Percutaneous left ventricular assist support is associated with less pulmonary congestion and lower rate of pneumonia in patients with cardiogenic shock

Sandra Haberkorn,1 Angelika Uwarow,1 Jean Haurand,1 Christian Jung,1 Malte Kelm,1,2 Ralf Westenfeld,1 Patrick Horn ∗1

ABSTRACT

Objectives The aim of this study was to investigate the impact of acute left ventricular unloading by percutaneous left ventricular assist device on pulmonary congestion and pneumonia in patients with cardiogenic shock (CS).

Methods In this retrospective study, we analysed patients with CS who received the Impella percutaneous left ventricular assist device (n=50) compared with those who received intra-aortic balloon pump (IABP) support (n=50). Pulmonary congestion was longitudinally assessed while on support by calculating characteristic findings on the chest X-ray using the Halperin score. The rate of pneumonia and early mortality were assessed as a secondary endpoint.

Results The groups (Impella vs IABP) did not differ in terms of age, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology, Chronic Health Evaluation (APACHE) II score or serum lactate levels. Pulmonary congestion decreased in patient treated with Impella at each time point postimplantation. No change in congestion status was observed in patients supported with IABP. Multivariate analysis indicated Impella support as an independent predictor for pulmonary decongestion (OR 4.06, 95% CI 1.15 to 14.35, p=0.030). The rate of early pneumonia was lower in the Impella group compared with the IABP group (54% vs 74%, p=0.037). Failure of pulmonary decongestion during mechanical circulatory support independently predicted early pneumonia (OR 0.28, 95% CI 0.12 to 0.70, p=0.006).

Conclusion Pulmonary decongestion may facilitate treatment of pneumonia in patients with CS. Left ventricular unloading by Impella device might support pulmonary decongestion, although a larger prospective trial in this patient population is required.

INTRODUCTION

Cardiogenic shock (CS) is defined by inadequate tissue perfusion due to reduced cardiac output. Despite early revascularisation strategies, the mortality rates of CS remain high at approximately 50%.1 Two out of three patients with CS will develop pulmonary congestion subsequent to left ventricular failure.2 Impaired left ventricular function leads to a back-up of fluid in the lungs and increased pulmonary artery and pulmonary capillary pressure causing pulmonary oedema.

Pneumonia often results from persistent pulmonary congestion and reduced alveolar bacterial clearance.3 Pneumonia progressing to severe sepsis may escalate into respiratory distress syndrome with inherent high mortality. Treating pneumonia in patients with CS is particularly challenging because increased left ventricular filling pressure and pulmonary congestion hamper antibiotic...
 approaches. Refractory pneumonia is common in this patient population.\textsuperscript{3-5}

Counterpulsation therapy with intra-aortic balloon pump (IABP) has been typically used in CS in addition to inotropic drug therapy.\textsuperscript{6} While a small increase in cardiac output is observed, IABP does not result in a marked decrease of left ventricular filling pressure and would not affect pulmonary congestion.\textsuperscript{7}

Percutaneous ventricular assist devices like the microaxial Impella pump unload the left ventricle and augment cardiac output which maintains blood pressure and improves end-organ perfusion.\textsuperscript{6,8,9} The benefit of mechanical circulatory support (MCS)-dependent enhanced forward blood flow may extend beyond its impact on cardiac function. Data demonstrate that the use of Impella in patients with myocardial infarct complicated by CS lowers pulmonary capillary wedge pressure.\textsuperscript{10} This would be expected to decrease pulmonary congestion.

However, to date, no data exist about the impact of counterpulsation with IABP or ventricular unloading by MCS on pulmonary congestion and on the incidence of pneumonia. Therefore, in this study, we assessed the occurrence and course of pulmonary congestion and pneumonia in a cohort of patient with CS supported with Impella pump compared with patients with CS receiving IABP.

METHODS
In this retrospective observational study, we assessed pulmonary congestion in patients with CS receiving Impella or an IABP device. Between January 2013 and June 2017, 127 patients with CS were included. The decision for IABP or Impella was left to the discretion of the interventional cardiologist. From 2013 to 2015, the IABP device was the dominant haemodynamic support in our centre. Beginning in 2015, our centre shifted away from IABP in favour of the Impella as a response to the IABP SHOCK trial (figure 1).

CS was defined as a systolic blood pressure <90 mm Hg or the need for continuous infusion of inotropes or vaso-pressors to maintain a systolic blood pressure >90 mm Hg with clinical and laboratory evidence of end-organ damage (oliguria, altered mental state, cool extremities).\textsuperscript{11} We excluded patients who arrived under ongoing resuscitation, those who died immediately on admission or those who were upgraded on extracorporeal life support (ECLS) in the first 48 hours. The duration of mechanical support was individual and was dependent on clinical, haemodynamic and biological parameters. All data were collected from patient charts and medical records until primary discharge including laboratory parameters, complications and therapy strategies. All participants who survived gave written informed consent for the use of their anonymous medical data relating to the defined hospitalisation.

