Percutaneous Left Ventricular Support With the Impella 2.5 Assist Device in
Acute Cardiogenic Shock - Results of the Impella EUROSHOCK-Registry

Lauten et al: Impella EUROSHOCK-Registry

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DOI: 10.1161/CIRCHEARTFAILURE.112.967224

Subject Codes: [4]; [11]; [24]; [25]; [37]
Abstract

Background—Acute cardiogenic shock (CS) following myocardial infarction (AMI) is associated with high in-hospital mortality due to persisting low cardiac output. The Impella-EUROSHOCK-registry evaluates the safety and efficacy of the Impella-2.5 percutaneous left ventricular assist device (pLVAD) in patients with CS following AMI.

Methods and Results—This multicenter registry retrospectively included 120 patients (63.6±12.2 years; 81.7% male) with CS from AMI receiving temporary circulatory support with the Impella-2.5-pLVAD. The primary endpoint evaluated mortality at 30 days. The secondary endpoint analyzed the change of plasma lactate after institution of hemodynamic support, the rate of early major adverse cardiac and cerebrovascular events (MACCE) as well as long-term survival.

30-day mortality was 64.2% in the study population. After Impella-2.5-pLVAD-implantation, lactate levels decreased from 5.8±5.0mmol/l to 4.7±5.4mmol/l (p=0.28) and 2.5±2.6mmol/l (p=0.023) at 24 and 48 hours. Early MACCE were reported in 18(15%) patients. Major bleeding at the vascular access site, hemolysis and pericardial tamponade occurred in 34 (28.6%), 9 (7.5%) and 2 (1.7%) patients, respectively. The parameters age>65 and lactate level >3.8mmol/l at admission were identified as predictors of 30day-mortality. After 317±526days of follow-up, survival was 28.3%.

Conclusions—In patient with acute CS from AMI, Impella 2.5-treatment is feasible and results in a reduction of lactate levels suggesting improved organ perfusion. However, 30-day mortality remains high in these patients. This likely reflects the last-resort character of Impella-2.5-application in selected patients with a poor hemodynamic profile and a greater imminent risk of death. Carefully conducted randomized controlled trials are necessary to evaluate the efficacy of Impella-2.5-support in this high-risk patient group.

Key Words: cardiogenic shock, mechanical circulatory support, Impella 2.5 device, percutaneous left ventricular assist device
Historically, cardiogenic shock (CS) due to acute myocardial infarction (AMI) has been associated with in-hospital mortality rates as high as 80%. Even in the era of prompt revascularization, mortality rates for CS remain high and many patients with severe and profound CS succumb to multiple organ failure secondary to persistent inadequate end-organ perfusion. In addition to early revascularization and pharmacologic therapy, mechanical support by means of intra-aortic balloon counterpulsation (IABP) is recommended (Class I) by the current guidelines. However, as the IABP augments native cardiac function, this treatment provides only limited hemodynamic support in patients with severely depressed myocardial function or cardiac arrest. Thus, several clinical trials as well as a recent meta-analysis have failed to demonstrate a benefit of IABP therapy on left ventricular function or survival.

New percutaneous left ventricular assist devices (pLVAD) have been developed for mechanical circulatory support, including the Impella 2.5 system (Abiomed Europe GmbH, Aachen, Germany). These devices unload the left ventricle and partially replace myocardial function, thus potentially promoting myocardial recovery. The Impella 2.5 is a catheter-mounted axial-flow pump which can be inserted percutaneously and provides a maximum flow of 2.5l/min. Short-term circulatory support with the device has been demonstrated to be safe and feasible in high-risk percutaneous coronary intervention as well as in the setting of hemodynamically stable large anterior ST-elevation myocardial infarction (STEMI). In patients with CS, a small randomized clinical trial of Impella 2.5 versus IABP demonstrated an improvement in cardiac index in Impella-treated patients. The purpose of the multicenter Impella EUROSHECK-registry was to assess procedural safety and outcome of Impella-2.5-support in a large cohort of patients with acute CS.
Methods

Study design and collection of data

A total of 14 tertiary cardiovascular centers located in 5 countries across Europe contributed data to the Impella EUROSHOCK registry. Data were collected at each site using a standardized case report form to record demographic and clinical characteristics, as well as procedural and follow-up data. Follow-up was obtained at 30 days and at the time of registry enrolment based on medical records and on physician or patient interviews. The study was approved by the Institutional Review Board of the University Heart Center Jena and supported by Abiomed Europe GmbH (Aachen, Germany) for the identification of sites of enrolment. The investigators had full access to the data and control of the data analysis.

