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# Unloading of the Left Ventricle During Venoarterial Extracorporeal Membrane Oxygenation Therapy in Cardiogenic Shock

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## ABSTRACT

**OBJECTIVES** This report relates the authors' ongoing experience with percutaneous left ventricular (LV) unloading by using a transaortic LV assist device in combination with venoarterial extracorporeal membrane oxygenation (VA-ECMO) and provides an in-depth analysis of the hemodynamic benefit of this approach.

**BACKGROUND** VA-ECMO is increasingly used in cases of severe cardiogenic shock. However, increase in afterload with subsequent LV overload is a major drawback of VA-ECMO.

**METHODS** Consecutive patients were treated with a transaortic LV assist device in addition to VA-ECMO for cardiogenic shock. The primary endpoint was 30-day all-cause mortality. Additional endpoints included weaning from VA-ECMO and safety endpoints.

**RESULTS** Between September 2013 and January 2018, 106 patients were treated with percutaneous LV unloading, using a transaortic LV assist device in combination with VA-ECMO. Successful weaning from VA-ECMO support was achieved in 51.9% of all patients. In the overall cohort, survival at day 30 was 35.8%, which was higher than predicted by the SAVE score (20%) or by the SAPS-II score (6.9%). Right heart catheterization indicated a marked decrease of PCWP after addition of the device to VA-ECMO.

**CONCLUSIONS** The strategy of percutaneous LV unloading using a transaortic LV assist device in combination with VA-ECMO improved outcome in an all-comers cohort compared to established risk scores. A prospective, randomized study is needed to further investigate this approach. (J Am Coll Cardiol HF 2018;6:1035–43) © 2018 by the American College of Cardiology Foundation.

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is established for treatment of severe cardiogenic shock (CS) (1). One of the main mechanisms contributing to mortality in CS is the impairment of end-organ perfusion due to the inability of the heart to generate an adequate cardiac output with consecutive low arterial and high pulmonary and central venous pressures. Although VA-ECMO therapy can reduce central venous pressure and improve end-organ perfusion, it also causes a marked increase in left ventricular (LV) afterload (2) due to a retrograde perfusion of the aorta, which may inhibit aortic valve opening and suppress LV ejection. Consequently, LV

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**ABBREVIATIONS AND ACRONYMS**

**CS** = cardiogenic shock

**ECMELLA** = Impella used in combination with venoarterial extracorporeal membrane oxygenation

**LV** = left ventricle

**VA-ECMO** = venoarterial extracorporeal membrane oxygenation

end-diastolic and pulmonary venous pressures increase, and the already failing myocardium can be further impaired by LV diastolic distension. Accordingly, one early sign of significantly impaired LV function and distension is loss of arterial pulsatility against the VA-ECMO flow. In clinical practice, pulmonary edema, LV dilation, LV stasis, and finally LV thrombus formation may occur as therapy-limiting consequences of increased LV afterload (3).

To avoid these complications, an LV venting strategy should be used. The authors recently proposed the use of a percutaneous, retrograde, and transaortic LV assist device (Impella, Abiomed, Danvers, Massachusetts) to achieve LV unloading during VA-ECMO support. This strategy was termed "ECMELLA" (4). The Impella is a percutaneously deployed, microaxial flow pump which pumps blood from the LV to the aortic root, thus reducing LV afterload and consecutively decreasing LV end-diastolic and pulmonary venous pressures (5). Using a propensity-matched analysis, a mortality reduction and superiority of other outcome measurements were shown in patients treated with ECMELLA compared to that in patients treated with VA-ECMO alone (4).

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The current study reviews the pathophysiology and reports the authors' ongoing experience with the ECMELLA approach for treatment of severe cardiogenic shock.

## METHODS

The present study follows tenets of the Declaration of Helsinki and was approved by the local ethics committee.

**STUDY DESIGN.** We report outcomes for all consecutive patients who were treated with VA-ECMO in combination with Impella (ECMELLA) at our institution. Laboratory and clinical data were collected following a standardized protocol and entered into a dedicated database. In addition to the mechanical circulatory support strategy described below, all patients received optimal medical therapy in accordance with guidelines and local practice.

