Abstract

Microaxial LVADs are increasingly used for cardiogenic shock treatment. We compared the short-term outcome of patients supported with different microaxial devices for cardiogenic shock.

A retrospective propensity score-adjusted analysis was performed in cardiogenic shock patients treated with either the Impella CP (n=64) or the Impella 5.0/5.5 (n=62) at two tertiary cardiac care centers between 1/14 and 12/19.

Patients in the Impella CP group were significantly older (69.6±10.7 vs 58.7±11.9 years, p=0.001), more likely in an INTERMACS level 1 (76.6% vs 50%, p=0.003) and post CPR (36% vs 13%, p=0.006). The unadjusted 30-day survival was significantly higher in Impella 5.0/5.5 group (58% vs 36%, p=0.021, odds ratio (OR) for 30-day survival on Impella 5.0/5.5 was 3.68 (95% CI [1.46-9.90], p=0.0072). After adjustment, the 30-day survival was similar for both devices (OR 1.23, 95% CI [0.34-4.18], p=0.744).
Lactate levels above 8 mmol/L and preoperative CPR were associated with a significant mortality increase in both cohorts (OR=10.7, 95% CI [3.45-47.34], p<0.001; OR=13.2, 95% CI [4.28-57.89], p<0.001, respectively).

Both Impella devices offer a similar effect with regards to survival in cardiogenic shock patients. Preoperative CPR or lactate levels exceeding 8 mmol/L immediately before implantation have a poor prognosis on Impella CP and Impella 5.0/5.5.

Introduction

The mortality in patients suffering from cardiogenic shock (CS) is high; the overall 30−day mortality for patients with CS associated with acute myocardial infarction (AMI) is approximately up to 50%.[1,2] Medical treatment with high-dose inotropic support and vasoactive agents is essential for acute stabilisation, but may lead to ventricular arrhythmias and further myocardial injury due to an increased afterload and myocardial workload.[3] In this setting, the role of temporary mechanical circulatory support (tempMCS) is becoming increasingly important.[1]

TempMCS can provide full haemodynamic support and improve organ perfusion, which may prevent or reverse multi-organ failure.[4] Left ventricular unloading reduces myocardial oxygen consumption and may increase the chances of myocardial recovery or at least prevent further injury.[5]

Veno-arterial extracorporeal life support (v-a ECLS) is the most common temporary MCS device. V-a ECLS is available in most tertiary care centres, is relatively simple to implant and can be applied during cardiopulmonary resuscitation (CPR).[6] Patients with biventricular or cardiorespiratory failure after CPR may benefit from ECLS therapy.[7] However, v-a ECLS therapy cannot sufficiently unload the left ventricle and hence generates an extremely high afterload, which in turn increases left ventricular wall stress, myocardial oxygen demand and impairs coronary perfusion. In the absence of ventricular contractility, this can lead to pulmonary hypertension and subsequently to interstitial lung oedema.[8] Therefore, in case of isolated left ventricular failure, microaxial left ventricular assist devices such as the Impella (Abiomed Inc., MA, USA) can be used as an alternative to or in combination with ECLS.[9]

The Impella-devices are a family of microaxial pumps that can provide a flow of up to 5.5 L/min, achieving partial or full haemodynamic support, depending on the patient's needs. By percutaneous access or vascular cut-down, Impella devices can be placed in the left ventricular outflow tract and effectively unload the left ventricle. Left ventricular unloading is a key factor for potential myocardial recovery and prevention of pulmonary oedema.[8]

One of the most commonly used Impella device is the Impella CP, which can generate up to 3.5 L/min of flow and is implanted percutaneously via femoral artery access. The Impella 5.0 and 5.5 LVAD are able to provide full haemodynamic support of up to 5.5 L/min. Due to their size, they require surgical implantation, usually via an axillary artery access.

Despite the fact that both devices are commonly used in cardiogenic shock patients, the optimal indication and correct patient selection for the type of support remain undefined. Therefore, we performed a retrospective analysis with the aim of comparing the effectiveness of both Impella CP and Impella 5.0/5.5 LVADs in cardiogenic shock patients.

Methods

The study is a retrospective analysis of 126 consecutive patients supported with the Impella CP or Impella 5.0/5.5 devices at two tertiary care centres. The study was approved by the institutional ethics committee (ES2/016/20).