Inclusion Criteria and Treatment:

At each site, all patients receiving emergent Impella 2.5-support over a 5-year-period (2005-2010) for acute CS following AMI were included. The diagnosis of AMI was based on the results of coronary angiography and on laboratory and electrocardiographic studies. CS was a clinical diagnosis based on the definition from the SHOCK trial including (1) the presence of a systolic blood pressure equal to or below 90 mmHg for at least 30 minutes or (2) vasopressors required to maintain blood pressure > 90 mmHg, (3) evidence of end-organ hypoperfusion (e.g.: urine output < 30 mL or cold, diaphoretic extremities or altered mental status) and (4) evidence of elevated filling pressures (e.g. pulmonary congestion on examination or chest radiograph)\(^\text{19}\). In each patient, therapy was tailored to the rapidly changing hemodynamic status and included mechanical ventilation, fluid administration, pharmacologic treatment (inotropes, vasopressors) and/or IABP-support if considered necessary. The amount of fluid administration as well as the choice of inotropes and vasopressors was based on current guidelines and on individual experience and insitutional
policy. Doses were titrated to achieve a systolic blood pressure of at least 80mmHg \(^{20, 21}\). The decision to institute circulatory support with the Impella-2.5 was made in patients with refractory CS unresponsive to high-dose inotropes and/or IABP support at the time of primary percutaneous coronary intervention (PCI).

After hemodynamic improvement weaning from circulatory support was considered in absence of hemodynamic or clinical signs of CS. Weaning criteria included a mean arterial pressure > 70mmHg and a cardiac index > 2.2l/min/m\(^2\) without a requirement of inotropic support and evidence of endorgan hypoperfusion. Weaning was performed by decreasing the pump performance level in 2 steps in intervals of 30 to 60 min. After reduction to performance level P2 (range: P1 to P9; P9= maximum flow) for 10 min without hemodynamic instability, the Impella pump was pulled back into the aorta and explanted.

**Device**

The Impella 2.5 device has been described previously \(^{15}\). In brief, it is a catheter-mounted microaxial rotary blood pump designed for rapid percutaneous insertion under fluoroscopy to allow for temporary left ventricular (LV) support. The device is inserted through a 13F femoral sheath and positioned retrogradely across the aortic valve in the LV. Equipped with a pigtail-tip to avoid myocardial injury and to ensure a stable position in the LV, the Impella 2.5 provides a maximum flow of 2.5L/min by expelling blood from the LV into the ascending aorta. The degree of support can be managed by graduation of pump speed up to a maximal rotation speed of 51.000 rpm. The device has received CE-approval in Europe for 5 day use.

**Study end-points**

The primary endpoint of the study was all-cause mortality at 30 days. The secondary endpoints were long-term survival and parameters of device efficacy and safety. The
secondary efficacy endpoint evaluated the change in level of plasma lactate within 24 and 48 hours after the beginning of Impella 2.5 support. Secondary endpoints also included procedural feasibility, the incidence of major cardiac and cerebral events (recurrent myocardial infarction or cardiovascular interventions [PCI, CABG] and stroke), device-related vascular complications (bleeding requiring transfusion or surgery), haemolysis, cardiac tamponade and device malfunction.

**Statistics**

Continuous data are presented as mean +/- standard deviation (SD), categorical variables are presented as percentages and numbers. All variables were tested for normal distribution with the Shapiro-Wilk test. Univariate logistic regression was performed among established predictors of 30-day mortality. Age was dichotomized to above and below the median of 65 years. Systolic blood pressure was dichotomized to above and below the median of 90 mmHg. Lactate at baseline was dichotomized to above and below the median of 3.8 mmol/L. All covariates with a p-value of <0.1 were included in the multivariate regression model. Backward stepwise logistic regression analysis was subsequently performed, to identify independent predictors for 30-day mortality. A covariate was removed from the model if the p-value exceeded 0.10. All p values <0.05 were considered statistically significant. Kaplan-Meier curves were constructed and stratified according to lactate levels above and below the median. Survival differences were tested using the log-rank statistic. All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA, version 18.0).
Results