**MECHANICAL CIRCULATORY SUPPORT STRATEGY.** The technical aspects of the ECMELLA approach have been described previously (4). Briefly, both VA-ECMO and the Impella (Impella CP or Impella 2.5) are implanted percutaneously in contralateral femoral arteries. After implantation of both devices, patients were transferred to our cardiovascular intensive care unit. Chest radiography or echocardiography was performed at least once per day to assess device position. The Impella was repositioned as needed to ensure the inflow port was approximately 4 cm below the aortic valve and that the outflow port was above the aortic valve as recommended by the manufacturer. Targeted VA-ECMO flow was 5 l/min for at least the first 24 h depending on the patient's need. Impella rotational speed was titrated up to achieve best unloading of the LV as assessed by echocardiography. There was no mandatory protocol for sedation or mechanical ventilation. The aim was to achieve the patient's spontaneous breathing and a conscious state as soon as possible. General medical treatment with inotropes and other supportive therapies was performed according to clinical needs based on current guidelines.

In case of hemodynamic stabilization (i.e., normalization of lactate levels and improvement of LV function on echocardiography), VA-ECMO flow was progressively reduced, and the patients were weaned as soon as possible. During weaning from VA-ECMO, the Impella support was increased to support the patient's blood pressure and cardiac output as needed. Inotropes were reduced to a minimum in this period, if possible. After successful weaning from VA-ECMO, the patient was weaned from the Impella through a stepwise reduction of Impella flow. In case of severe myocardial dysfunction without signs of recovery during the initial 5 to 7 days, the transition from a femoral access Impella CP or 2.5 to a subclavian access Impella 5.0 was performed. This transition allows for prolonged Impella treatment and for patient mobilization. In case there was still no myocardial recovery with prolonged Impella support, transition to a long-term LV assist device was performed, barring any contraindication to such therapy.

**OUTCOME MEASUREMENTS.** The primary endpoint of this study was 30-day all-cause mortality. The secondary endpoint was successful weaning from VA-ECMO. Safety endpoints included hypoxic brain damage, intracerebral bleeding, stroke (defined by positive neurologic symptoms and a positive computer tomography scan), vascular complication requiring an intervention (any surgical or catheter-based intervention), abdominal compartment with the need for laparotomy, mesenteric ischemia with the need for laparotomy, bleeding requiring an intervention (any surgical or catheter-based intervention), hemolysis (increase in lactate dehydrogenase serum levels above 1,000 U/l associated with a decrease of haptoglobin below 0.2 g/l in 2 consecutive blood samples within 24 h), sepsis (systemic inflammatory response syndrome and clinical signs of infection such as positive blood cultures or increased procalcitonin)

**TABLE 1 Baseline Parameters of 30-Day Survivors and 30-Day Nonsurvivors**

| | All Patients (N = 106) | Survivors (n = 38) | Nonsurvivors (n = 68) | p Value |
|---|---|---|---|---|
| Age, yrs | 53.0 (48.0, 65.0) | 50.0 (43.0, 54.2) | 59.5 (49.0, 67.0) | <0.01 |
| Males | 87 (82.1) | 26 (68.4) | 61 (89.7) | <0.01 |
| Cause of cardiogenic shock | | | | |
| Myocarditis | 10 (9.4) | 6 (15.8) | 4 (5.9) | 0.16 |
| Acute coronary syndrome | 63 (59.4) | 23 (60.5) | 40 (58.8) | 1.00 |
| Decompensated heart failure | 21 (19.8) | 8 (21.1) | 13 (19.1) | 0.80 |
| Sudden cardiac death | 9 (8.5) | 1 (2.6) | 8 (11.8) | 0.15 |
| Cardiopulmonary resuscitation | 87 (82.0) | 29 (76.3) | 58 (85.3) | 0.30 |
| Out-of-hospital CPR | 56 (52.8) | 17 (44.7) | 39 (57.4) | 0.23 |
| Duration of CPR | 45.0 (20.0, 90.0) | 20.0 (10.0, 41.7) | 60.0 (30.0, 101.7) | <0.01 |
| CPR during VA-ECMO implantation | 51 (48.1) | 11 (28.9) | 40 (58.8) | <0.01 |
| Hemodynamics before VA-ECMO | | | | |
| Mean arterial pressure, mm Hg | 50.5 (44.9, 60.0) | 53.0 (45.7, 65.0) | 50.0 (40.7, 56.0) | 0.17 |
| Systolic arterial pressure, mm Hg | 70.0 (55.0, 85.2) | 74.0 (56.0, 88.3) | 66.0 (52.7, 76.7) | 0.15 |
| Diastolic arterial pressure | 44.0 (38.0, 52.1) | 46.0 (39.0, 60.7) | 40.0 (30.0, 50.0) | 0.11 |
| Heart rate, beats/min | 102.0 (80.7, 120.0) | 110.0 (98.3, 123.7) | 91.0 (76.7, 110.3) | 0.04 |
| Lactate before VA-ECMO, mmol/l | 9.7 (5.0, 15.0) | 9.1 (4.5, 13.8) | 10.0 (6.0, 15.8) | 0.18 |
| pH before VA-ECMO | 7.1 (7.0, 7.3) | 7.3 (7.0, 7.3) | 7.1 (7.0, 7.3) | 0.04 |
| Creatinine clearance before VA-ECMO | 40.6 (27.0, 59.9) | 57.9 (37.5, 77.4) | 35.1 (25.2, 49.2) | <0.01 |
| SAVE score, points | −12.5 (−17.0, −8.0) | −8.5 (−13.1, −5.8) | −14.0 (−18.0, −10.4) | <0.01 |
| SAPS-II score; points | 81.0 (74.0, 88.6) | 77.0 (62.7, 81.0) | 85.0 (79.0, 91.0) | <0.01 |