The percutaneous left ventricular assist device (Impella 2.5 or CP; Abiomed, Aachen, Germany) is a microaxial flow pump and is placed percutaneously via femoral artery and crosses the aortic valve into the left ventricle. The system aspirates blood from the left ventricle and expels it into the ascending aorta. The Impella 2.5 and CP deliver up to 2.5 and 3.5 L/min of antegrade flow, respectively.

The IABP (Arrow International, Reading, Pennsylvania, USA) is inserted percutaneously using a femoral approach (7F). The 40 cubic centimetre balloon is positioned in the descending aorta and is rapidly inflated.
during diastole and deflated during systole. Due to
diastolic inflation and displacement of the blood, coro-
nary blood flow and systemic perfusion are improved.

The primary endpoint of our study was absolute pulmo-
nary congestion. This was assessed by calculating the
Halperin score using the characteristic findings of the
patient chest X-ray. Serial computerised chest X-rays
were analysed at baseline (0h), 24hours and 72hours
after implantation of MCS support by a radiologist and
two cardiologists who were blinded to the image order.
Each lung was divided into three regions and were scored
with 0–65 points (0 points= no congestion; 65 points=frank alveolar oedema). The Halperin score is the
summation of all six regional scores and ranges from 0
to 390. Severity of pulmonary congestion was further clas-
sified by the Halperin score such that 0, normal; 10–60,
mild congestion; 61–119, moderate congestion, 120–179,
severe congestion; 180–269, interstitial oedema; ≥270, interstitial and alveolar oedema. Marked pulmonary
decongestion was defined as a reduction of the Halp-
erin score by a minimum of 60 points (10 points for each
region) during the first 72hours. For each time point,
the average of the measurements from the three observers
was used for analysis.

The rate of pneumonia was assessed as a secondary
endpoint. Pneumonia was defined as a new infiltrate
on chest X-ray plus two of three additional criteria: a
temperature greater than 38.5°C or less than 36.0°C,
and a leucocyte count of more than 10x10⁹/L or
less than 3x10⁹/L and new purulent sputum (thick
yellow, green, brown or blood-stained mucus).

Safety endpoints included severe or life-threatening
bleeding and moderate bleeding during the hospital
stay, as assessed according to the Global Use of Strategies
to Open Occluded Coronary Arteries (GUSTO) and
peripheral ischaemic vascular complications requiring
surgical or interventional therapy.

Statistical analysis was performed using SPSS statistics,
V.24 (IBM, Armonk, USA). Categorical variables are
reported as absolute values and percentages, whereas
continuous data are expressed as median with IQR. Cate-
gorical data were compared by χ² test or Fisher’s exact
test. Continuous variables were tested for normal distribu-
tion with the D’Agostino and Pearson omnibus normality
test. Continuous variables were tested for normal distribu-
tion were compared using the Mann-
Whitney U

Univariate and multivariate logistic regression analyses
were used to identify clinical predictors for pulmonary
decongestion and pneumonia. Candidate variables for
the multivariable model were those with a p value<0.1 in
the univariate analysis. All tests were two-tailed, and a p
value of <0.05 was considered to be statistically significant.

RESULTS
We screened 129 patients receiving MCS for CS at our
institution, with 67 patients considered for IABP and
62 patients for Impella support. In the IABP group,
11 patients died during the first 24 hours, 4 patients
were upgraded to ECLS and 2 patients were referred
to the operating theatre for surgical revascularisation.
In the Impella group, nine patients died during the
first 24 hours, two patients were upgraded to ECLS and
one patient did not get a chest X-ray (figure 1). Taken
together, 50 patients in both the Impella and the IABP
groups were enrolled into this study. In 27 patients,
the Impella 2.5 and in 23 patients the Impella CP was
implanted.

In the majority of cases, CS was related to acute myocar-
dial infarction (64% in the Impella group vs 78% in the
IABP group, p=0.181) (table 1). In patients with non-
myocardial infarction, CS was based on decompensated
dilated cardiomypathy in 11 out of 17 patients (65%)
in the Impella group and in 7 out of 11 patients in the
IABP group (63%) (p=0.954). The overall resuscitation
rate was 54%. Patients in both the Impella and the IABP
groups were severely ill, as reflected in the Acute Phys-
iology, Chronic Health Evaluation (APACHE II) score
(22 (17; 26) vs 25.5 (18; 29), respectively, p=0.076) and
the Sequential Organ Failure Assessment (SOFA) score
(9 (7; 11) vs 8.5 (6; 12), p=0.572). There was no major
difference in baseline laboratory values or comorbid-
ties between the groups (table 1). Prophylactic antibi-
otics were given in almost all patients in the study with
no difference between the groups (n=42 in the Impella
group and n=40 in the IABP group, p=0.603). Further,
40 patients (80%) of the Impella group and 38 patients
(76%) of the IABP group were mechanically ventilated
during MCS support (table 2).