Patient selection

Patients (n=126) underwent Impella CP, 5.0 or 5.5 implantation between January 2014 and December 2019. Patients supported with va-ECLS were not included into the analysis. The indication for Impella implantation was cardiogenic shock (INTERMACS profile 1, 2, 3 or SCAI level E, D, and C); all patients were over 18 years old.[2,10] Patients were retrospectively divided into two groups according to the device type: an Impella CP group (n=64) and an Impella 5.0/5.5 group (n=62). Impella device selection depended on the medical institution: patients treated in the cardiological department of one centre received only Impella CP, in the cardiothoracic surgical department of another Impella 5.0/5.5 implantations were performed. Patients' admission to the participating centres underwent independently.

The 30-day cut-off was arbitrarily chosen on the basis of several comparable shock studies.[4,5]

Data collection

Demographic, clinical and last available haemodynamic data and laboratory values prior to Impella implantation were retrospectively collected from the patients' charts and analysed. A 20% limit for missing data was set to exclude variables for which an excessive amount of data was missing. No relevant parameter had >10% missing data. The patients' follow-up data from at least 30 postoperative days were collected.

The MELD-XI score was calculated using the formula: $5.11 \times \ln(\text{bilirubin}) + 11.79 \times \ln(\text{creatinine}) + 9.44$.[11]

Statistical procedures

Continuous variables are summarised as mean and standard deviation (SD) or as median and interquartile range [IQR] in the case of skewed data. For categorical variables, numbers and percentages are presented. Patient groups were compared using Student's t-test for normally distributed continuous data and the Mann-Whitney-U test for non-normally distributed continuous data. For categorical data, Chi^2 tests with Yates' continuity correction were used. To account for imbalances in preoperative data in the Impella CP, 5.0 and 5.5 groups, a propensity score was calculated with sex, age, aetiology of cardiogenic shock, INTERMACS level (The Interagency Registry of Mechanically Assisted Circulatory Support), CPR, CAD, IABP, AHT, DM, renal insufficiency, COPD, liver insufficiency, lactate, WBC, creatinine and INR. The influence of Impella CP, 5.0 and 5.5 on 30-day survival was calculated using logistic regression adjusting for the propensity score. Due to the small patient number no propensity score matching was performed.

A receiver operating characteristic (ROC) curve was plotted for preoperative lactate. The area under the ROC curve was calculated as a measure for discrimination ability. Survival in different patient groups was analysed using Kaplan-Meier estimates with 95% confidence intervals (CIs). Log-rank testing was used to compare patient groups.

We assumed a p-value of <0.05 as the threshold for statistical significance. The analysis was exploratory in nature. R software version 4.0.2 was used for statistical analyses.

Implantation technique

For Impella CP placement, the right or left femoral artery was punctured and dilated, following which a 14 Fr introducer was placed. The 0.018 inch 260 cm placement guidewire was inserted and pushed through the aortic valve into the left ventricle (LV), after which the Impella CP pump was inserted under fluoroscopic guidance. The inlet cannula was placed approx. 3.5-4.5 cm below the level of the aortic valve.

For Impella 5.0/5.5 placement, patients were intubated and operated under general anaesthesia. The axillary artery was surgically exposed and a 10-mm Hemashield graft (MAQUET Ltd., Rastatt, Germany) was anastomosed end-to-side and tunnelled under the skin to allow primary wound closure. The pump was inserted through the graft under fluoroscopic and transoesophageal echocardiographic guidance as described by Boll et al.[12] The inlet was positioned approx. 4.5 cm below the level of the aortic valve annulus. After optimal positioning the pump speed was increased stepwise to P9 (33,000 rpm) under a consistent reduction of inotropic support with a target mean arterial pressure (MAP) of 60-70 mmHg.

Impella 5.0 implantation was performed in 53 (42%) patients, 9 (7%) were treated with Impella 5.5. In three (2%) cases, left axillary artery access and in 59 (47%) cases, the right axillary artery were chosen resp.

Anticoagulation

Anticoagulation was maintained by intravenous heparin and monitored by aPTT and anti-Xa levels (target: 70-90 s and 0.3-0.5 IU/mL, respectively).

Device management:

During the acute phase of the CS maximal support level of P9 was targeted in both groups, achieving up to 3.5L/min and 5.5L/min for Impella CP and Impella 5.0/5.5 respectively. The support level was adapted to patients' demand, aiming to achieve inotropic support free status with target MAP of 60-70 mmHg.

Results

Demographic characteristics are presented in Table 1.
The last available pre-implantation haemodynamic characteristics and laboratory data not older than 24h prior to Impella implantation are presented in Table 2.
Complications under Impella support are listed in Table 3.