Values are median (1st, 3rd quartile) or n (%). Baseline parameters of 30-day survivors and 30-day nonsurvivors of cardiogenic shock treated with Impella in addition to VA-ECMO.

CPR = cardiopulmonary resuscitation; VA-ECMO = venoarterial extracorporeal membrane oxygenation therapy; SAPS-II = Simplified Acute Physiology Score II; SAVE = Survival After Veno-arterial extracorporeal membrane oxygenation score.

(6), and need for any renal replacement therapy during the hospital stay. Lactate levels were measured from days 1 to 5 after VA-ECMO implantation.

**STATISTICS.** Continuous variables were described as median (1st, 3rd quartile) and categorical variables as absolute numbers and percentages. Student's *t*-test (for continuous variables) or Fisher exact test (for categorical variables) was used for between-group comparisons. Thirty-day all-cause mortality rates were estimated using Kaplan-Meier analysis, with the date of the first device implanted defined as the starting point. Any death within 30 days was counted as an event, regardless of whether the patient had been weaned from VA-ECMO or not. Patients who were weaned from VA-ECMO or who went on to durable LV assist device were not censored. Outcome measurements between groups were compared using the log-rank test. All computations were performed using R version 3.5.1. software (R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

**PATIENTS.** ECMELLA, the concept of adding a transaortic LV assist device to a patient receiving VA-ECMO therapy, was first used in September 2013 and was initially used in selected patients who had experienced severe cardiogenic shock and impaired LV function. Data for the first 19 patients were published previously (4). Since 2015, this approach has become the standard of care at our institution, with a total of 106 patients treated as of January 2018. A total of 82.0% of these patients were males of 52.0 (1st, 3rd quartile: 48.0, 65.0) years of age. Primary causes of cardiogenic shock were myocardial infarction (59.4%) and acute decompensated heart failure (19.8%); 82% of patients had had cardiac arrest before onset of mechanical circulatory support devices. Additionally, 48.1% of patients had a refractory cardiac arrest with the need for VA-ECMO implantation during ongoing cardiopulmonary resuscitation (eCPR). High lactate levels and a low pH were observed in all patients. Detailed baseline characteristics are summarized in Table 1. During the study period, there were 5 cases in which implantation of a transaortic LV assist device in addition to VA-ECMO was intended but could not be performed (2 cases of severe peripheral artery disease, 2 cases of severe aortic valve stenosis, 1 case of aortic valve endocarditis).

**IMPLANTATION CHARACTERISTICS AND CLINICAL COURSE.** In 60.3% of the cases, VA-ECMO and Impella were implanted simultaneously during the index procedure. This group of patients represents a