During MCS lactate, lactate dehydrogenase, glutamate-
oxaloacetate transaminase and glutamate-pyruvate trans-
aminase decreased in both groups (online supplemental
tables 1 and 2).

At baseline, patients in both groups had similarly
marked pulmonary congestion as indicated by the Halp-
erin score of 233 (168; 280) points in the Impella group
and 200 (164; 250) points in the IABP group (p=0.926).
Further, 64% of the patients in the Impella group and
60% of the patients in the IABP group (p=0.680) had
pulmonary congestion classified as interstitial oedema or
worse using the definition of congestion severity outlined
in the Methods section.

Pulmonary congestion continually declined in
patients while on Impella support as indicated by the
Halperin score (figure 2A) (p=0.001): At 24 hours post-
implantation, the Halperin score declined to 180 (138;
236). At the 72 hours time point, further decrease was
observed (175 (130; 210) points, t24h vs t72h). On the
contrary, in the IABP group pulmonary congestion did not change with time and was 220 (160; 275) points after 24 hours and 205 (154; 250) points after 72 hours (p=0.510) (figure 2B). This distribution of congestion severity also shifted more in the Impella-supported patients. More patients in the Impella group were decongested to a lower classification of congestion using the definition of congestion severity outlined in the Methods section (figure 2C,D). In the Impella group, the percentage of patients with pulmonary

Table 1 Baseline characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Impella (n=50)</th>
<th>IABP (n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65 (56; 72)</td>
<td>73 (64; 77)</td>
<td>0.69</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>38 (76)</td>
<td>35 (70)</td>
<td>0.499</td>
</tr>
<tr>
<td>Acute myocardial infarction, n (%)</td>
<td>33 (66)</td>
<td>39 (78)</td>
<td>0.181</td>
</tr>
<tr>
<td>PCI, n (%)</td>
<td>31 (62)</td>
<td>36 (73)</td>
<td>0.287</td>
</tr>
<tr>
<td>OHCA, n (%)</td>
<td>12 (24)</td>
<td>13 (26)</td>
<td>0.198</td>
</tr>
<tr>
<td>IHCA, n (%)</td>
<td>12 (24)</td>
<td>17 (34)</td>
<td>0.378</td>
</tr>
<tr>
<td>Severely reduced LV function, n (%)</td>
<td>41 (82)</td>
<td>36 (72)</td>
<td>0.235</td>
</tr>
<tr>
<td>PAD, n (%)</td>
<td>10 (20)</td>
<td>6 (12)</td>
<td>0.315</td>
</tr>
<tr>
<td>Prior CABG, n (%)</td>
<td>4 (8)</td>
<td>6 (12)</td>
<td>0.44</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>17 (34)</td>
<td>20 (40)</td>
<td>0.386</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>8 (16)</td>
<td>6 (12)</td>
<td>0.621</td>
</tr>
<tr>
<td>Chronic renal failure, n (%)</td>
<td>29 (58)</td>
<td>27 (54)</td>
<td>0.683</td>
</tr>
<tr>
<td>Serum lactate (mmol/L)</td>
<td>3.2 (1.7; 6.3)</td>
<td>2.9 (1.4; 5.7)</td>
<td>0.415</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.3 (1.1; 1.7)</td>
<td>1.35 (1; 2)</td>
<td>0.539</td>
</tr>
<tr>
<td>Lactate dehydrogenase (U/L)</td>
<td>523 (309; 938)</td>
<td>368 (288; 789)</td>
<td>0.073</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>130.2 (110.3; 140.8)</td>
<td>120.8 (100.7; 140.1)</td>
<td>0.221</td>
</tr>
<tr>
<td>SOFA score</td>
<td>9 (7; 11)</td>
<td>8.5 (6.12)</td>
<td>0.572</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>22 (17; 26)</td>
<td>25.5 (18; 29)</td>
<td>0.076</td>
</tr>
<tr>
<td>Baseline inotropic score</td>
<td>21.6 (5.5; 57.8)</td>
<td>16.5 (0; 37.8)</td>
<td>0.126</td>
</tr>
</tbody>
</table>

Categorical variables are reported as absolute values and percentages, whereas continuous data are expressed as median with IQR.

APACHE II, Acute Physiology, Chronic Health Evaluation; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; IHCA, in-hospital cardiac arrest; LV, left ventricular; OHCA, out-of-hospital cardiac arrest; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; SOFA, Sequential Organ Failure Assessment.