Patient Characteristics at Hospital Admission

The Impella EUROSHOCK-registry included a total of 120 patients with AMI and CS treated with the Impella 2.5 in 14 European cardiovascular centers. Baseline characteristics are detailed in Table 1. Mean age was 63.6±12.3 years, 98 (81.7%) patients were male. In accordance with the inclusion criteria all patients were in profound CS with a low mean arterial blood pressure (68.3±17.3mmHg), an elevated plasma lactate (5.8±5.0mmol/l) and a severely reduced LV ejection fraction (0.27±0.11; determined by either echocardiography or ventriculography). At the time of device implantation, 102 (85%) patients received vasopressors and/or inotropics and 35 (29.0%) were on IABP support. In addition, 40.8% (n=49) of the patients had been resuscitated for out-of-hospital cardiac arrest. The majority of patients (n=81, 67.5%) presented with multivessel disease with a severely reduced mean TIMI- (thrombolysis in myocardial infarction) flow at the culprit lesion of 0.4±0.8, which improved after PCI to 2.6±0.9.

Thirty-day mortality

Thirty-day mortality in this study cohort was 64.2% (77/120 patients). Multivariate logistic regression analysis was performed to identify independent parameters for 30-day mortality (Table 2). After stepwise backward analysis, the parameters age> 65 (OR 5.46; p=0.008) and blood lactate >3.8mmol/l (p=0.012) remained in the model as independent predictors for 30-day mortality with odds ratios of 5.245 (95%CI 1.473-18.677, p=0.011) and 5.245 (95% CI 1.473-18.677, p=0.011), respectively (Table 3).
Clinical Course

The mean duration of Impella 2.5 support was 43.5±49.6 hours in the overall study cohort. Fifty patients (42%) deceased during Impella 2.5 support. Within the overall study group, 53 (44.5%) patients were successfully weaned from the device after a mean support duration of 66.3±54 hours. Within the subgroup of successfully weaned patients, 18/53 (34%) patients had deceased after further treatment at 30 days. In 6 patients (5.0%), circulatory support with the Impella 2.5 was discontinued due to associated complications (vascular:5; haemolysis:1).

After device implantation mean plasma lactate levels decreased from 5.8±5.0mmol/l to 4.7±5.4mmol/l (p=0.28) at 24 hours and to 2.5±2.6mmol/l (p=0.023) at 48 hours of device support, respectively. In patients presenting with a lactate above the median of 3.8mmol/l, plasma lactate decreased from 9.3±4.9mmol/l to 6.4±6.3mmol/l (p=0.06) after 24 hours and to 4.0±4.0mmol/l (p=0.007) after 48 hours, respectively. Further details on laboratory measurements are presented in Table 2. Survival after a mean follow-up of 317±526 days was 28.3%. The Kaplan-Meier-Curves for the overall-group, as well as Kaplan-Meier curves stratified by plasma lactate at admission and with or without CPR < 72 hours are provided (Figures 1 and 2).

In the overall study population, 10 patients (8.4%) required upgrading to other circulatory assist devices with a higher maximum pump flow (Impella 5.0: n=6; extracorporeal membrane oxygenation: n=2; surgical LVAD: n=2). Decisions for upgrade were influenced by clinical judgement and the persistence of severe hypotension or suboptimal cardiac output despite Impella 2.5 - and inotropic support. The 30-day mortality in the subgroup of patients upgraded to other devices was 60% (n=6).
Patients requiring CPR within 72 hours before Impella 2.5-implantation had a significantly lower survival at 30 days compared to patients not requiring CPR (24.5% vs. 43.7%; p=0.002; Figure 2B). However, the requirement of CPR prior to institution of hemodynamic support was no independent predictor of early mortality in the multivariate logistic regression analysis (Table 3).

**Feasibility and Safety**

The Impella 2.5 was successfully implanted in 119 (99.2%) patients. The implantation procedure was considered easy or suitable by the implanting physician in 114 (95%) patients. In one patient (0.8%), transfemoral placement of the Impella 2.5 failed and intraaortic counterpulsation was used subsequently. In patients successfully weaned or upgraded to other devices, the explantation procedure was rated easy or suitable in 66 (95.7%) patients. Major adverse cardiac and cerebrovascular events in the overall study group were reported in 18 (15%) cases (myocardial infarction: n=8; Re-PCI: n=13; coronary artery bypass grafting: n=3; stroke: n=2). Complications associated with Impella 2.5 support included bleeding at the vascular access site requiring transfusion in 29 (24.2%) and vascular surgery in 5 (4.2%) patients. Haemolysis resulting in blood transfusion was reported in 9 (7.5%) cases. In 2 (1.7%) patients pericardial drainage was necessary due to hemodynamically relevant pericardial tamponade after Impella placement. Device malfunction necessitating explantation occurred in 3 (2.5%) patients during long-term support. Details on safety endpoints are presented in Table 4.
Discussion