**TABLE 2 Characteristic of Mechanical Circulatory Support**

| | All Patients (N = 106) | Survivors (n = 38) | Nonsurvivors (n = 68) | p Value |
|---|---|---|---|---|
| Onset of shock to VA-ECMO, h | 5.0 (2.0, 1.0) | 5.0 (2.9, 10.5) | 4.0 (2.0, 10.0) | 0.75 |
| Timing of Impella implantation | | | | |
| Impella first, VA-ECMO staged | 22 (20.8) | 9 (23.7) | 13 (19.1) | 0.62 |
| VA-ECMO first, Impella staged | 20 (18.9) | 4 (10.5) | 16 (23.5) | 0.12 |
| Concomitant implantation | 64 (60.3) | 25 (65.8) | 39 (57.4) | 0.42 |
| Initial Impella device | | | | |
| Impella 2.5 | 23 (21.7) | 9 (23.7) | 14 (20.6) | 0.81 |
| Impella CP | 83 (78.3) | 29 (76.3) | 54 (79.4) | 0.81 |
| Duration of VA-ECMO support, days | 6.0 (3.0, 10.1) | 9.0 (5.0, 15.1) | 4.0 (1.0, 9.0) | <0.01 |

Values are median (1st, 3rd quartile) or n (%). Characteristic of mechanical circulatory support in 30-day survivors and 30-day nonsurvivors of cardiogenic shock treated with Impella in addition to VA-ECMO.

Abbreviations are as in Table 1.

cohort with severe cardiogenic shock and impaired LV function; 59.4% of these patients were cases of eCPR. In 20.8% of the cases, the Impella was the first device implanted with a staged VA-ECMO implantation. These patients were initially deemed to be sufficiently treated using only a transaortic LV assist device strategy. However, these patients deteriorated and were upgraded to ECMELLA. In the remaining 18.9% of patients, VA-ECMO was the first device implanted, followed by a staged Impella implantation. These patients either received VA-ECMO implantation at another hospital or were later upgraded with a transaortic LV assist device at our institution (35.0%). In the remaining patients, Impella implantation was delayed because of urgently needed diagnostics or interventions after VA-ECMO implantation (Table 2).

An Impella CP was used in 78.3% of the cases. Upon implantation of the VA-ECMO, the median SAVE score was −12.5 (1st, 3rd quartile: −17.0, −8.0), and the median SAPS-II score was 81.0 (1st quartile, 3rd quartile: 74.0, 88.6), indicating a survival rate of 20% and 6.9%, respectively. Right-heart catheterization data were available from 3 patients during the index procedure. Original tracings from 1 patient shows that pulmonary capillary wedge pressure (PCWP) increased above its already high level with the initiation of VA-ECMO support. With the addition of Impella, PCWP decreased rapidly (Figure 1). Similar PCWP reductions were noted in all 3 patients for which data were available. Overall, lactate levels were slightly lower in survivors (Figure 2). The median duration of VA-ECMO support was 6.0 (1st, 3rd quartile: 3.0, 10.1) days with a median duration of Impella support of 6.0 (1st, 3rd quartile: 2.7, 12.0) days.

**OUTCOME AND COMPLICATIONS.** Successful weaning from VA-ECMO support was achieved in 51.9% of the patients. In 12 patients (22%), an upgrade from an Impella CP to an Impella 5.0 was necessary to wean from VA-ECMO. Of these 12 patients, 5 received implants with a durable LV assist device, whereas the other 7 patients could be weaned from Impella 5.0. Among the remaining patients successfully weaned from VA-ECMO, 7 underwent direct implantation with a durable LV assist device. There were no heart transplantations in the overall cohort. Weaning from VA-ECMO was less often observed after eCPR (35.3% vs. 67.3%, respectively; $p < 0.01$). The 30-day all-cause mortality in the overall cohort was 64.2%, with a significantly higher mortality rate in patients with eCPR (Figure 3). Overall survival was higher (35.8%) than predicted by either the SAVE or SAPS-II score. Patients not weaned from VA-ECMO had a significantly higher rate of 30-day all-cause mortality than those who were successfully weaned from VA-ECMO (98.0% vs. 32.7%, respectively; $p < 0.01$).

Although there was a high incidence of vascular complications and bleedings requiring an intervention, both complications were equally divided among survivors and nonsurvivors. Hypoxic brain damage was more often prevalent in nonsurvivors, whereas sepsis was significantly more often present in survivors. There was a trend toward a higher incidence of stroke, abdominal compartment, mesenteric ischemia, and hemolysis among nonsurvivors. Detailed data for complications are displayed in Table 3.

## DISCUSSION

The prime finding of this study was that addition of an Impella to VA-ECMO (ECMELLA) for treatment of severe cardiogenic shock was feasible for patients in an all-comers cohort. Although mortality remained high, the ECMELLA approach resulted in better survival rates as predicted by 2 different risk scores.