Table 2 Clinical outcomes

<table>
<thead>
<tr>
<th></th>
<th>Impella (n=50)</th>
<th>IABP (n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of support (days)</td>
<td>3 (2; 5)</td>
<td>3 (2; 3)</td>
<td>0.020*</td>
</tr>
<tr>
<td>Peripheral ischaemic complications requiring intervention in hospital</td>
<td>3 (6)</td>
<td>2 (4)</td>
<td>1</td>
</tr>
<tr>
<td>Moderate bleeding in hospital</td>
<td>10 (20)</td>
<td>9 (18)</td>
<td>1</td>
</tr>
<tr>
<td>Life-threatening or severe bleeding in hospital</td>
<td>5 (10)</td>
<td>2 (4)</td>
<td>0.436</td>
</tr>
<tr>
<td>Dialysis, n (%)</td>
<td>26 (52)</td>
<td>20 (40)</td>
<td>0.225</td>
</tr>
<tr>
<td>Mechanical ventilated, n (%)</td>
<td>40 (80)</td>
<td>38 (76)</td>
<td>0.233</td>
</tr>
<tr>
<td>Duration of ventilation (hours)</td>
<td>197 (105; 381)</td>
<td>182 (63; 321)</td>
<td>0.376</td>
</tr>
<tr>
<td>Hospitalisation (days)*</td>
<td>18 (8; 34)</td>
<td>16 (9; 22)</td>
<td>0.155</td>
</tr>
<tr>
<td>ICU length of stay (days)*</td>
<td>12 (4; 18)</td>
<td>8 (2; 17)</td>
<td>0.323</td>
</tr>
</tbody>
</table>

Categorical variables are reported as absolute values and percentages, whereas continuous data are expressed as median with IQR.

*p<0.05 between the groups.

ICU, intensive care unit.
congestion classified as interstitial oedema or worse decreased after 72 hours support to 42% (p=0.026). Patients with the presence of alveolar oedema deceased from 26% at baseline to 2% by 72 hours (p=0.001). Additionally, the distribution of patients with mild, moderate or severe congestion increased from 36% at baseline to 58% by 72 hours (p=0.028). This distribution did not change in the IABP group (60% of the patients with pulmonary congestion classified as interstitial oedema or worse pre-support and post-support, p=1.0).

Marked pulmonary decongestion (reduction of more than 60 points of Halperin score) was achieved in 24 patients with Impella support and in 11 patients with IABP support (47% vs 20%, p=0.006).

Halperin score did not differ between mechanically ventilated patients and non-ventilated patients (online supplemental table 3). The ratio of the partial pressure of oxygen in arterial blood/fraction of inspired oxygen (pO₂/FiO₂) as a marker of oxygenation disturbance did not differ between the Impella group and the IABP group at each time point (pO₂/FiO₂ at t0: p=0.137; pO₂/FiO₂ at t24h: p=0.707; pO₂/FiO₂ at t72h: p=0.823) (online supplemental tables 1 and 2). In the mechanically ventilated patients, there was also no difference in the positive end-expiratory pressure (PEEP) between the Impella and the IABP groups (PEEP at t0: p=0.067; PEEP at t24h: p=0.064; PEEP at t72h: p=0.248).

The Halperin score did neither correlate with pO₂/FiO₂ ratio at the corresponding time points (p=0.881 (t0); p=0.141 (t24h); p=0.969 (t72h)) nor with the PEEP values (p=0.547 (t0); p=0.174 (t24h); p=0.177 (t72h)).

Total fluid balance was net positive in both groups and did not differ between the groups (Impella vs IABP): +0.5 (–0.4; 2.3) L vs +0.9 (0.1; 3.0) L, p=0.702 in the first 24 hours; +0.1 (–0.7; 1.4) L vs +0.1 (–0.6; 0.9) L/24 hours, p=0.98 in the following 48 hours. To identify predictors of pulmonary decongestion, we performed an...
univariate logistic regression analysis with those parameters supposed to be relevant (online supplemental table 4). In the multivariate analysis, Impella support was an independent predictor for pulmonary decongestion in a model including age and percutaneous coronary intervention (table 3).

The incidence of early pneumonia during MCS support was lower in the Impella group compared with the IABP group. Early pneumonia developed in 27 patients with Impella support compared with 37 patients with IABP support (54% vs 74%, p=0.037) (figure 3A). Impella support had a number needed to treat of 5 to avoid one case of early pneumonia. Diagnosis of pneumonia was made after 3.2±1.3 days in the Impella group and after 3.1±1.3 days in the IABP group (p=0.6813). The incidence of pneumonia did not differ between mechanically ventilated patients and non-ventilated patients (online supplemental table 3).

When analysing the full cohort, patients with pulmonary decongestion regardless of the applied MCS device displayed lower incidences of pneumonia: 15 out of 35 patients with pulmonary decongestion developed early pneumonia, whereas 49 out of 65 patients without pulmonary-decongestion developed pneumonia (43% vs 75%, p=0.0012) (figure 3B). To identify predictors of early pneumonia, we performed a univariate logistic regression analysis with those parameters supposed to be relevant (online supplemental table 5). In the multivariate analysis, early pneumonia was independently predicted by failure of pulmonary decongestion during MCS (table 3).

There were no statistically differences between the Impella group and the IABP group regarding rates of moderate or life-threatening bleedings and ischaemic peripheral vascular complications (table 2).