In the Impella CP cohort 19 patients could be weaned from support, 1 was bridged to durable MCS and 44 died on support. In Impella 5.0/5.5 group in 16 cases the pump was removed for myocardial recovery, in 24 cases durable LVADs were implanted, and 22 patients died on support. The median support time was 2.0 [0.0, 5.3] days in the CP group vs 8.5 [4.3, 15.8] days in the 5.0/5.5 group. The 30-day survival was 31% and 58%, respectively, in the unadjusted cohort. After propensity score adjustment the survival was similar between the groups (OR=1.23, 95% CI [0.34-4.18], p=0.74).
Because both devices showed a similar 30-day survival, Kaplan-Meier estimates for the risk of 30-day mortality for lactate ≥ 8 mmol/L (OR=10.7, 95% CI [3.45-47.34], p<0.001) and preoperative CPR (OR=13.2, 95% CI [4.28-57.89], p<0.001) were calculated for the combined cohort (Figures 1 and 2).[9] Figure 3 illustrates the ROC

curve for preoperative lactate for the 30-day mortality: the specificity and sensitivity for the cut-off of 8 mmol/L were 94.8% and 36.9%, respectively.

The median lactate level in patients surviving 24h after implantation was similar between the groups: 1.67 mmol/L [1.11, 3.83] for Impella CP and 1.72 mmol/L [1.16, 3.16] for Impella 5.0/5.5 (adjusted p-value=0.91) (Figure 4, Figure 5).

A comparison of the effects of Impella CP and Impella 5.0/5.5 on postoperative lactate levels 24h after implantation revealed no significant difference in paired patient samples: -0.94 mmol/L [-2.89, 0] for Impella CP and -0.22 mmol/L [-1.58, 0.36] for Impella 5.0/5.5 (adjusted p-value=0.65) (Figure 5).

Discussion:

The Impella CP and Impella 5.0/5.5 are widely used microaxial tempMCS devices. The Impella CP is frequently used in protected PCI and may be a risk modifier if used in acute cardiogenic shock.[13,14] The Impella 5.0/5.5 devices were developed as an alternative to v-a ECLS for patients with left ventricular failure. Less need for anticoagulation and effective LV unloading as well as the option for active patient mobilization are arguments for its use.[15]

Despite the fact that tempMCS is considered an effective CS therapy and is recommended in the European Society of Cardiology (ESC) guidelines, the scientific evidence remains scarce.[16,17]

Although the Impella CP provides only partial circulatory support, our study demonstrated no difference for full haemodynamic support with Impella 5.0/5.5. A number of aspects such as differences in patient populations and implantation techniques need to be discussed. The main advantage of Impella CP system is the rush percutaneous implantation, which can be performed even under running CPR. Surgical placement of Impella 5.0/5.5 is more challenging and time consuming, but allows longer support duration in combination with patients' mobilisation. The Impella CP cohort in our study predominantly included patients with acute myocardial infarction CS (AMICS) who underwent PCI and the system was implanted in the cath-lab to stabilise the patient. Patients supported with an Impella 5.0/5.5 were more likely to suffer from acute on chronic heart failure (ac-HF). The therapeutic goal in AMICS patients differs considerably from ac-HF: while revascularisation mostly restores myocardial perfusion and leads to partial myocardial recovery, ac-HF patients require long-term support and are more likely to be bridged to durable LVAD or heart transplantation.[10,18,19] Therefore, in the context of ac-HF with a dilated left ventricle, full support with Impella 5.0/5.5 might be more beneficial, while AMICS patients might be adequately treated with immediate Impella CP support.

A recently published study by Kerami et al. demonstrated no significant survival benefit in cardiogenic shock patients supported with v-a ECLS compared to those on Impella CP and 5.0 support. At the same time, v-a ECLS patients showed a significantly higher prevalence of vascular complications.[20] Due to the small cohort and significant differences in patient demographics, no statistical analysis of complications under support was performed (Table 3). The complications on Impella CP or Impella 5.0/5.5 support depend predominantly on the implantation technique: while the Impella CP is usually inserted percutaneously through the femoral artery, the Impella 5.0/5.5 requires surgical implantation through a vascular prosthesis

sewed to the axillary artery. Therefore, the Impella CP might be associated with a higher risk of leg ischaemia and vessel dissection, while Impella 5.0/5.5 implantation may lead to brachial plexus injury and access site infection as well as bleeding due to the vascular prosthesis remaining in the wound.

Despite the fact that our study demonstrated no reduction in the 30-day mortality in CS patients compared with the results of the SHOCK II trial, an indirect comparison between previous trials and our analysis is not appropriate.[21] The mortality rates in Impella CP and Impella 5.0/5.5 cohorts are expected to be high due to a high percentage of patients in advanced CS correlating with SCAI stages D and E, which are associated with an in-hospital mortality of 40% and 67%, respectively.[2,22] Moreover, around 25% of our patients underwent preoperative CPR. Resuscitated patients exhibit inferior outcomes with in-hospital mortality rates of around 90%.[23] For these patients, strict therapy decision protocols based on preoperative risk profiling should be established in order to identify subgroups that still benefit from Impella implantation and those who require more advanced support.