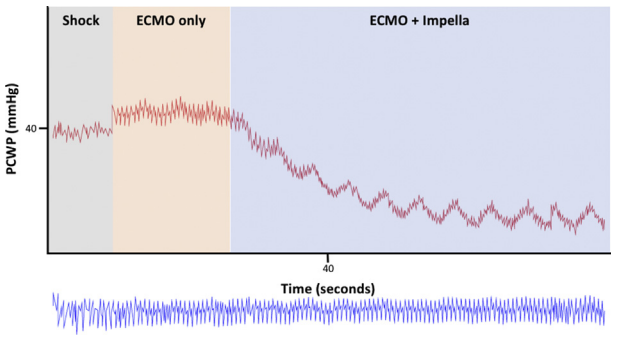
The principles underlying the impact of VA-ECMO on systemic hemodynamics, LV mechanics, and LV energetics are well documented (7), well appreciated in the clinical setting, and validated in preclinical studies (8) (Figure 4). The fundamental issue with VA-ECMO alone is that venous return to the LV (through residual flow through the pulmonary circuit, venous return from the bronchial circulation, and Thebesian flow) must exit the LV through the aortic valve; however, the increased systemic flow provided by VA-ECMO and resultant increased blood pressure (both beneficial effects for oxygen delivery to the end organs) must be overcome by the weak LV. In patients with insufficient contractile reserve, LV preload, end-diastolic pressure, and thus PCWP increase until, through the Frank-Starling mechanism, LV stroke volume matches venous return to the LV (Figure 4).

Thus, as a consequence of LV contractile dysfunction, pulmonary venous pressure increases, and this increase is proportional to VA-ECMO flow. Therefore, a support strategy for cardiogenic shock must not only address improved oxygen delivery to the end organs but must also provide unloading of the LV. In addition to a reduction in pulmonary venous pressure, cardiac unloading reduces myocardial oxygen demand and has the potential to reduce myocardial infarct size (9–11). Furthermore, reductions of pulmonary venous pressure (relief of pulmonary edema) enhances arterial blood oxygen content and reduces risks of other pulmonary complications (e.g., infection, acute respiratory distress syndrome, and others).

In addition to simply reducing VA-ECMO flow (which is not always clinically possible), there are at least 7 different LV unloading strategies that have been used during VA-ECMO support (12), including positive inotropic agents, pharmacologic afterload reduction (i.e., vasodilators), intra-aortic balloon pumping (13–15), atrial septostomy (16–18), percutaneous transseptally placed left atrial vent (19), surgical LV vent (12,20,21), and use of the Impella (4,22–27). Most VA-ECMO patients receive pharmacologic agents as standard of care, but these strategies tend to increase myocardial workload, heart rate, and oxygen consumption and should thus be used with caution. Of all other options, Impella support appears to provide the greatest and most direct means of LV decompression, while simultaneously providing additional active blood flow to the systemic circulation (**Figures 4C and 4D**). This allows for early partial weaning of VA-ECMO and, as illustrated in our patients, full VA-ECMO weaning even if continued circulatory support is needed. Finally, potential permanent aortic valve closure during VA-ECMO support represents a risk of blood stagnation and thrombus formation in the LV, left atrium, and aortic root (27). Of note, LV maximum pressure decreased with the addition of Impella due to lower LV pre- and afterload. Consequently, the aortic valve would not open during systole, in case the aortic pressure was higher than LV maximum pressure (**Figures 4C and 4D**). In that case, the arterial pressure signal was a flat line, but still there was no stagnation of blood in either the LV or aortic root, and the risk of thrombus formation is decreased. A flat arterial pressure signal during ECMELLA, therefore, reflects maximal LV unloading, whereas a flat arterial pressure signal during VA-ECMO alone reflects maximal LV overload.