DISCUSSION

We report for the first time the course of pulmonary congestion in patients with CS treated with MCS. Successful decongestion was dependent on the type of MCS and was improved in the Impella group. Furthermore, the rate of early pneumonia was lower in patients with pulmonary decongestion compared with patients without decongestion.

### Table 3

<table>
<thead>
<tr>
<th>Effects of pulmonary decongestion and pneumonia by multivariate regression analysis</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effects of pulmonary decongestion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impella</td>
<td>4.06</td>
<td>1.15 to 14.35</td>
<td>0.030*</td>
</tr>
<tr>
<td>Age</td>
<td>0.96</td>
<td>0.91 to 1.01</td>
<td>0.263</td>
</tr>
<tr>
<td>PCI</td>
<td>0.48</td>
<td>0.14 to 1.66</td>
<td>0.243</td>
</tr>
<tr>
<td>Adjusted R² 0.282</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Effects of pneumonia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impella</td>
<td>0.55</td>
<td>0.22 to 1.34</td>
<td>0.188</td>
</tr>
<tr>
<td>Pulmonary decongestion</td>
<td>0.28</td>
<td>0.12 to 0.70</td>
<td>0.006*</td>
</tr>
<tr>
<td>Adjusted R² 0.156</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p≤0.05.

PCI, percutaneous coronary intervention.

**Figure 3** Incidence of early pneumonia was lower in patients with Impella support/pulmonary decongestion. (A) Incidence of early pneumonia in patients with Impella support compared with intra-aortic balloon pump (IABP) support. (B) Incidence of early pneumonia in patients with markedly pulmonary decongestion compared patients without decongestion regardless of the type of mechanical circulatory support (MCS). "p≤ 0.05,"p≤ 0.001.
In patients with CS, pulmonary congestion is caused by reduced stroke volume, which leads to an increase in pulmonary capillary hydrostatic pressure. Clinically, patients in CS with pulmonary oedema, decreased cardiac index and an elevated pulmonary capillary wedge pressure are classified as ‘cold and wet’ by the Forrester classification and exhibit a high in-hospital mortality of approximately 60%. Our data indicate that patients with CS treated with Impella support displayed significant pulmonary decongestion, while patients treated with IABP did not. Total fluid balance was positive in both groups, thus Impella support might prevent fluid accumulation in the lungs. The decongestion most likely occurs actively by recovery of cardiac function or passively by ventricular unloading both leading to reduced ventricular and concomitant pulmonary capillary hydrostatic filling pressure.

The IABP has been the most common MCS device for years. However, the randomised controlled IABP-SHOCK II trial did not show any beneficial effects of IABP support on short-term or long-term survival in patients with CS.

This has been suggested to result from the inability of this device to improve patient haemodynamics, particularly cardiac output. In contrast, the Impella, a transaortic axial flow pump, provides superior haemodynamic support compared with IABP. This is achieved by directly unloading the left ventricle and augmenting cardiac output and mean arterial pressure which improves end-organ perfusion. Directly unloading the left ventricle decreases ventricular wall stress, external work and myocardial oxygen consumption while enhancing myocardial recovery.

Our study did not capture complete haemodynamic data in this patient population. As these were CS patients in need of emergent treatment, the Swan-Ganz catheter capable of capturing pulmonary capillary wedge pressure was not deployed. However, it is known that the pulmonary capillary wedge pressure decreases in patients on Impella support while IABP does not. Indeed, in a pig model of subacute heart failure, Ishikawa et al directly measured left atrial unloading while on Impella support. Unloading of left atrial pressure haemodynamically favours forward flow through the pulmonary circulation, thereby promoting decongestion. We believe this is the best explanation for the difference we observed here in pulmonary decongestion comparing Impella-treated and IABP-treated patients with CS.

Pappalardo et al demonstrated that the addition of Impella in patients with ECLS was associated with reduced left ventricular pressure, thus preventing worsening of pulmonary oedema. In six patients treated with a combination of ECLS and Impella-CP support, increased total blood flow and a reduction of pulmonary capillary wedge pressure resulted in a reduced right ventricular afterload and in improved gas exchange.

Limited data exist on the incidence of pneumonia in patients with CS. Previous studies have demonstrated that pneumonia is partly responsible for the acute worsening of pre-existing cardiac comorbidities. Data have shown that pneumonia can lead to new cardiac events like acute coronary syndrome and reduced myocardial function due to increased coronary and systemic inflammation as well as vasoconstriction, endothelial dysfunction and increased metabolic demand. In this context, the development of pneumonia and sepsis adds to the high risk of mortality in patients with CS. Thus, optimal management of these complications may translate into improved survival.

This study shows that the rate of successful pulmonary decongestion was significantly higher in patients treated with the Impella compared with those treated with IABP. Successful pulmonary decongestion could prevent the incidence of early pneumonia.