Mechanical support for CS

In current practice, CS complicates 5-15% of cases with acute myocardial infarction and is still associated with high in-hospital mortality rates\(^1\), \(^5\), \(^7\), \(^22\). Intraaortic counterpulsation is considered the first line of treatment for patients requiring mechanical support and is recommended with a class I recommendation according to AHA/ACC and ESC guidelines\(^8\), \(^23\). Contemporary IABP usage ranges from 11% to 86% in patients with CS\(^1\), \(^11\), \(^19\), \(^24\), \(^25\). However, so far there is no data from randomized controlled trials demonstrating a survival benefit of IABP-therapy and its efficacy has recently been questioned\(^10\), \(^26\), \(^27\).

Ventricular assist devices are a promising alternative for patients with CS as they provide hemodynamic support by replacing LV function and thus may allow for recovery of hibernating or stunned myocardium. However, surgical LVADs frequently require time-consuming and complex implantation procedures. They are themselves associated with a significant morbidity and mortality and their invasiveness precludes urgent implantation upon presentation in patients with acute CS\(^28\)-\(^30\). Therefore, percutaneous devices have been developed, including the Impella 2.5 system.

Current Evidence for Hemodynamic Support with the Impella 2.5 in Acute CS

In contrast to other percutaneous devices, the Impella 2.5 is a less invasive system that allows for rapid transcatheter introduction using standard catheterization techniques and that provides a maximal pump flow of 2.5l/min. A larger version of the Impella system is available as well, which is capable of providing a maximum flow of 5.0 l/min. However, this device requires a surgical cut-down of the femoral artery. The Impella 2.5 has been demonstrated to be safe and feasible in elective use during high-risk PCI as well as in patients...
with STEMI without CS\textsuperscript{14-17}. It has been demonstrated to promote myocardial recovery by LV unloading and to result in an immediate reduction of diastolic LV wall stress and pulmonary capillary wedge pressure\textsuperscript{17, 18, 31}. Further, beneficial effects of the system on cerebral perfusion during cardiac arrest have been reported in the experimental setting\textsuperscript{32}.

However, clinical data on efficacy of the Impella 2.5 in patients with CS is still limited. In a small series in six patients with CS after STEMI circulatory support with the Impella system resulted in hemodynamic improvement with a decrease of blood lactate levels\textsuperscript{33}. In the small randomized ISAR-Shock-trial comparing hemodynamic support with the Impella 2.5 and IABP (Impella: n= 12; IABP: n=13) the device resulted in an improved cardiac index, however, failed to improve survival\textsuperscript{18}.

The present report based on data from the Impella EUROSHOCK-registry is the largest series to date investigating emergency support with the Impella 2.5 device for treatment-refractory CS. Although survival rates in patients with CS vary among the current literature, 30-day survival in the present study was 35.8\% and seems rather low\textsuperscript{6, 18, 34, 35}. The excess mortality is likely the result of a selection bias favouring critically ill patients with a particularly poor hemodynamic profile and a greater imminent risk of death. Although rather disappointing, this data reflect the outcome in a subgroup of patients who have failed to improve with first-line treatment and in whom the pLVAD is frequently used as “last resort” option. This observation is also in line with the results of a recent study by Engstroem et al. reporting an even lower 30-day survival rate of 24\% in a series of 34 patients with CS after STEMI\textsuperscript{36}.

Indeed, compared the ISAR-Shock trial, patients enrolled in the Impella EUROSHOCK registry had a poorer hemodynamic profile at the time of device implantation with a lower
systolic and diastolic blood pressure (106±22 and 64±15mmHg vs. 91±21 and 57±17mmHg)
18. Compared to other reports, a larger proportion of the study population had been
resuscitated for cardiac arrest and plasma lactate levels were higher (4.7±2.6 vs. 5.97±5.0) at
admission, thus reflecting refractory CS with severe organ hypoperfusion at this time37.