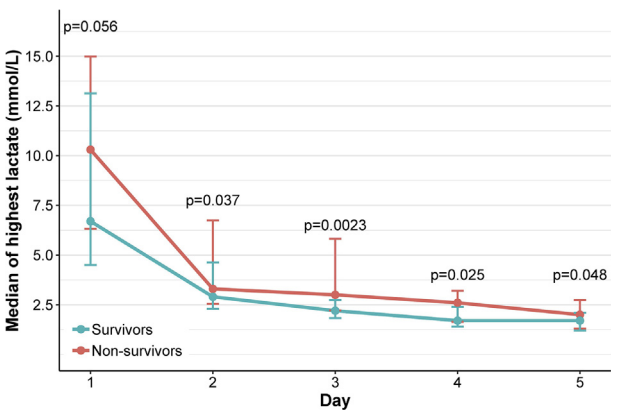
Several case reports and case series reported outcomes for the use of Impella to decompress the LV in CS patients undergoing VA-ECMO alone and in a canine model of CS (2). Additionally, Lim et al. (28) showed that addition of Impella to VA-ECMO reduced pulmonary pressures (including PCWP) and improved right ventricular function in a series of 6 CS patients (28). Donker et al. (29) performed a closed-loop real-time computer model of CS. In their model, VA-ECMO therapy led to LV overload (expressed as an increase in LV end-diastolic volume and PCWP), which was then compensated by addition of Impella with subsequent reduction in LV end-diastolic volume and PCWP. The present authors were the first to compare CS patients treated with the ECMELLA approach with those undergoing VA-ECMO only (4). In a propensity

**FIGURE 1 Hemodynamic Effect of Impella Support in Combination With VA-ECMO**




With the initiation of VA-ECMO, PCWP **(red)** increased above pre-support levels, reaching ~45 mm Hg. Upon initiation of Impella support, PCWP decreased rapidly and significantly. ECG shown in **blue**. ECG = electrocardiography; PCWP = pulmonary wedge pressure; VA-ECMO = venoarterial extracorporeal membrane oxygenation therapy.

**FIGURE 2 Lactate Clearance in Survivors and Nonsurvivors**




Lactate clearance in survivors and nonsurvivors of cardiogenic shock treated with Impella in addition to venoarterial extracorporeal membrane oxygenation therapy.

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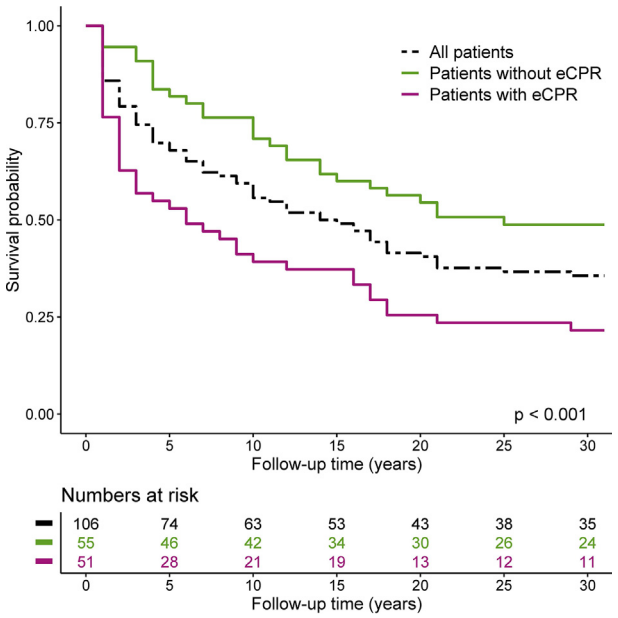
**FIGURE 3** Kaplan-Meier Curve For 30-Day All-Cause Mortality




Kaplan-Meier curves for 30-day all-cause mortality in patients with cardiogenic shock treated with Impella in addition to VA-ECMO. Separate curves are shown for patients with and without VA-ECMO implantation during ongoing cardiopulmonary resuscitation (eCPR). VA-ECMO = venoarterial extracorporeal membrane oxygenation therapy.

matched analysis of 63 patients, the ECMELLA approach significantly improved weaning from VA-ECMO (48% vs. 28%, respectively; p = 0.05) and reduced in-hospital mortality (48% vs. 74%; p = 0.04). Furthermore, although a higher rate of hemolysis (76% vs. 33%, respectively; p < 0.01) was observed, this did not translate into a higher incidence of bleeding (38% vs. 29%, respectively; p = 0.60). Interestingly, Patel et al. (23) found comparable results regarding this topic in a U.S.-based cohort of CS patients. In that study, 36 patients treated with VA-ECMO only were compared to 30 patients treated with VA-ECMO and Impella concomitantly. Again, mortality rates were significantly lower in the ECMELLA group (57% vs. 78%, respectively; p = 0.02) without an increase in bleeding complications. Importantly, the mortality advantages of the ECMELLA cohort occurred despite the use of a surgical LV vent in 58% of the patients receiving VA-ECMO only.