It is important to emphasise that the present study focused on the development of early pneumonia, which occurred during the first days of MCS support. We chose this as an endpoint because this type of pneumonia is associated with pulmonary oedema. As pulmonary congestion can be mitigated by the left ventricular unloading, this made of a more ideal target for investigation. We also hypothesised that the above described effective decompression of the left ventricle, left atrium and the resulting pulmonary decongestion in patients on Impella support might promote alveolar bacterial clearance and, consequently, leads to less early pneumonia.

While we observed a numerical trend in 90-day survival of patients with Impella support, our study was not powered to detect a mortality difference. It remains unclear whether early pulmonary decongestion by MCS and lower risk of pneumonia affects survival in patients with CS. In a retrospective analysis of patients with myocardial infarction-related CS, the use of an Impella device was not associated with lower 30-day mortality compared with matched patients from the IABP-SHOCK II trial treated with an IABP or medical therapy. The prospective randomised DanGer shock trial is ongoing and compares the outcome of patients with myocardial infarction-related CS treated by Impella versus medical therapy.

Our study is limited by the retrospective study design and the inherent limitations of such an approach. Our study did not capture complete haemodynamic data in this patient population, which could underline the mechanism of the observed effects.

In conclusion, in this retrospective observational analysis, pulmonary decongestion may facilitate treatment of pneumonia in patients with CS. Left ventricular unloading by Impella device might support pulmonary decongestion, although a larger prospective trial in this patient population is required to decipher the potential prognostic value of MCS-induced decongestion on the development of pneumonia.

Contributors SH: data curation, validation, formal analysis, investigation, writing—original draft. AU: data curation, validation, investigation. JH: data curation, validation, investigation. CJ: data curation, validation, investigation. MK:...
supervision; writing—review and editing. RW: supervision, writing—review and editing. PH: formal analysis, conceptualisation; project administration; writing—original draft, writing—review and editing. Conception and design: SH, PH, RW, MK. Data collection: SH, AU, JH, CJ, RW, PH. Data analysis and interpretation: SH, AU, PH. Drafting of the article: SH, MK, PH. Critical revision and final approval: all authors.

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Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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REFERENCES
23 Lim HS. The effect of Impella CP on cardiopulmonary physiology during venoarterial extracorporeal membrane oxygenation support. Artif Organs 2017;41:1109–12.
SUPPLEMENTAL MATERIAL
**Supplemental Table 1.** Clinical follow up of the Impella group. Continuous data are expressed as median with interquartile range. * indicates p ≤ 0.05 among the time points.

<table>
<thead>
<tr>
<th>Metric</th>
<th>t0</th>
<th>t24</th>
<th>t72</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum lactate (mmol/L)</td>
<td>3.2 (1.7; 5.9)</td>
<td>1.6 (1.2; 3.2)</td>
<td>1.5 (1.1; 2.1)</td>
<td>*0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.35 (7.27; 7.43)</td>
<td>7.41 (7.34; 7.46)</td>
<td>7.43 (7.39; 7.46)</td>
<td>*0.001</td>
</tr>
<tr>
<td>Laktatdehydrogenase (U/l)</td>
<td>515 (305; 937)</td>
<td>1266 (895; 1549)</td>
<td>673 (661; 1624)</td>
<td>*0.011</td>
</tr>
<tr>
<td>C-reactive protein (mg/dl)</td>
<td>3.6 (0.7; 11.3)</td>
<td>10.5 (6.4; 15.5)</td>
<td>14.7 (8.6; 14.7)</td>
<td>*0.022</td>
</tr>
<tr>
<td>Leukocytes (1000x/µl)</td>
<td>14.8 (10.9; 19.1)</td>
<td>12.9 (10; 16.5)</td>
<td>13.1 (9.6; 16.1)</td>
<td>0.163</td>
</tr>
<tr>
<td>GOT (U/l)</td>
<td>166 (68; 468)</td>
<td>560 (233; 1649)</td>
<td>350 (117; 1189)</td>
<td>*0.018</td>
</tr>
<tr>
<td>GPT (U/l)</td>
<td>98 (96; 437)</td>
<td>192 (72; 1175)</td>
<td>191 (63; 878)</td>
<td>0.106</td>
</tr>
<tr>
<td>Bilirubine (mg/dl)</td>
<td>0.8 (0.46; 1.1)</td>
<td>1.9 (0.93; 2.59)</td>
<td>1.51 (1.06; 2.73)</td>
<td>*0.019</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>53 (36; 71)</td>
<td>39 (24; 66)</td>
<td>41 (27; 62)</td>
<td>0.167</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.2 (11.3; 14.7)</td>
<td>10.3 (8.7; 11.8)</td>
<td>9.8 (8.3; 10.5)</td>
<td>*0.001</td>
</tr>
<tr>
<td>Inotropic Score</td>
<td>21.57 (5.51;)</td>
<td>29.74 (7.75;)</td>
<td>11.85 (4.22;)</td>
<td>0.073</td>
</tr>
<tr>
<td>pO₂/FiO₂ (mmHg)</td>
<td>210 (172; 261)</td>
<td>231 (216; 294)</td>
<td>247 (161; 430)</td>
<td>0.487</td>
</tr>
<tr>
<td>PEEP in ventilated patients (mmHg)</td>
<td>9 (8.1; 9.9)</td>
<td>8 (7.8; 9.5)</td>
<td>8 (7.6; 9.5)</td>
<td>0.902</td>
</tr>
</tbody>
</table>