The observations made in the Impella EUROSHOCK registry confirm that use of the Impella
2.5 is feasible in the emergency setting and represents a rapid method of instituting
hemodynamic support- also in less experienced centers. The device was easy to implant with
a high procedural success rate and performed well. Despite the prolonged duration of support
(43.5, range 0-210h) the rate of device-associated complications was acceptable in this study
population- although higher than reported from non-emergent pLVAD application14.
Bleeding complications requiring transfusion occurred in 24.2% (n=29) patients, whereas
surgical treatment of bleeding complications was required in 5 (4.2%) patients (Table 4).
Although Seyfarth et al. did not observe any vascular or bleeding complications in the ISAR-
Shock-trial, this was a relatively small trial performed in an highly experienced center18.
Importantly, complication rate of Impella 2.5 treatment is low when compared to the
TandemHeart pLVAD37,38.

Clinical implications
The Impella EUROSHOCK registry reflects the real-world use of the Impella 2.5 in
contemporary practice outside of randomized trials. Based on these data, this potentially
effective therapy is currently rather restricted to patients with refractory CS who have failed
to improve with first-line treatment. This is due to the current lack of data demonstrating a
clinical benefit with these devices as well as the current guidelines recommending intraaortic
counterpulsation as first-line for patients requiring mechanical support\textsuperscript{39, 40}. Another issue are the higher costs of pLVADs when compared to IABP-therapy\textsuperscript{25}.

The present study demonstrates the feasibility and ease of Impella 2.5-implantation in patients requiring urgent hemodynamic support even in less experienced centers. Also not based on randomized trials, this type of hemodynamic support should be considered early in patients failing to improve with first-line therapy. Further, plasma lactate at the time of Implantation has a prognostic impact and may also be used as metabolic marker of hypoperfusion aiding in guiding therapy. A significant decrease in plasma lactate after the beginning of Impella treatment suggests at least partial reversal of hypoperfusion and supports the hemodynamic efficacy of the device. These findings are in line with data reported in the literature\textsuperscript{40}. Possibly, patients with lactate levels on admission above 3.8 mmol/L, as well as patients who continue to have high plasma lactate levels on Impella 2.5 support should be considered for upgrading to more powerful assist devices (e.g. the Impella 5.0), although this recommended strategy is rather based on experience than actual data\textsuperscript{36}. The present analysis failed to demonstrate a survival benefit for patients upgraded to other devices. This may be due to the small number of patients as well as cofounding factors, such as the time delay associated with the decision to upgrade.

\textbf{Study limitations}

This study represents the by far largest real-world cohort of patients treated with the Impella 2.5 in CS to date. However, several limitations should be acknowledged with regard to the current report. First of all, the lack of a control group as typical for a registry hampers definite conclusions on efficacy of Impella 2.5 support. Secondly, due to the retrospective nature of data collection, detailed hemodynamic data after Impella implantation, in particular...
cardiac output, are not available. In emergency situations in patients requiring circulatory support an extensive hemodynamic evaluation is often not possible and not performed outside of randomized trials. The availability of data was limited to standard parameters recorded during clinical routine in all participating centers. However, this might be of minor significance as the hemodynamic benefit of LVAD-support is well-documented and similar effects may be assumed in the Impella EUROSHOCK population. Thirdly, selection bias may have influenced the outcome, as treatment with the Impella 2.5 has preferentially been given to the most severely ill patients. Finally, patients were included retrospectively over a period of five years also covering the learning curve of the participating center in use of the Impella 2.5. This may impact selection of patients as well as the timepoint of device-implantation in the individual centers.

In conclusion, the use of the Impella-2.5 for hemodynamic support in refractory CS is feasible although associated with a high complication rate. The high 30-day mortality rate may reflect the selection of patients with major hemodynamic compromise and high risk of imminent death. In a severely ill patient population with lactic acidosis, this device may not provide adequate ventricular unloading or systemic perfusion. Particularly in patients with profound CS the Impella 2.5 may need to be upgraded early to more powerful devices. Further studies and adequately powered clinical trials are necessary to improve selection and timing for device support for this indication.
Sources of Funding

The study was funded by the University Heart Center Jena/Germany.

Disclosures

JPH has received an unrestricted research grant from Abiomed Europe GmbH, Aachen, Germany. All other authors report no conflict of interest.