Blood lactate is a well-known parameter for CS evaluation and mirrors the level of end-organ ischaemia.[4,5,9] A comparison of lactate levels 24h after implantation demonstrated that both systems can lead to restoration of organ perfusion and fulfil metabolic demands. The median level of lactate reduction was compared between paired samples using a propensity score-adjusted analysis and revealed no significant difference in effect between the devices. Based on previous publication we evaluated the impact of preoperative lactate on the patients' outcomes.[24] In our study we demonstrated that lactate levels above 8 mmol/L are associated with a significantly higher mortality rate in cardiogenic shock patients supported with Impella CP and Impella 5.0/5.5. The high specificity of almost 95% allows us to use this parameter as a cut-off for the preoperative identification of patients who may require more advanced support than Impella CP or 5.0/5.5 alone.

Still, patients with high preoperative lactate levels or after CPR and patients with biventricular failure or cardiorespiratory failure represent a clinical challenge and are associated with poor outcomes on Impella CP or 5.0/5.5 support.[9] In this setting, a combination with v-a ECLS as ECMELLA concept might be the best treatment providing both biventricular unloading and blood oxygenation.[8,25] The multicentre study by Schrage et al. demonstrated a significant improvement in survival in ECMELLA patients compared to isolated v-a ECLS support if LV unloading with Impella is initiated within 2h after v-a ECLS implantation.[26] Further, the novel ECMELLA 2.0 technique, using a single arterial access for v-a ECLS cannulation and Impella implantation, may potentially reduce the incidence of vascular complications associated with conventional femoral cannulation, simultaneously allowing mobilisation and de-escalation.[27]

Based on the current analysis and recently published studies we developed a new algorithm for selecting the optimal mechanical circulatory support in cardiogenic shock (Figure 6).[9,19,26,27]

Conclusion:

Our study demonstrated a similar effect of mechanical circulatory support with Impella CP and Impella 5.0/5.5 in patients with profound cardiogenic shock after

adjustment for significant confounders. Both cohorts differed significantly in age, aetiology of heart failure, resuscitation time, as well as renal and liver function, which are important determinants for survival and might influence the results of this study. Patients supported during or after CPR or with lactate levels ≥ 8 mmol/L immediately before implantation showed poor survival on both devices. A standardised operational protocol including preoperative criteria and therapy targets may facilitate the tempMCS device selection. Whether the use of Impella CP as treatment for ac-HF differs from Impella 5.0/5.5 support in the setting of acute MI and vice versa warrants further investigation. A prospective randomised trial is required to compare partial and full haemodynamic support outcomes on Impella CP and 5.0/5.5 devices.

Limitations:

Retrospective, non-randomised study. Small patient cohorts with different patient populations.

Conflict of interest:

E. Potapov reports institutional grants and fees and non-financial support from Abbott and Medtronic during the conduct of the study; institutional grants, fees and non-financial support from Berlin Heart and Abiomed outside the submitted work.

C. Tschöpe has received speaker fees and/or contributions to congresses from Abbott, Abiomed, Astra Zeneca, Bayer, Berlin Chemie, Pfizer, and Servier outside the submitted work.

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Figure legends:

Figure 1. Cumulative survival for preoperative lactate level

Legends for Figure 1:

Figure 2. Cumulative survival for CPR during or immediately before Impella implantation

Legends for Figure 2:

CPR – cardiopulmonary resuscitation

Figure 3. Receiver operating characteristic curve for preoperative lactate

Legends for Figure 3:

Figure 4. Box plot diagrams for pre- and postoperative lactate

Legends Figure 4:

Figure 5. Box plot diagrams for postoperative lactate reduction

Legends for Figure 5:

IQR – interquartile range

Figure 6. Algorithm for optimal temporary mechanical circulatory support selection in cardiogenic shock

Legends for Figure 6:

AVR – aortic valve replacement

CPR – cardiopulmonary resuscitation

LVEF – left ventricular ejection fraction

ROSC – return of spontaneous circulation

TI – tricuspid valve insufficiency

VIS – vasoactive inotropic score

VT/VF – ventricular tachycardia/ fibrillation

LV – left ventricle; RV – right ventricle

VSD – ventricular septal defect

(v) v-a ECLS – (veno) veno-arterial extracorporeal life support

RVAD – right-ventricular assist device