The standard treatment strategy when a patient is diagnosed with PCCS consists of inotropic therapy, afterload reduction and IABP placement, which has been suggested to be beneficial\textsuperscript{13,14}. However, as an adequate working of the IABP depends on the residual cardiac pump function, as well as a stable heart rhythm, PCCS may persist despite IABP treatment.

Ventricular assist devices for PCCS

For PCCS, a wide range of surgically implantable VADs have been investigated. In a review by Goldstein and Oz, published in 2000, 8 studies evaluating the outcomes of VAD treatment in PCCS were outlined\textsuperscript{15}. Overall, 25% of patients survived through discharge, regardless of the device that was applied. More recently, several other studies have been conducted, in which more favorable mortality rates were observed. In 2009, Xiao et al reported on a series of 17 patients treated with the Luo-Ye VAD in China\textsuperscript{16}. Weaning rate was 47.1%, and 41.2% of patients survived through hospital discharge. In another study, by Hoy et al, 62 patients with PCCS were supported with a centrifugal VAD\textsuperscript{17}. Weaning rate in this study was 68%, whereas 44% of patients survived through discharge. Potapov et al described the experience with over 1000 ventricular assist devices\textsuperscript{18}; in 173 patients, a VAD was implanted for PCCS. Early mortality was 50.9% in those patients. A report from Hernandez et al from the Society of Thoracic Surgeons’ national database describes the outcome of postcardiotomy VAD placement from 1995 to 2004\textsuperscript{5}. A total of 5735 patients had a VAD placed after cardiac surgery; overall survival to discharge was 54.1% in this large study. Importantly, in this study, survival rates improved significantly over time. Another small report from Curtis et al, in 21 patients undergoing VAD implantation for PCCS, showed a 52.4% discharge rate\textsuperscript{19}. Although in general, results from VAD implantation seem relatively favorable, the applicability of such a treatment is limited by the complex and high-risk implantation procedures in the setting of PCCS. Furthermore, bleeding rates are high and the availability and cost of such devices may be a problem, as well as the availability of an experienced team to perform the implantation procedure. Therefore, the role of less invasive modalities for mechanical circulatory support has become more and more pronounced.

Extracorporeal membrane oxygenation (ECMO)

A large amount of research has been conducted with regard to ECMO support in PCCS, both in the setting of general cardiac surgery and in the setting of cardiac transplant. A recent report by Rastan et al describes treatment with ECMO for 517 patients with PCCS\textsuperscript{7}. Although 63% of patients could be weaned from the ECMO, only 25% could
be discharged. Complications included leg ischemia (5.4%), major bleeding (mean transfusion rate of 13 units per patient during the first 48 hours) and cerebrovascular events (17.4%). However, long-term outcome for in hospital survivors (25% of overall study population) was favourable, with an additional mortality at 7% and 8% at 6 months and 1 year, respectively. Another recent paper by Beiras-Fernandez et al on ECMO support for refractory PCCS in 108 patients, including 73 adults and 35 children, showed an overall 30-day survival of 40.2%. Causes of death included multi-organ failure (40.6%), bleeding (23.2%), persistent low cardiac output (21.7%) and thromboembolic events (8.7%)\textsuperscript{20}. Wu et al also investigated the use of ECMO for severe treatment-refractory PCCS, in a retrospective analysis of 110 adult patients. In-hospital survival was 41.8%. Age >60 years, the need for prolonged ECMO support, the need for dialysis and a high bilirubin level were identified as independent predictors for mortality\textsuperscript{21}. In another large retrospective study by Elsharkawy et al, of all patients requiring ECMO after cardiac surgery from 1995 through 2005 (n=233), overall in-hospital survival was 36%\textsuperscript{22}. Liden et al investigated ECMO support in cardiogenic shock, including PCCS and other etiologies\textsuperscript{23}. Thirty-three patients suffered from PCCS; early survival in the PCCS group was 45%, as opposed to 63% in the non-postcardiotomy group. Another small study by Wang et al which included 62 patients who received ECMO for PCCS, in-hospital survival was 54.8%, after a mean duration of hospital stay of 44 ± 18 days\textsuperscript{24}. In a report by Doll et al, which included 219 patients with ECMO for PCCS, 60% of patients could be weaned from ECMO support, whereas 24% survived through discharge\textsuperscript{6}. Complication rate was high in this report as well. An overview of outcomes in ECMO-treated patients with PCCS is provided in Table 2. Although the ECMO is a potentially acceptable modality of mechanical circulatory support, it is a complex device, which is associated with significant complications and survival seems lower compared to LVAD treated patients, although the patient population may differ.