References


Table 1. Baseline characteristics (n=120)

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<tr>
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<th>Baseline (N=120)</th>
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<tbody>
<tr>
<td>Age, years±SD</td>
<td>63.6 ±12.2</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>98 (81.7)</td>
</tr>
</tbody>
</table>

**Cardiac risk factors**
- Body mass index >25kg/m², n (%) 75 (57.3)
- Hypertension, n (%) 66 (55.0)
- Diabetes, n (%) 37 (30.8)
- Current smoker, n (%) 33 (27.5)
- Hypercholesterolemia, n (%) 41 (34.2)

**Previous medical history**
- Chronic obstructive pulmonary disease, n (%) 13 (10.8)
- Renal Insufficiency, n (%) 27 (22.5)
- Atrial Fibrillation, n (%) 25 (20.1)
- Stroke, n (%) 2 (1.7)
- Peripheral Vascular Disease, n (%) 13 (10.8)
- Previous Myocardial Infarction, n (%) 35 (29.2)
- Myocardial Infarction within 90days, n (%) 17 (14.2)
- Previous Coronary Artery Bypass Grafting, n (%) 7 (5.8)

**Additional treatment upon admission**
- Inotropes and/or vasopressors, n (%) 102 (85.0)
- Mechanical ventilation, n (%) 83 (69.2)
- Intraaortic counterpulsation, n (%) 35 (29.2)
- Primary PCI, n (%) 101 (93.2)
- CPR within 72hours before device implantation 49 (40.8)

**Hemodynamics and lab measurements**
- Systolic blood pressure, mmHg±SD 90.2±22.3
- Diastolic blood pressure, mmHg±SD 56.6±17.3
- Mean blood pressure, mmHg±SD 68.1±17.9
- Heart rate, bpm±SD 100±23
- Ejection fraction ±SD 0.27±0.12
- Lactate, mmol/l±SD 5.8±4.9

**Coronary status**
- Multivessel disease, n (%) 81 (67.5)
- Number of lesions treated 1.7±1.2
- TIMI-flow before intervention 0.4±0.8
- TIMI-flow after intervention 2.6±0.9

Values as mean ± SD or n(%)
Table 2. Mortality at 30 days and secondary efficacy end points

<table>
<thead>
<tr>
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<th>Baseline (N=120)</th>
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<tbody>
<tr>
<td><strong>Primary end point:</strong></td>
<td></td>
</tr>
<tr>
<td>Mortality at 30 days</td>
<td>77 (64.2)</td>
</tr>
<tr>
<td>Death on circulatory support</td>
<td>50 (42.0)</td>
</tr>
<tr>
<td>Successfully weaned from support</td>
<td>53 (44.5)</td>
</tr>
<tr>
<td>Long-term survival (after 317±526days)</td>
<td>34 (28.3)</td>
</tr>
</tbody>
</table>

**Secondary end points:**

<table>
<thead>
<tr>
<th></th>
<th>Overall group</th>
<th>Subgroup with initial lactate &gt; 3.8mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful Implantation Procedure</td>
<td>119 (99.2)</td>
<td></td>
</tr>
<tr>
<td>Procedure rated “easy” or “suitable”</td>
<td>114 (95%)</td>
<td></td>
</tr>
<tr>
<td>Duration of Impella 2.5 support, hours</td>
<td>43.5±49.6</td>
<td></td>
</tr>
</tbody>
</table>

Plasma lactate at admission, mmol/l

<table>
<thead>
<tr>
<th></th>
<th>Overall group</th>
<th>Subgroup with initial lactate &gt; 3.8mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.8±5.0</td>
<td>9.3±4.9</td>
</tr>
<tr>
<td>Plasma lactate after 24 hours, mmol/l</td>
<td>4.7±5.4</td>
<td>6.4±6.3</td>
</tr>
<tr>
<td>Plasma lactate after 48 hours, mmol/l</td>
<td>2.5±2.6*</td>
<td>4.0±4.0*</td>
</tr>
</tbody>
</table>