GFR = Glomerular filtration rate. GOT = Glutamate-Oxaloacetate Transaminase. GPT = Glutamate-Pyruvate Transaminase. pO₂ = partial pressure of oxygen in arterial blood. FiO₂ = Fraction of inspired oxygen. PEEP = positive end-expiratory pressure.
**Supplemental Table 2.** Clinical follow up of the IABP group. Continuous data are expressed as median with interquartile range. * indicates \( p \leq 0.05 \) among the time points.

<table>
<thead>
<tr>
<th></th>
<th>t0</th>
<th>t24</th>
<th>t72</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum lactate (mmol/L)</td>
<td>2.9 (1.4; 5.7)</td>
<td>1.6 (1.2; 2.3)</td>
<td>1.3 (1; 1.8)</td>
<td>*0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.38 (7.30; 7.43)</td>
<td>7.42 (7.34; 7.47)</td>
<td>7.43 (7.37; 7.45)</td>
<td>0.357</td>
</tr>
<tr>
<td>Laktatdehydrogenase (U/l)</td>
<td>368 (288; 789)</td>
<td>797 (356; 1135)</td>
<td>457 (330; 911)</td>
<td>0.052</td>
</tr>
<tr>
<td>C-reactive protein (mg/dl)</td>
<td>3.5 (1.1; 10.3)</td>
<td>9.7 (3.6; 15.4)</td>
<td>14.7 (8.8; 24.7)</td>
<td>*0.001</td>
</tr>
<tr>
<td>Leukocytes (1000x/µl)</td>
<td>12.7 (9.8; 16)</td>
<td>11.6 (8.8; 14.8)</td>
<td>10.4 (7.7; 13.4)</td>
<td>*0.010</td>
</tr>
<tr>
<td>GOT (U/l)</td>
<td>97 (42; 227)</td>
<td>171 (58; 662)</td>
<td>201 (54; 461)</td>
<td>0.347</td>
</tr>
<tr>
<td>GPT (U/l)</td>
<td>58 (28; 136)</td>
<td>70 (33; 196)</td>
<td>106 (43; 703)</td>
<td>0.095</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>0.66 (0.34; 1.28)</td>
<td>0.8 (0.49; 1.36)</td>
<td>0.88 (0.64; 1.41)</td>
<td>0.085</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>45 (25; 60)</td>
<td>47 (27; 65)</td>
<td>47 (32; 60)</td>
<td>0.727</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>12.8 (10.7; 14.1)</td>
<td>11.1 (9.4; 12.8)</td>
<td>10.8 (9.2; 11.7)</td>
<td>*0.001</td>
</tr>
<tr>
<td>Inotropic Score</td>
<td>16.5 (0; 37.82)</td>
<td>15.32 (4.66; 28.66)</td>
<td>14.7 (3.87; 40.48)</td>
<td>*0.010</td>
</tr>
<tr>
<td>pO2/ FiO2 (mmHg)</td>
<td>237 (161; 292)</td>
<td>254 (157; 331)</td>
<td>257 (218; 321)</td>
<td>0.188</td>
</tr>
<tr>
<td>PEEP in ventilated</td>
<td>8 (7.1; 11.1)</td>
<td>8 (6.9; 10.5)</td>
<td>8 (6.0; 9.2)</td>
<td>0.486</td>
</tr>
</tbody>
</table>
GFR = Glomerular filtration rate, GOT = Glutamate-Oxaloacetate Transaminase, GPT = Glutamate-Pyruvate Transaminase. \( pO_2 \) = partial pressure of oxygen in arterial blood. \( FiO_2 \) = Fraction of inspired oxygen. PEEP = positive end-expiratory pressure
**Supplemental Table 3:** Characteristics of mechanically-ventilated patients and non-ventilated patients.