**Impella**

A less invasive system for mechanical circulatory support is the Impella system. Safety and feasibility of Impella treatment have been demonstrated in the setting of high-risk PCI and acute myocardial infarction\textsuperscript{25,11}. It has been investigated in the setting of PCCS as well, although only small reports have been published (Table 2). In 2003, Meyns et al reported on their initial experiences with the Impella device for CS in 16 patients\textsuperscript{26}. Ten of those patients suffered from PCCS, three of whom were additionally supported with ECMO. An improvement in cardiac output and mean arterial pressure was observed, as well as a significant decrease in wedge pressure after 6 hours of support in the 13 Impella-treated patients. Eight of those patients could be weaned from the device, 6 of whom survived through discharge. All three patients with combined support could be weaned successfully; however, all three deceased due to multi-organ failure. Overall
30-day survival was 37%. In 2004, Siegenthaler et al reported on their experience with the Impella recover device for 24 patients with PCCS. They compared these patients with 198 patients that had undergone IABP insertion for PCCS. In-hospital mortality for the Impella-treated patients was 54%. Importantly, the subgroup of patients who had a residual native cardiac output of 1L/min or more showed a significant reduction in mortality. Jurmann et al reported on a small group of 6 patients with PCCS that were treated with the Impella device. Although only 2 patients eventually survived through discharge, the device was easy to implant and remove and associated with low anticoagulation requirements. In all of those studies, the predecessor of the current Impella device was investigated. Our findings are largely in accordance with previously conducted studies, including the studies evaluating VAD- and ECMO support. Mortality rates remain high, reflecting the high-risk characteristics of the study populations under investigation. The outcomes of ECMO-treatment have been directly compared with the outcomes of Impella treatment by Lamarche et al, in a retrospective analysis. In this study, 29 patients with cardiogenic shock from various etiologies, supported with either Impella 5.0 or Impella RD, were compared with 32 patients supported with ECMO. Thirty-day survival rates for ECMO and Impella were 56% versus 62%, respectively. Importantly, the prevalence of PCCS was 44% versus 14% in ECMO and Impella-groups, respectively, which may have led to substantial bias. However, in this study, blood transfusion rates were significantly lower in the Impella-treated patients. Recently, a study of Impella 5.0 treatment for PCCS has been conducted for FDA-approval, the RECOVER I trial. This

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Treatment modality</th>
<th>30-day/In-hospital survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beiras-Fernandez 2011</td>
<td>108</td>
<td>ECMO</td>
<td>40.2%</td>
</tr>
<tr>
<td>Wu 2010</td>
<td>110</td>
<td>ECMO</td>
<td>41.8%</td>
</tr>
<tr>
<td>Elsharkawy 2010</td>
<td>233</td>
<td>ECMO</td>
<td>36%</td>
</tr>
<tr>
<td>Wang 2009</td>
<td>62</td>
<td>ECMO</td>
<td>54.8%</td>
</tr>
<tr>
<td>Liden 2009</td>
<td>52</td>
<td>ECMO</td>
<td>52%</td>
</tr>
<tr>
<td>Rastan 2010</td>
<td>517</td>
<td>ECMO</td>
<td>24.8%</td>
</tr>
<tr>
<td>Doll 2003</td>
<td>219</td>
<td>ECMO</td>
<td>24%</td>
</tr>
<tr>
<td>RECOVER I 2012</td>
<td>16</td>
<td>Impella 5.0</td>
<td>94%</td>
</tr>
<tr>
<td>Lamarche 2011</td>
<td>29</td>
<td>Impella 5.0/Impella RD</td>
<td>56%</td>
</tr>
<tr>
<td>Lamarche 2011*</td>
<td>32</td>
<td>ECMO</td>
<td>62%</td>
</tr>
<tr>
<td>Jurmann 2004</td>
<td>6</td>
<td>Impella recover</td>
<td>33%</td>
</tr>
<tr>
<td>Siegenthaler 2004</td>
<td>24</td>
<td>Impella recover</td>
<td>46%</td>
</tr>
<tr>
<td>Meyns 2003</td>
<td>16</td>
<td>Impella recover</td>
<td>37%</td>
</tr>
</tbody>
</table>

*This study included patients with CS from variable causes; the proportion of PCCS patients was small; ECMO denotes extracorporeal membrane oxygenation; PCCS denotes postcardiotomy cardiogenic shock.
study included 16 patients, 94% of whom survived through 30 days\textsuperscript{10}. These results are clearly much more favourable than results from all previously conducted studies in this patient category. Importantly, cardiogenic shock is a continuum, ranging from mild degrees of hemodynamic instability without evident peripheral organ hypoperfusion, through severe treatment-refractory shock with multi-organ failure. Obviously, mortality rates are higher in patients with treatment-refractory shock and multi-organ failure. In the RECOVER I trial, support was initiated early after the patient met the hemodynamic criteria for shock, which may potentially explain the large difference in clinical outcomes. Nevertheless, this study further supports the conclusion from the available preliminary data, that Impella 5.0 support is a suitable treatment option in this challenging category of patients. Outcomes are comparable to or even better than in patients supported with other devices. Importantly, the Impella device has a less invasive implantation technique and low morbidity profile compared to surgical VADs or ECMO. The minimal invasiveness may allow for relatively early institution of hemodynamic support, in order to improve patient outcomes.

\textbf{Study limitations}

Several limitations with regard to the current report should be acknowledged. First of all, the report is limited by its relatively small sample size. Nevertheless, it represents a real-world population of patients with severe PCCS from three tertiary care centers across Europe and it is the largest cohort reported to date. Due to the retrospective nature of data collection, several important parameters, including detailed hemodynamic parameters, are lacking. Timing of Impella implantation varied amongst patients, as well as the type of cardiac surgery.

\textbf{CONCLUSIONS}

Mechanical support with the Impella devices in patients with PCCS was associated with a 39.5\% survival rate at 30 days, which is in accordance with survival rates from previously conducted studies evaluating other mechanical circulatory support devices. The relatively low survival rate throughout different studies evaluating different modalities for mechanical circulatory support reflects the challenging nature and the clinical severity of the PCCS syndrome. As the Impella device is much less invasive and much more easily available than surgical assist devices, whereas survival seems comparable, it may form a suitable alternative treatment modality in patients with PCCS.
REFERENCES


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