**TABLE 3** Complications During Mechanical Circulatory Support

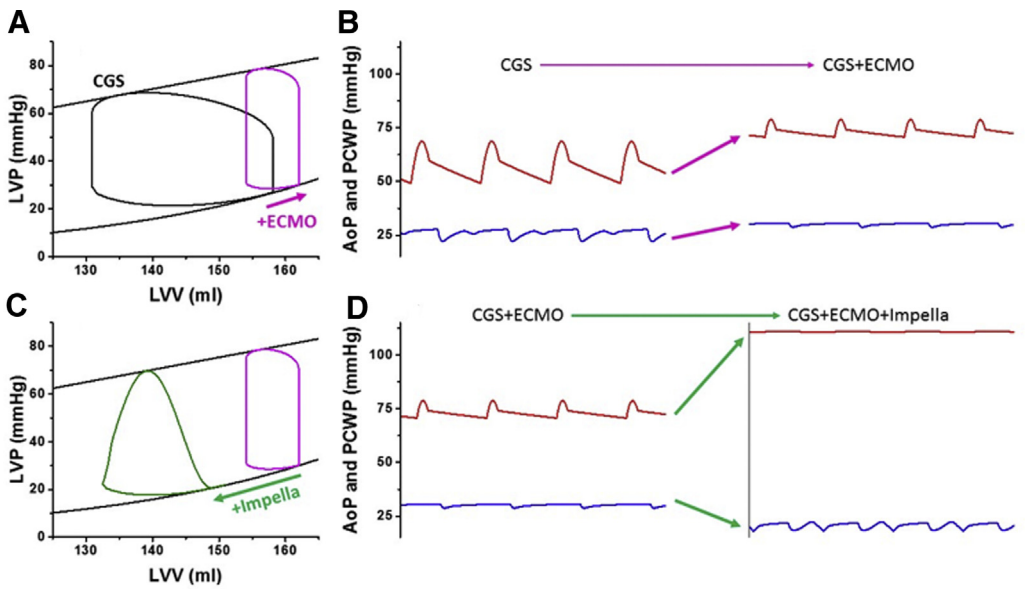
| | All Patients (N = 106) | Survivors (n = 38) | Nonsurvivors (n = 68) | p Value |
|---|---|---|---|---|
| Hypoxic brain damage | 17 (19.1) | 0 (0) | 17 (32.7) | <0.01 |
| Intracerebral bleeding | 3 (3.4) | 1 (2.7) | 2 (3.9) | 1.00 |
| Stroke | 10 (11.4) | 2 (5.4) | 8 (15.7) | 0.18 |
| Vascular complication requiring an intervention | 36 (34.3) | 12 (31.6) | 24 (35.8) | 0.83 |
| Abdominal compartment with the need of laparotomy | 24 (22.9) | 6 (15.8) | 18 (26.9) | 0.23 |
| Mesenteric ischemia | 10 (9.5) | 1 (2.6) | 9 (13.4) | 0.09 |
| Bleeding requiring an intervention | 26 (24.8) | 11 (28.9) | 15 (22.4) | 0.49 |
| Hemolysis | 48 (47.1) | 13 (36.1) | 35 (53.0) | 0.15 |
| Sepsis | 44 (41.9) | 23 (60.5) | 21 (31.3) | <0.01 |
| Renal replacement therapy during hospital stay | 63 (59.4) | 20 (52.6) | 43 (63.2) | 0.31 |

Values are n (%). Complications during mechanical circulatory support in 30-day survivors and 30-day nonsurvivors of cardiogenic shock treated with Impella in addition to venoarterial extracorporeal membrane oxygenation therapy.

The present study extends the findings of a smaller, propensity-matched analysis to a larger all-comers cohort of patients treated with Impella in combination with VA-ECMO for severe CS. In this severely diseased patient population, the combined approach resulted in a significantly lower 30-day mortality rate than predicted by 2 widely used risk scores. Several mechanisms could contribute to the benefits of the ECMELLA approach. First, the marked decrease in PCWP (a surrogate marker for the LV filling pressures) after Impella implantation indicates active LV unloading during VA-ECMO therapy (**Figure 1**). Although the number of cases with available PCWP is limited, this is further supported by the underlying hemodynamic principles presented above. Second, Impella support during weaning from VA-ECMO may increase the chances and speed of a successful weaning, which has already been shown by the authors' previous analysis (4). This is possible because Impella provides the necessary flow to the systemic circulation while VA-ECMO flow is withdrawn. Therefore, Impella use can reduce the duration of VA-ECMO support, which is independently associated with a poor outcome (30). A marked decrease in lactate levels is crucial after establishing VA-ECMO therapy. A similar decrease in survivors and nonsurvivors, however, indicates that hemodynamic stabilization is only 1 component of successful therapy. Myocardial recovery and successful weaning are a necessary next step, both of which could be optimized with Impella support.