Values as n(%) or mean ± SD; * p=0.023 compared to baseline; #p=0.007 compared to baseline
Table 3. Regression analysis of predictors of 30 day mortality (n=120)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65</td>
<td>2.085(0.969-4.484)</td>
<td>0.06</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.641(0.642-4.193)</td>
<td>0.30</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.045(0.465-2.349)</td>
<td>0.92</td>
</tr>
<tr>
<td>COPD</td>
<td>0.881(0.269-2.883)</td>
<td>0.83</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>0.421(0.176-1.007)</td>
<td>0.052</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.553(0.034-9.063)</td>
<td>0.68</td>
</tr>
<tr>
<td>Previous MI</td>
<td>0.394(0.175-0.885)</td>
<td>0.024</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1.339(0.603-2.976)</td>
<td>0.473</td>
</tr>
<tr>
<td>CPR</td>
<td>2.390(1.071-5.331)</td>
<td>0.033</td>
</tr>
<tr>
<td>IABP</td>
<td>2.362(0.961-5.808)</td>
<td>0.061</td>
</tr>
<tr>
<td>Systolic BP &lt;90 mmHg</td>
<td>2.250(1.018-4.972)</td>
<td>0.045</td>
</tr>
<tr>
<td>Lactate &gt;3.8 mmol</td>
<td>3.750(1.225-11.481)</td>
<td>0.021</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95%CI)</th>
<th>p</th>
<th>OR (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65</td>
<td>6.658 (1.616-27.432)</td>
<td>0.009</td>
<td>5.245 (1.473-18.677)</td>
<td>0.011</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>0.733 (0.148-3.628)</td>
<td>0.703</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous MI</td>
<td>0.412 (0.107-1.588)</td>
<td>0.198</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPR</td>
<td>1.899 (0.451-8.007)</td>
<td>0.382</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IABP</td>
<td>2.209 (0.475-10.27)</td>
<td>0.312</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP &lt;90 mmHg</td>
<td>1.523 (0.372-6.228)</td>
<td>0.558</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactate &gt;3.8 mmol</td>
<td>4.986 (1.24-20.053)</td>
<td>0.024</td>
<td>5.245 (1.473-18.677)</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Logistic regression analysis of predictors of 30-day mortality. OR: odds ratio. CPR: cardiopulmonary resuscitation
## Table 4. Secondary safety end points

<table>
<thead>
<tr>
<th></th>
<th>Baseline (N=120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACCE (total)</td>
<td>18 (15.0)</td>
</tr>
<tr>
<td><em>Myocardial Infarction</em></td>
<td>8 (6.7)</td>
</tr>
<tr>
<td><em>Re-PCI</em></td>
<td>13 (10.8)</td>
</tr>
<tr>
<td><em>CABG</em></td>
<td>3 (2.5)</td>
</tr>
<tr>
<td><em>Stroke</em></td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Bleeding requiring transfusion</td>
<td>29 (24.2)</td>
</tr>
<tr>
<td>Bleeding requiring surgery</td>
<td>5 (4.2)</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>9 (7.5)</td>
</tr>
<tr>
<td>Pericardial drainage</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Device malfunction</td>
<td>3 (2.5)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>38 (31.7)</td>
</tr>
<tr>
<td>Renal failure requiring dialysis</td>
<td>28 (23.8)</td>
</tr>
<tr>
<td>Multiple organ failure</td>
<td>37 (30.8)</td>
</tr>
</tbody>
</table>

MACCE = Major adverse cardiac and cerebrovascular events, values as n(%) or mean ± SD
Figure Legends

**Figure 1.** Overall Long-Term Survival: Kaplan-Meier curve of 120 patients showing survival after 317±526 days (survival rate 28.3%).

**Figure 2.** (A) Kaplan-Meier survival curves stratified by plasma lactate levels below and above median (3.8 mmol/l) at admission demonstrate a lower 30 day survival in patients with lactate ≥3.8 mmol/l compared to patients with a lactate <3.8 mmol/l (18.2 vs. 46%; p<0.001). (B): 30-day survival in patients requiring cardiopulmonary resuscitation (CPR) <72 hours prior to Impella 2.5-implantation is significantly lower compared to patients without CPR (24.5% vs. 43.7%; p=0.002).
Percutaneous Left Ventricular Support With the Impella 2.5 Assist Device in Acute Cardiogenic Shock - Results of the Impella EUROSHOCK-Registry
Alexander Lauten, Annemarie E. Engström, Christian Jung, Klaus Empen, Paul Erne, Stéphane Cook, Stephan Windecker, Martin W. Bergmann, Roland Klingenberg, Thomas F. Lüscher, Michael Haude, Dierk Rulands, Christian Butter, Bengt Ullmann, Laila Hellgren, Maria Grazia Modena, Giovanni Pedrazzini, Jose P.S. Henriques, Hans R. Figulla and Markus Ferrari

Circ Heart Fail. published online December 4, 2012;
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3289. Online ISSN: 1941-3297

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