<table>
<thead>
<tr>
<th></th>
<th>Mechanically ventilated</th>
<th>Non-ventilated</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=78</td>
<td>n=22</td>
<td></td>
</tr>
<tr>
<td>Halperin Score t0</td>
<td>215 (199; 230)</td>
<td>220 (172; 249)</td>
<td>0.943</td>
</tr>
<tr>
<td>Halperin Score t24h</td>
<td>210 (195; 213)</td>
<td>205 (158; 221)</td>
<td>0.546</td>
</tr>
<tr>
<td>Halperin Score t72h</td>
<td>183 (171; 199)</td>
<td>195 (151; 214)</td>
<td>0.853</td>
</tr>
<tr>
<td>Decongestion n, (%)</td>
<td>27 (35)</td>
<td>8 (36)</td>
<td>0.879</td>
</tr>
<tr>
<td>pO$_2$/FiO$_2$ at t0 (mmHg)</td>
<td>218 (187; 259)</td>
<td>209 (167; 278)</td>
<td>0.452</td>
</tr>
<tr>
<td>pO$_2$/FiO$_2$ at t24h (mmHg)</td>
<td>246 (225; 286)</td>
<td>252 (212; 292)</td>
<td>0.865</td>
</tr>
<tr>
<td>pO$_2$/FiO$_2$ at t72h (mmHg)</td>
<td>247 (190; 358)</td>
<td>255 (221; 312)</td>
<td>0.934</td>
</tr>
<tr>
<td>Pneumonia n, (%)</td>
<td>50 (64)</td>
<td>14 (64)</td>
<td>0.832</td>
</tr>
</tbody>
</table>

Categorical variables are reported as absolute values and percentages, whereas continuous data are expressed as median with interquartile range. \( pO_2 \) = *partial pressure of oxygen in arterial blood*. \( FiO_2 \) = *Fraction of inspired oxygen*. \( PEEP \) = *positive end-expiratory pressure*.
**Supplemental Table 4.** Univariate logistic regression analysis for pulmonary decongestion. * indicates $p \leq 0.05$.

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.95</td>
<td>0.90-0.99</td>
<td>*0.021</td>
</tr>
<tr>
<td>Impella 2.5/CP</td>
<td>3.27</td>
<td>1.37-7.81</td>
<td>*0.008</td>
</tr>
<tr>
<td>Impella CP</td>
<td>0.51</td>
<td>0.166-1.592</td>
<td>0.249</td>
</tr>
<tr>
<td>MCS support length</td>
<td>1.31</td>
<td>0.98-1.64</td>
<td>0.201</td>
</tr>
<tr>
<td>Reduced left ventricular function</td>
<td>0.83</td>
<td>0.23-2.94</td>
<td>0.768</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0.71</td>
<td>0.18-2.85</td>
<td>0.630</td>
</tr>
<tr>
<td>GFR</td>
<td>0.99</td>
<td>0.97-1.02</td>
<td>0.581</td>
</tr>
<tr>
<td>Total fluid balance t24h</td>
<td>1.00</td>
<td>0.99-1.00</td>
<td>0.277</td>
</tr>
<tr>
<td>Total fluid balance t72h</td>
<td>1.01</td>
<td>0.98-1.01</td>
<td>0.577</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>1.50</td>
<td>0.43-5.23</td>
<td>0.525</td>
</tr>
<tr>
<td>Central venous pressure</td>
<td>0.98</td>
<td>0.87-1.11</td>
<td>0.756</td>
</tr>
<tr>
<td>PCI</td>
<td>0.33</td>
<td>0.11-1.01</td>
<td>0.056</td>
</tr>
</tbody>
</table>

CI = confidence interval; OR = Odds ratio; GFR = Glomerular filtration rate; PCI = Percutaneous coronary intervention.
**Supplemental Table 5.** Univariate logistic regression analysis for the risk of pneumonia. * indicates $p \leq 0.05$.

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.00</td>
<td>0.97-1.05</td>
<td>0.660</td>
</tr>
<tr>
<td>Pulmonary decongestion</td>
<td>0.25</td>
<td>0.10-0.59</td>
<td>*0.002</td>
</tr>
<tr>
<td>Impella 2.5/CP</td>
<td>0.42</td>
<td>0.18-0.96</td>
<td>*0.039</td>
</tr>
<tr>
<td>Impella CP</td>
<td>1.21</td>
<td>0.39-3.69</td>
<td>0.741</td>
</tr>
<tr>
<td>MCS support length</td>
<td>1.01</td>
<td>0.83-1.31</td>
<td>0.702</td>
</tr>
<tr>
<td>GFR</td>
<td>0.99</td>
<td>0.97-1.01</td>
<td>0.238</td>
</tr>
<tr>
<td>Total fluid balance t24h</td>
<td>1.00</td>
<td>0.99-1.01</td>
<td>0.308</td>
</tr>
<tr>
<td>Total fluid balance t72h</td>
<td>1.00</td>
<td>1.00-1.00</td>
<td>0.681</td>
</tr>
<tr>
<td>Central venous pressure</td>
<td>1.07</td>
<td>0.95-1.20</td>
<td>0.269</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1.37</td>
<td>0.36-5.19</td>
<td>0.641</td>
</tr>
<tr>
<td>Reduced left ventricular function</td>
<td>0.60</td>
<td>0.16-2.28</td>
<td>0.445</td>
</tr>
<tr>
<td>PCI</td>
<td>1.75</td>
<td>0.55-5.56</td>
<td>0.343</td>
</tr>
</tbody>
</table>

CI = confidence interval; OR = Odds ratio; GFR = Glomerular filtration rate; PCI = Percutaneous coronary intervention.