Other important considerations are the incidence and severity of complications, as 2 mechanical circulatory support devices are used with the ECMELLA approach. In the present analysis, there was an overall high incidence of vascular complications and bleeding events. However, these were equally distributed among survivors and nonsurvivors. In contrast, hypoxic brain damage, stroke, hemolysis, abdominal compartment, and mesenteric ischemia were more frequent among nonsurvivors. Comparison of the current findings to previously published data for

**FIGURE 4 Pressure-Volume Loops During Cardiogenic Shock**




**(A)** Idealized PVLs in CGS **(black)** and its rightward shift toward higher filling volumes and pressure (LV loading) with the addition of VA-ECMO **(pink)** due to the increase in afterload. **(B)** In the time domain, addition of VA-ECMO in CGS increases AoP **(red)**, which can also be associated with an increase in PCWP **(blue)**. **(C)** The addition of Impella support for active, direct LV venting caused a marked shift of the PVL to lower volumes and pressures (LV unloading). Note the **triangular shape** of the PVL, indicating loss of isovolumic periods during contraction and relaxation. **(D)** In the time domain, the marked reduction of PCWP (consistent with clinical data shown in Figure 1) and further increase of arterial pressure as flow from the Impella will add to that of VA-ECMO. Note that the AoP is significantly higher than peak LV pressure seen on the PVL **(C)**. This AoP-LV pressure uncoupling is associated with aortic valve closure but not with the risk of LV or aortic root thrombosis because there is no stagnation of blood in either location due to inflow and outflow locations of the Impella pump. AoP = aortic pressure; CGS = cardiogenic shock; PVL = pressure-volume loops; LV = left ventricular; other abbreviations are as in Figure 1.

VA-ECMO only therapy is complicated, largely because definitions of events and data availability vary among studies (31). However, results of available studies generally show that addition of a transaortic LV assist device to VA-ECMO leads to a higher rate of hemolysis without an increased risk of major bleeding (4). Future studies should continue to evaluate the impact of the Impella on complication rates.

**STUDY LIMITATIONS.** First, the data carry all the drawbacks of a nonrandomized single-center analysis. It is therefore impossible to extract which findings are indeed related to the presented mechanical circulatory support strategy and which findings are related to other therapeutic measures. Second, the observational design of these data is prone to selection bias. Although there is a standardized protocol for this therapeutic approach at our institution, final decision was always left to the treating physician. Third, although data from 106 cases are presented, the limited sample size of this observational study does not provide enough statistical power to evaluate important subgroups, especially as multiple testing further limits interpretation of the data. Fourth, the present analysis does not offer a control group. Therefore, the presented results may only be exploratory and hypothesis generating.

## CONCLUSIONS

Implantation of a transaortic LV assist device in combination with VA-ECMO resulted in better outcome in an all-comers cohort than predicted by 2 established risk scores. We hypothesize that this relates to the reduction in LV filling pressures, which is supported by the underlying physiological principles. Ultimately, a randomized, controlled trial comparing ECMELLA, conventional VA-ECMO, and Impella treatment is needed to further define the optimal approach in different patient subgroups.

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## PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** Percutaneous unloading of the LV counteracts the negative hemodynamic consequences of VA-ECMO support during cardiogenic shock. Impella implantation seems to be most promising in this setting, as this device provides an active LV unloading. Additionally, this approach seems to facilitate the VA-ECMO weaning and seems to improve outcome measures.

**TRANSLATIONAL OUTLOOK:** Future research needs to clarify open questions of optimal timing of device implantation, best weaning strategies, and strategies to reduce complications. Furthermore, comparison of different unloading strategies, for example, Impella versus surgical LV venting, need to be investigated in a randomized fashion.

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**KEY WORDS** cardiogenic shock, left ventricular unloading, VA-ECMO